T.K. Lim

Edible Medicinal And Non-Medicinal Plants

Volume 7, Flowers

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Contents

Introduction

This book continues as volume 7 of a multi-compendium on *Edible Medicinal and Non-Medicinal Plants*. It covers plants with edible flowers whose floral parts including the stalk and flower nectar are eaten as conventional or functional food, as spice, and may provide a source of food colourant, additive or nutraceuticals. According to Health Canada (2002), a *functional food* is similar in appearance to, or may be, a conventional food that is consumed as part of a usual diet and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, i.e. they contain bioactive compound. A *nutraceutical* is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with foods and is demonstrated to have a physiological benefit or provide protection against chronic disease. Biologically active components in functional foods that may impart health benefits or desirable physiological effects include the following: carotenoids (β-carotene, lutein, lycopene), dietary fibres (β-glucans, soluble fibre), fatty acids (omega fatty acids, conjugated linoleic acid), flavonoids (anthocyanins, flavanols, flavanones, flavonols, proanthocyanidins), isothiocyanates, phenolic acids, plant sterols, polyols and prebiotics/probiotics (fructooligosaccharides—inulin), vitamins and phytoestrogens (isoflavones—diadzein, genistein). Many plants with edible flowers contain many of these bioactive components and essential mineral elements (Mlcek and Rop 2011; Rop et al. 2012), carbohydrates and amino acids in the flowers and other plant parts, imparting a wide array of health benefits and pharmacological properties. According to the Global Industry Analyst Inc., global nutraceuticals market is anticipated to exceed US 243 billion by 2015 (GIA 2012). The United States, Europe and Japan dominate the global market, accounting for a combined market share of more than 85 %. Spurred by the growing affluence, rising disposable income and increasing awareness, particularly in China and India, the Asia-Pacific region is projected to see significant growth in the long term. Functional foods that constitute the faster growing segment in the nutraceuticals market are rising in popularity, as the segment offers a cheaper alternative to dietary supplements. Value-added food products that feature edible flowers offer additional marketing opportunities.

This volume covers selected plant species with edible flowers from families Acanthaceae to Facaceae in a tabular form (Table 1) and 75 such species from the families Amaryllidaceae, Apocynaceae, Asclepiadaceae, Asparagaceae, Asteraceae, Balsaminaceae, Begoniaceae, Bignoniaceae, Brassicaceae, Cactaceae, Calophyllaceae, Caprifoliaceae, Caryophyllaceae, Combretaceae, Convolvulaceae, Costaceae, Doryanthaceae and Fabaceae in detail. Some plants with edible flowers, but are better known for their edible fruits, have been covered in earlier volumes and for other non-floral parts will be covered in subsequent volumes. Other plants with edible flowers from the family Geraniaceae to Zygophyllaceae will be covered in volume 8. The edible flower

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Table 1 Plants with edible flowers in the families Acanthaceae to Fagaceae

Scientific name	English/common vernacular name	Flower edible uses	References
Acanthaceae			
Adhatoda vasica Nees	Malabar nut	Flowers are eaten	Sawian et al. (2007)
Beloperone californica Benth.	Red Justicia, Chuparosa	Red flowers are eaten raw or cooked	Clarke (1977), Facciola (1990)
Justicia adhatoda L.	Malabar Nut; Boga Bahak (Assamese); Nongmangkha Angouba (Manipur)	Flowers are eaten fried in Assam	Patiri and Borah (2007), Yumnum and Tripathi (2012)
Phlogacanthus curviflorus (Wallich) Nees	Dhapa Tita (Assamese)	Young inflorescences and flowers are eaten as vegetables in Assam	Patiri and Borah (2007), Medhi and Borthakur (2012)
Phlogacanthus thyrsiformis (Roxb. ex Hardow) Mabb.	Ronga Bhahak, Titaphul, Titabahak (Assamese); Nongmankha (Manipur)	Flowers are bitter in taste and eaten as roasted vegetable by covering with banana leaf. Sometimes flowers are kept dried for future use. In Manipur, the people use the flowers in a dish called 'kangngou', a dry-fried dish. Another popular dish is 'sumtak', a bitter-tasting dish in which the flowers are fried in oil with small fish	Patiri and Borah (2007), Hauzel (2012)
Phlogacanthus tubiflorus Nees		Dry/fresh inflorescences eaten in Assam	Medhi and Borthakur (2012)
Rhinacanthus nasutus (L.) Kurz.	Snake Jasmine; Thong Phan Chang (Thai)	Flowers reported edible	Wongwattanasathien et al. (2010)
Strobilanthes scaber Nees	Raspatia (Assamese); Sam Siphra (Meghalaya)	Flowers are commonly eaten by the Garo communities in assam and in Meghalaya	Patiri and Borah (2007)
Adoxaceae			
Sambucus callicarpa Greene = *Sambucus racemosa* var. *arborescens* (Torr. & A. Gray) A. Gray	Red Coast Elder	Flowers are eaten raw or cooked	Huxley et al. (1992), Fern (1992–2003)
Sambucus canadensis L.	American Elder, Canadian Elderberry	Flowers are dried and used for tea	Fernald et al. (1958), Facciola (1990), Barash (1997), Lauderdale and Evans (1999), McCullough (2007)
Sambucus cerulea Raf. = *Sambucus nigra* var. *cerulea* (Raf.) B.L. Turner	Blue Elderberry	Blossoms added to pancake to lighten batter and add flavour, used in tea and muffins	Barash (1997), Schofield (2003)
Sambucus gaudichaudiana DC.	White Elderberry	Flowers are eaten raw or cooked	Wikipedia (2012)

Sambucus glauca Nutt. = *Sambucus cerulea* Raf.	Blue Elderberry, Blue Elder	Blossoms added to pancake to lighten batter and add flavour, also ingredient for cakes and waffles. Dried flowers can be ground and added to baking mixes and flour. Also used for elder fritters	Schofield (2003)
Sambucus javanica Reinw. ex Blume	Chinese Elder	Flowers are eaten raw or cooked	Facciola (1990)
Sambucus melanocarpa A. Gray = *Sambucus racemosa* var. *melanocarpa* (A. Gray) McMinn	Black Elder	Blossoms added to pancake to lighten batter and add flavour, also ingredient for cakes and waffles. Dried flowers can be ground and added to baking mixes and flour. Also used for elder fritters	Schofield (2003)
Sambucus mexicana auct. = *Sambucus cerulea* Raf.	Mexican Elder	Flowers eaten raw or cooked. Flower clusters dipped in batter, fried and sprinkled with sugar. Flowers shaken from stem to add flavour to pancakes, muffins and cakes	Uphof (1968), Clarke (1977), Facciola (1990)
Sambucus microbotrys Rydb. = *Sambucus racemosa* var. *microbotrys* (Rydb.) Kearney and Peebles	Red Elder	Flowers eaten raw or cooked	Kunkel (1984), Moerman (1998)
Sambucus nigra L.	Elderberry	Flowers fried in fritters, blossom eaten as sweet fritter or added to steamed fruit, jams, jellies, vinegar, make into elderflower wine, sparkling champagne. Blossoms added to pancake to lighten batter and add flavour, also ingredient for cakes and waffles. Dried flowers can be ground and added to baking mixes and flour. Also for elder fritters	MacNicol (1967), Hedrick (1972), Cribb and Cribb (1975), Tanaka (1976), Low (1989), Facciola (1990), Garland (1993), Burnie and Fenton-Smith (1996), Schofield (2003)
Sambucus pubens Michx. = *Sambucus racemosa* subsp. *pubens* (Michx.) House	American Red Elder	Blossoms added to pancake to lighten batter and add flavour	Schofield (2003)
Sambucus racemosa subsp. *kamtschatica* (E.L. Wolf) Hulten	Red Elder	Blossoms added to pancake to lighten batter and add flavour	Schofield (2003)
Sambucus racemosa L.	Red Elder	Blossoms added to pancake to lighten batter and add flavour	Schofield (2003)
Sambucus sieboldiana (Miq.) Blume ex Graebn.	Elderberry	Buds boiled and eaten as vegetables or used as substitute for tea	Tanaka (1976)
Viburnum edule Raf.	Mooseberry, Highbush Cranberry	Flowers added to pancake and cake batters. Blossoms can also be batter-dipped and fried	Schofield (2003)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Viburnum trilobum Marshall	American Cranberrybush Viburnum, American Cranberrybush, Kalyna, Highbush, Highbush Cranberry	Flowers can be mixed with pancake or muffin batter or can be made into fritters	Deane (2007–2012u)
Aizoaceae			
Carpobrotus deliciosus (L. Bolus) L. Bolus	Sweet Hottentot Fig, Pigface	Edible flowers, also fruits and leaves (pickled)	King (2007)
Carpobrotus edulis (L.) N.E.Br.	Hottentot Fig, Ice Plant	Edible flowers, also fruits and leaves (pickled)	King (2007)
Carpobrotus glaucescens (Haw.) Schwantes	Coastal Noon Flower, Pigface	Pink flowers eaten, also fruits and leaves (pickled)	King (2007)
Alismataceae			
Limnocharis flava (L.) Buchenau	Yellow Burhead	Young unopened inflorescence and peduncle eaten	Ochse and van den Brink (1980), Tanaka and Nguyen (2007), van den Bergh (1994)
Sagittaria latifolia Willd.	Wapato, Duck Potato, Indian Potato	White flowers edible	Deane (2007–2012f)
Amaranthaceae			
Alternanthera sessilis (L.) R.BR. ex DC.	Dwarf Copperleaf, Sessile Joyweed; Chuk-Tsit-Tsoi (Chinese)	Flowers are eaten in China	Facciola (1990), Uphof (1968), Tanaka (1976)
Amaranthus cruentus L.	Blood Amaranth, Purple Amaranth, Red Amaranth	Flowers are used to colour ceremonial maize bread in Guatemala	Facciola (1990)
Amaranthus quitensis Kunth	Ataco, Sangorache	Red inflorcences—source of dye used for colouring chicha and ceremonial maize dishes	Kunkel (1984), Facciola (1990)
Amaranthus sp. (*Amaranthus cruentus* × *Amaranthus powelli*)	Hopi Red Dye Amaranth	Water extract of flower clusters used to colour the pink maize wafer bread	Facciola (1990)
Amaranthus viridis L.	Green Amaranth, Slender Amaranth	Leaves, leafy stem and flower cluster used as spinach substitute.	Tanaka (1976), Cribb and Cribb (1987), Kunkel (1984), Ochse and van den Brink (1980), Facciola (1990)
Atriplex canescens (Pursh.) Nutt.	Four-Wing Salt Bush, Grey Sage Bush	Yellow flowers edible	Wilson (2012)
Atriplex spp.	Salt Bush	All parts including flowers are edible	McCullough (2007)
Celosia argentea L.	Plumed Cockscomb, Quailgrass, Soko	Leaves, stem and young inflorescences steamed and eaten as potherb or finely cut and used in soups	Dalziel (1937), Ochse and Bakhuizen van den Brink (1980), Faccciola (1990)
Celosia cristata L. = *Celosia argentea var. cristata* (L.) Kuntze	Toreador Cockscomb; Maendrami Hwajeon (Korean)	Flowers used in 'hwajeon' cake in Korea	Anonymous (2012b)
Chenopodium album L.	Fat Hen	Young inflorescences are cooked	Fernald et al. (1958), Facciola (1990)

Chenopodium bonus-henricus L.	Good King Henry	Young flower buds are cooked	Organ (1960), Hedrick (1972), Facciola (1990)
Chenopodium cornutum (Torr.) Benth. and Hook.f. ex Watson	Goosefoot	Flowers eaten in Arizona	Yanovsky (1936)
Chenopodium ficifolium Sm.	Fig-Leaved Goosefoot	Flower buds eaten in soups, vegetable dishes, fried, roasted or parboiled and as potherb	Tanaka (1976), Facciola (1990)
Chenopodium nuttalliae Saff. = *Chenopodium quinoa* Willd.	Quinoa; Huauzontle	Flower clusters eaten cooked, used like broccoli; they are considered a gourmet food	Phillips and Rix (1998), Facciola (1990)
Suaeda maritima (L.) Dumort.	Annual Sea Blite	Green flowers eaten	Maisuthisakul et al. (2008), Maisuthisakul (2012)
Amaryllidaceae			
Allium acuminatum Hook.	Hooker's Onion, Tapertip Onion	Flowers raw, used as a garnish on salads	Moerman (1998), Fern (1992–2003)
Allium aflatunense B. Fedtsch.	Ornamental Onion; Kirgislök (Swedish)	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium akaka S. G. Gmel. ex Schult. and Schult. F.	None	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium altaicum Pall.	Altai Onion; Songino (Mongolia)	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium ampeloprasum var. *babingtonii* (Borrer) Syme = *Allium ampeloprasum* L.	Babbington's Leek, Wild Leek	Flowers raw, used as a garnish on salads. Flowers best used as a flavouring in cooked food	Fern (1992–2003)
Allium ampeloprasum L.	Leek	Flowers raw, used as a garnish on salads	Fern (1992–2003), Sulistiorini and van der Meer (1994)
Allium angulare Pall. = *Allium angulosum* L.	None	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium angulosum L.	Mouse Garlic	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium ascalonicum L.	Red Shallots; Hom (Thai)	Young inflorescences eaten	Ochse and van den Brink (1980), Maisuthisakul et al. (2008), Maisuthisakul (2012)
Allium atropurpureum Waldst. and Kit.	Purple-Flowered Onion	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium bisceptrum S. Watson	Aspen Onion	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium bodeanum auct. = *Allium walteri* Regel.	None	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium bolanderi S. Watson	Bolander's Onion	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium brevistylum S. Watson	Short-Style Onion	Flowers raw, used as a garnish on salads	Fern (1992–2003)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Allium canadense L.	Canadian Garlic	Flowers raw, used as a garnish on salads	Fern (1992–2003)
Allium carinatum L.	Keeled Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium carolinianum DC.	Jambo-Pharan, Janglee Piyaz, Ladam, Markua	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium cepa L.	Garden Onion, Bulb Onion, Onion, White Onion	Flowers eaten raw, used as garnish on salads; flowers simmered in soups, eaten in salads or dipped in batter and fried as fritters	Schofield (2003), Fern (1992–2003), van der Meer and Leong (1994)
Allium cepa var. *aggregatum* G.Don	Potato Onion	Young inflorescence and flowers eaten raw; used as a garnish on salads	Fern (1992–2003), Permadi and van der Meer (1994), Maisuthisakul et al. (2008)
Allium cernuum Roth	Nodding Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium chinense G. Don	Rakkyo	Flowers and young seedpods eaten raw; flowers used as a garnish on salads	Read (1946), Fern (1992–2003), van der Meer and Agustina (1994)
Allium condensatum Turcz.	None	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium cupani Raf.	None	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium douglasii Hook.	Douglas' Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium dregeanum Kunth	Wild Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium drummondii Regel	Prairie Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium fistulosum L.	Welsh Onion	Flowers eaten raw, used as garnish on salads	Oyen and Soenoeadji (1994), Fern (1992–2003)
Allium flavum L.	Small Yellow Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium galanthum Kar. and Kir.	None	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium geyeri var. *tenerum* M.E. Jones	Bulbil Onion, Geyer's Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium giganteum Regel	Giant Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium grayi Regel = *Allium macrostemon* Bunge	Chinese Garlic, Japanese Garlic, Water Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium hookeri Thwaites	Hooker Chives	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium kunthii G.Don	Kunth's Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium kurrat Schweinf. Ex K. Krause	Kurrat, Egyptian Leek	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium ledebourianum Schult. and Schult. F.	Giant Siberian Chives; Asatsuki (Japanese)	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)

Allium macleanii Baker	Maclean Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium macropetalum Rydb.	Large Flower Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium macrostemon Bunge	Macrostemon Onion, No-Binu	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium moly L.	Golden Garlic	Flowers eaten raw, have a pleasant onion flavour and used as garnish on salads	Fern (1992–2003)
Allium monanthum Maxim.	Wild Chive; Dan Hua Xie (Chinese); Hime Nira (Japanese)	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium mutabile Michx. = *Allium canadense* var. *canadense*	Canada Garlic, Meadow Garlic, Wild Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium neapolitanum Cirillo	Daffodil Garlic	Flowers eaten raw or cooked, excellent in salads	Fern (1992–2003)
Allium obliquum L.	Twisted leaf Garlic, Lopsided Ornamental Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium oleraceum L.	Field Garlic	Flowers eaten raw, used as garnish on salads and as flavouring in soups and stews	Facciola (1990), Fern (1992–2003)
Allium orientale Boisse	Oriental Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium oschaninii O. Fedtsch.	French Gray Shallot	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium paradoxum (M. Bieb.) G. Don	Few-Flowered Leek	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium pendulinum Ten.	Italian Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium platycaule S. Watson	Flat-Stem Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium porrum L. = *Allium ampeloprasum* L.	Leek, Garden Leek	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium przewalskianum Regel	Ladakh Onion, Flowering Onion, Przewalski's Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium ramosum L.	Flowering Leek, Fragrant-Flowered Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium roseum L.	Rosy Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium rubellum M. Bieb	None	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium rubrum Osterh. = *Allium geyeri* var. *tenerum* M.E. Jones	Bulbil Onion, Geyer's Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium ruhmerianum Asch. ex E.A. Durand and Barratte	None	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium sacculiferum Maxim.	None	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Allium sativum L.	Garlic	Flower peduncles used as vegetable	Tanaka (1976), Facciola (1990), Woodward (2000), van der Meer and Permadi (1994)
Allium sativum var. *ophioscorodon* (Link) Döll	Ophio Garlic, Spanish Garlic	Flower peduncles used as vegetable	Facciola (1990), Fern (1992–2003)
Allium schoenoprasum L.	Garden Chives	Flowers eaten fresh, tossed in salads or made into herb vinegars and butters; flowers simmered in soups, eaten in salads or dipped in batter and fried as fritters; flowers eaten in omelette, cheese and fish dishes or used as garnish	Burnie and Fenton-Smith (1996), Schofield (2003), Tanaka (1976), Facciola (1990), Lauderdale and Evans (1999), Roberts (2000), Newman and O'Connor (2009)
Allium schoenoprasum subsp. *sibiricum* Hayek and Markgraf = *Allium schoenoprasum* L.	Garden Chives	The bulb, root, leaves and flowers of most *Allium* plants are edible, although only the bulbs or leaves are usually consumed, depending on species	Facciola 1990)
Allium scorodoprasum L.	Rocambole	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium scorodoprasum subsp. *rotundum* (L.) Stearn = *Allium rotundum* subsp. *rotundum*	Sand Leek; Ail Arrondi (French)	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium semenovii Regel	Semenov's Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium senescens L.	German Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium sphaerocephalon L.	Round-Headed Leek, Round-Headed Garlic, Ball-Head Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium splendens Willd.ex Schult. and Schult.f.	Glittering Onion; Miyama-Rakkyo (Japanese)	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium stellatum Nutt. Ex Ker Gawl.	Prairie Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium stipitatum Regel	Persian Shallot	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium stracheyi Baker	Dunna, Pharan (Central Himalaya)	Flowers eaten raw; used as a garnish on salads; used as condiment in Central Himalaya	Laferriere (1992), Fern (1992–2003)
Allium suaveolens Jacq.	Fragrant Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium subhirsutum L.	Hairy Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium textile A. Nelson and J. F. Macbr.	Textile Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium thunbergii G. Don	Japanese Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)

Allium tricoccum Sol.	Wood Leek	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium triquetrum L.	Angled Onion, Three-Cornered Garlic	Flowers eaten raw; juicy with a mild garlic flavour, they make a tasty and decorative garnish on salads	Fern (1992–2003)
Allium tuberosum Rottler ex Spreng.	Garlic Chives	Inflorescence, flowers, unopened flower buds and flower peduncle used in Asian cooking	Van der Meer (1994), Facciola (1990), Woodward (2000), Tanaka and Nguyen (2007), Newman and O'Connor (2009), Anonymous (2012a)
		Chive flowers have a mild onion flavour and are surprisingly crunchy. They are widely used tossed in salads, pasta, omelettes and scrambled eggs. They can be added to white fish dishes or to cheese sauce to give that extra bite	
Allium unifolium Kellogg	One-Leaved Onion	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium ursinum L.	Wild Garlic	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium validum S. Watson	Pacific Onion, Pacific Mountain Onion, Swamp Onion, Wild Onion,	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium victorialis L.	Alpine Leek	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium wallichii Kunth	Jimbur	Flowers eaten raw, used as garnish on salads	Fern (1992–2003)
Allium × *proliferum* (Moench) Schrad. ex Willd.	Beltsville Bunching Onion, Egyptian Onion, Top Onion	Inflorescence bulbils, bulbs and leaves used as spice	Siedmann (2005)
Narcissus jonquilla L.	Jonquil	Flowers eaten raw or candied and made into desserts	Crowhurst (1972), Facciola (1990)
Tulbaghia alliacea L.f.	Society Garlic	Flowers regarded as a delicacy by the native Zulu women	Facciola (1990), Newman and O'Connor (2009)
Tulbaghia violacea Harv.	Society Garlic	Flowers eaten raw or cooked; added to salads, used as a garnish or as a flavouring in cooked foods	Facciola (1990), Harris (1975)
Anacardiaceae			
Mangifera indica L.	Mango	Flowers are edible	Facciola (1990)
Pistacia terebinthus L.	Turpentine Tree	Flowers edible raw	Deane (2007–2012w)
Spondias malayana Kostermans	Malaysian Hog, Malaysian Mombin Plum	Inflorescence used as food flavouring	Jansen (1999)
Spondias mangifera Willd. = *Spondias pinnata* (L.f.) Kurz	Hog Plum, Malayan Mombin, Amra, Buah Amra	Tender panicles eaten steamed or dressed as salad, sour flowers used as flavouring	Burkill (1966), Ochse and van den Brink (1980), Facciola (1990)
Anthericaceae			
Dichopogon fimbriatus (R.Br.) J.F. Macbride	Nodding Chocolate Lily		Harden (1993)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Dichopogon strictus (R.Br.) Baker	Chocolate Lily		Harden (1993)
Apiaceae			
Anethum graveolens L.	Dill	Inflorescences used to flavour pickled cucumbers, onions, vinegar, sauces, gravies, stews, pastries and bread. Flowers added to fish dishes and omelettes or sprinkle over cooked vegetables. Whole flowers are added to pickled gherkins, cucumbers or beetroots	Hedrick (1972), Facciola (1990), Garland (1993), Van den Bergh (1994a, b), Lauderdale and Evans (1999), Newman and O'Connor (2009), Anonymous (2012a)
Angelica archangelica L.	Angelica, Garden Angelica, Holy Ghost, Wild Celery, Norwegian Angelica	Flowers are excellent with fish and the flower stems are especially popular candied; flowers used in pastries, cakes and confectionary	Uphof (1968), Tanaka (1976), Facciola (1990), Deane (2007–2012x)
Anthriscus cerefolium (L.) Hoffm.	Chervil, French Parsley	Flowers used as seasoning	Hedrick (1972), Facciola (1990), Lauderdale and Evans (1999), Newman and O'Connor (2009)
Bunium bulbocastanum L.	Earth Chestnut, Pignut	Flowers and seeds used as condiment	Uphof (1968), Tanaka (1976), Kunkel (1984), Facciola (1990)
Carum carvi L.	Caraway	Flowers used in salads, peach 'pashka'	Roberts (2000)
Cogswellia nudicaulis M.E. Jones	Barestem Biscuitroot	Flowers used as beverage	Yanovsky (1936)
Coriandrum sativum L.	Coriander	The flowers are as adaptable as the leaves in a variety of different dishes. Flowers are scattered over cauliflower, added to the end of a stir-fry or added to cream cheese. A few flowers are scattered over an orange fruit salad to enhance the flavour. Some dishes include aubergine and coriander lunch dish; leeks, kale and coriander flower soup; green bean and potato salad with coriander flowers	Roberts (2000), Newman and O'Connor (2009), Kaisoon et al. (2011), Anonymous (2012a)
Crithmum maritimum L.	Samphire, Rock Samphire	Raw blossoms used in salad	Deane (2007–2012q)
Cryptotaenia canadensis (L.) DC.	Honewort, Wild Chervil	Young leaves, stems and flowers eaten raw or cooked as potherb	Tanaka (1976), Kunkel (1984), Facciola (1990)
Cryptotaenia japonica Hassk.	Mitsuba, Japanese Honewort, Japanese Parsley	Flowers are edible cooked	Deane (2007–2012p)
Daucus carota L.	Carrot, Queen Anne's Lace, Wild Carrot	The flower clusters can be french fried to produce a carrot-flavoured gourmet's delight	Facciola (1990)
Ferula assa-foetida L.	Asafoetida, Devil's Dung	Immature flower heads eaten fresh	Garland (1993)

Foeniculum vulgare Mill.	Fennel, Sweet Fennel	Flowers used in fruit pies	Barash (1997), Lauderdale and Evans (1999), Roberts (2000), Newman and O'Connor (2009)
Heracleum lanatum Michx.	Cow Parsnip, Indian Celery, Pushki	Young flowers eaten	Yanovsky (1936)
Heracleum maximum Bartr.	Common Cow Parsnip	Flower stalks and leaf petioles peeled and eaten fresh	Perry (1952), Turner et al. (1980)
Heracleum sphondylium subsp. *montanum* (Schleich. ex Gaudin.) Briq. = *Heracleum lanatum* Michx.	Cow Parsnip, Indian Celery, Pushki	Young flowers are eaten	Uphof (1968), Usher (1974), Tanaka (1976)
Levisticum officinale W.D.J. Koch	Lovage, Garden Lovage	Flowers are eaten	Facciola (1990), Lauderdale and Evans (1999)
Lomatium macrocarpum (Hook. & Arn.) J.M. Coult. and Rose = *Lomatium hallii* (S. Watson) J.M. Coult. and Rose	Bigseed Biscuit Root, Bigseed Lomatium	Tea prepared from flowers	Facciola (1990)
Lomatium nudicaule (Pursh) J.M. Coult. and Rose	Beach Dill, Hogfennel, Indian Celery, Naked Desert Parsley, Naked-Stemmed Pestle Parsnip, Wild Celery,	An infusion of leaves, stems and flowers used as a beverage	Hedrick (1972), Facciola (1990)
Myrrhis odorata (L.) Scop.	Sweet Cicely, Cicely, Greater Chervil, Roman Plant, Cow Chervil, Smooth Cicely, Sweet Fern, British Myrrh, Shepherd's Needle, Sweets	The sweet anise-flavoured flowers are lovely added to apple, plum or rhubarb tarts	Brown (2011)
Pimpinella saxifraga L.	Black Caraway, Burnet Saxifrage, Greater Burnet, Saxifrage Burnet	Flower heads made into wine	Facciola (1990)
Saposhnikovia divaricata (Turcz.) Schischk.	Siler Root, Fang Feng (Chinese)	Leaves, flowers boiled used as tea	Hu (2005)
Smyrnium olusatrum L.	Alexanders, Black Lovage	Flower buds eaten raw, added to salads	Larkcom (1980), Loewenfeld and Back (1978)
Smyrnium perfoliatum L.	Perfoliate Alexanders	Flower buds eaten raw, added to salads	Larkcom (1980), Loewenfeld and Back (1978)
Trachyspermum roxburghianum (DC.) H. Wolff	Wild Celery; Ajmod (Hindi); Ajamodika (Sanskrit); Phakchee Rai, Phak Sangae (Thai)	Young plants are harvested and consumed fresh as side dish or added to soup. Dried whole plant with inflorescence is used as spice to flavour curries	Jircas (2010)
Zizia aurea W.D.J. Koch.	Golden Alexanders	The flowers, minus pedicels, are tossed in green salad. They are also a delicious cooked vegetable when used in a similar manner to broccoli	Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Apocynaceae			
Asclepias asperula (Decne.) Woodson	Antelope Horns	Unopened flower buds eaten cooked. They taste somewhat like peas. They are used like broccoli. Flowers are used as a flavouring and a thickener in soups. The flower clusters can be boiled down to make a sugary syrup	Harrington (1974), Harris (1975), Facciola (1990), Kavasch (2005)
Asclepias galioides H. B. K.	Bedstraw Milkweed	Young buds eaten by boys of Zufii Indians of New Mexico	Yanovsky (1936)
Asclepias hallii A. Gray	Purple Silkweed	Flower buds eaten raw or cooked, taste like peas	Balls (1962), Usher (1974)
Asclepias incarnata L.	Swamp Milkweed	Unopened flower buds eaten cooked. They taste somewhat like peas. They are used like broccoli. Flowers are used as a flavouring and a thickener in soups. The flower clusters can be boiled down to make a sugary syrup	Yanovsky (1936), Uphof (1968), Usher (1974), Facciola (1990)
Asclepias lanceolata Walter	Purple Silkweed	Flowers edible	Wikipedia (2012)
Asclepias mexicana Cav.	Mexican Milkweed	Young blossoms eaten cooked	Yanovsky (1936), Kunkel (1984)
Asclepias ovalifolia Decne.	Oval-Leaved Milkweed, Dwarf Milkweed	Unopened flower buds eaten cooked. They taste somewhat like peas. They are used like broccoli. Flowers are used as a flavouring and a thickener in soups. The flower clusters can be boiled down to make a sugary syrup	Hedrick (1972), Harris (1975), Facciola (1990), Kavasch (2005)
Asclepias pumila (A. Gray) Vail.	Low Milkweed	As above	Harrington (1974), Facciola (1990), Kavasch (2005)
Asclepias purpurascens L.	Purple Milkweed	Flower buds eaten raw or cooked	Usher (1974), Elias and Dykeman (2009)
Asclepias quadrifolia Jacq.	Fourleaf Milkweed	Unopened flower buds eaten cooked. They taste somewhat like peas. They are used like broccoli. Flowers are used as a flavouring and a thickener in soups. The flower clusters can be boiled down to make a sugary syrup	Harrington (1974), Harris (1975), Kavasch (2005)
Asclepias rubra L.	Red Silkweed	The flower clusters can be boiled down to make a sugary syrup	Coffey (1993)

Asclepias speciosa Torr.	Showy Milkweed	Flowers eaten raw or boiled in Montana and California; buds boiled for soup or with meat	Yanovsky (1936), Balls (1962), Usher (1974)
Asclepias syriaca L.	Common Milkweed, Milkweed	Unopened flower buds eaten cooked. They taste somewhat like peas. They are used like broccoli. Flowers are used as a flavouring and a thickener in soups. The flower clusters can be boiled down to make a sugary syrup. Flowers stewed by Chippewa Indians	Yanovsky (1936), Harrington (1974), Harris (1975), Facciola (1990), Moerman (1998), Kavasch (2005)
Asclepias tuberosa L.	Butterfly Weed, Canada Root, Chigger Flower, Chiggerflower, Fluxroot, Indian Paintbrush, Indian Posy	Flowers produce so much nectar that crystallizes out into small lumps which can then be eaten like sweets. The flower clusters can also be boiled down to make a sugary syrup	Yanovsky (1936), Harrington (1974), Facciola (1990)
Asclepias viridiflora Raf.	Green Milkweed	Flowers eaten and used like common milkweed	Harris (1975), Facciola (1990)
Dregea volubilis (L.f.) Benth. ex Hook.f.	Sneeze Wort; Kratung-Maba (Thai)	Young shoot and inflorescence, which are available year-round, are cooked in a curry with dried, smoked fish	Jircas (2010)
Fernaldia pandurata (A. DC.) Woodson	Loroco, Quilite (El Salvador, Guatemala, Mexico)	Loroco is small green unopened flower buds used as an herb for flavouring in Central America. It is used in salads, rice dishes, stews and sauces. In El Salvador and in Honduras, it is added to the fillings in 'pupusas'	Facciola (1990), Morton et al. (1990)
Holostemma rheedii Wall.	Palay Keeray (Tamil); Pala Kura (Telugu)	Flowers eaten in India (Deccan)	Shortt (1887–1888), Watt (1908)
Hoya viridflora (R.Br.) Griff	Hoya; Cooringee Keeray (Tamil)	Flowers eaten uncooked or prepared into a 'bhaji'. Flower powder (said to be pollen) is removed from the flowers and used in the preparation of 'Dhoklas', a small, thick bread	Shortt (1887–1888), Gammie (1902), Paton and Dunlop (1904), Watt (1908)
Leichhardtia australis R.Br. = *Marsdenia australis* (R.Br.) Druce	Doubah, Bush Banana	Flowers, leaves, shoots, roots seed eaten	Low (1989)
Leptadenia hastata Vatke = *Leptadenia lancifolia* (Schumach. & Thonn.) Decne.	Idar; Cheila, Kayilla, Hayilla (Konsogna, Ethiopia); Moroh (Somali)	Flowers and tender shoots eaten like spinach	Dalziel (1937), Hedrick (1972), Facciola (1990)
Morrenia odorata (Hook. & Arn.) Lindl.	Milkweed Vine, Latex Plant, Strangler Vine	The flowers are very sweet and floral and can be eaten raw	Deane (2007–2012n)
Orbea namaquensis (N.E.Br.) Leach	Carrion Flower, Orbea; Aasblom, Bokhoring (Afrikaans)	Flowers eaten	Aiyambo (2010)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Pergularia daemia (Forsk.) Chiov.	Trellis-Vine; Utaran, Sagovani, Aakasan, Gadaria Ki Bel, Jutak (Hindi)	Flowers cooked as potherbs	Fox et al. (1982), Tanaka (1976), Facciola (1990)
Plumeria obtusa L.	Frangipani, Temple Flower, Pagoda Tree	Flowers popular in omelettes, fried, in salads, as dried herbal tea. The crispy and tasty flavour of the tempura style fried flowers may accompany 'Khanom Jeen Nam Ya' (Chinese spaghetti with fish curry soup). Flowers also eaten in sweetmeats	Wetwitayaklung et al. (2008), Wongwattanasathien et al. (2010), Kaisoon et al. (2011)
Plumeria rubra L.	Frangipani, Temple Flower, Temple Tree, Tree of Life, West Indian Jasmine,	Flowers used as above	Burkill (1966), Kunkel (1984), Hu (2005)
Rhyncharrhena linearis (Decne.) K.L. Wilson	Climbing Purple-Star, Purple Pentatrope	Flowers and buds eaten	Cribb and Cribb (1975)
Telosma cordata (Burm.f.) Merr.	Chinese Violet, Cowslip Creeper, Fragrant Telosma, Tonkin Creeper, Tonkin Jasmine; Thiên Lý, Hoa Lý, Hoa Lý (Vietnamese)	Flowers and young leaves eaten	Tanaka and Nguyen (2007)
Telosma minor (Andrews) Craib = *Telosma cordata* (Burm.f.) Merr.	Chinese Violet, Cowslip Creeper, Fragrant Telosma, Tonkin Creeper, Tonkin Jasmine	Flowers eaten raw or cooked in light curry, steamed or fried	Pongpangan and Poobrasert (1985), Wetwitayaklung et al. (2008), Kaisoon et al. (2011)
Telosma procumbens (Blanco) Merrill	Cowslip Creeper; Latok (Tagalog), Cam Thảo Đá Bia (Vietnamese)	Flowers eaten in the Philippines	Van den Bergh (1994a, b)
Vallaris heynei Spreng. = *Vallaris solanacea* (Roth) O Kuntze	Bread Flower	Flowers eaten in Thailand	Burkill (1966), Facciola (1990)
Vallaris solanacea (Roth) O Kuntze	Bread Flower	Flowers eaten in Thailand	Van den Bergh (1994a, b)
Wattakaka volubilis (L.f.) Stapf = *Dregea volubilis* (L.f.) Benth. ex Hook.f.	Green Milkwood Climber	Young leaves, tender stem and green flowers cooked locally as vegetables	Pongpangan and Poobarasert (1985)
Wrightia tinctoria R.Br.	Dyers's Oleander, Pala Indigo Plant, Sweet Indrajao	Flowers are edible	Jukema et al. (1992)

Aponogetonaceae			
Aponogeton distachyos L.f.	Cape Pond Lily, Cape Asparagus, Water Hawthorn; Waterblommetjie (Afrikaans)	Flowering spike—pickled or used as a spinach or asparagus substitute. The flowers are used as a flavouring and flower buds used as a key ingredient in tempura, 'waterblommetjies' and in the traditional South African dish of 'waterblommetjie bredie' (lamb stew)	Uphof (1968), Hedrick (1972), Facciola (1990), Roberts (2000)
Araceae			
Amorphophallus spp.	Corpse Flower, Snake Plant; Buk (Thai)	Non-stinking flowers cooked for food	Pongpangan and Poobarasert (1985)
Lasia spinosa (L.) Thaw.	Spiny Taro; Chengmora (Assam); Phak Naam (Thai)	Flower spadix eaten cooked as vegetable	Patiri and Borah (2007)
Peltandra virginica (L.) Schott	Green Arrow Arum	Spadix (the flowering stem) and berries—cooked. A great delicacy, but they must be thoroughly well cooked otherwise they are poisonous	Uphof (1968), Hedrick (1972), Tanaka (1976)
Schismatoglottis calyptrata (Roxb.) Zollinger and Moritzi	Guang Xi Luo Yan (Chinese); Dujaruk (Malay)	Inflorescences are eaten	Van den Bergh (1994a, b)
Spathiphyllum phryniifolium Schott.	Lirio, Busnay	Tender inflorescences eaten raw or used in soups or fried in egg batter	Martin and Ruberté (1975), Williams (1981), Facciola (1990)
Typhonium trilobatum (L.) Schott.	Bengal Arum, Lobed Leaf Typhonium; Syam Kachu, Sam Ghas, Sam Kochu (Assamese)	Spadix are eaten cooked as vegetable by Bodo and Rajbongshi people in Assam	Patiri and Borah (2007)
Wolffia globosa (Roxb.) Hartog and Plas	Asian Watermeal, Tropical Watermeal; Pham, Khai Nae, Khai Nam (Thai)	Inflorescences are eaten	Dadaung et al. (2011)
Araliaceae			
Aralia armata (Wallich ex G. Don) Seemann	Guang Dong Sonu Mu (Chinese); Tang Nok (Thai)	Young leaves, unopened flowers cooked, excellent	Pongpangan and Poobarasert (1985)
Eleutherococcus gracilistylus (W.W.Sm.) S.Y. Hu = *Eleutherococcus nodiflorus* (Dunn) S.Y.Hu	Wu Jia Pi, Xi Zhu Wu Jia (Chinese)	Flowers are edible	Kunkel (1984)
Trevesia palmata (Roxb. ex Lindl.) Vis.	Snowflake Aralia; Taang Luang (Thai)	Young flower buds, available by the end of rainy season, are eaten after cooking in hot and spicy curry in Thailand. Flower buds eaten cooked by Garos and Bodos peoples in Assam and in Meghalaya	Tanaka (1976), Facciola (1990), Patiri and Borah (2007), Jircas (2010), Medhi and Borthakur (2012)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Arecaceae			
Arenga ambong Becc. = *Arenga undulatifolia* Becc.	Ambung, Aren Gelora	Buds are edible	Brown (1954), Tanaka (1976), Facciola (1990)
Arenga engleri Becc.	Formosan Sugar Palm	Buds are eaten, sap from inflorescence made into sugar	Tanaka (1976), Facciola (1990)
Arenga pinnata (Wurmb) Merr.	Sugar Palm, Arenga Palm, Areng Palm, Black-Fibre Palm, Gomuti Palm, Aren	Sap from cut inflorescene stalk extracted to make palm sugar, jaggery, almost sap juice to make fresh drink, saguir or lightly fermented beverage, vinegar inflorescence peduncle tap for treacle, sugar, alcohol, toddy, tuba and vinegar; bids are cooked as a vegetable or pickled	Uphof (1968), Ochse and van den Brink (1980), Jones (1984), Facciola (1990), Smits (1996)
Astrocaryum mexicanum Lieb. ex Mart.	Chocho, Waree Palm	Flowers edible	Haynes and Mclaughlin (2000)
Borassus aethiopum Mart.	African Fan Palm, African Palmyra Palm, Deleb Palm, Ron Palm, Toddy Palm, Black Rhun Palm, Ronier Palm	Sap from cut inflorescene stalk extracted to make palm sugar, jaggery Sap from cut inflorescence provides a drink; sap also processed into wine, alcohol or vinegar and dried into sugar cakes	Tanaka (1976), Jones (1984), Facciola (1990), Haynes and Mclaughlin (2000)
Borassus flabellifer L.	Asian Palmyra Palm, Toddy Palm, Sugar Palm, Cambodian Palm	Sap from cut inflorescene stalk extracted to make palm sugar, jaggery, almost sap juice to make lightly fermented beverage, toddy	Menninger (1977), Jones (1984), Morton (1988), Facciola (1990), Haynes and Mclaughlin (2000)
Calyptronoma dulcis (C. Wright ex Griseb.) L.H. Bailey = *Calyptronoma plumeriana* (Mart.) Lourteig	Manaca, Palma Manaca (Spanish)	Flowers used for making candy in Cuba	Kunkel (1984), Facciola (1990)
Caryota urens L.	Fish Tail Palm	Sap from cut inflorescence stalk extracted to make palm sugar, jaggery	Jones (1984)
Chamaedorea costaricana Oerst.	Parlour Palms	Young inflorescences (flower stems) are eaten raw, deep fried in batter or boiled or use in soups in Costa rica	Williams (1981), Facciola (1990)
Chamaedorea elegans Mart.	Parlour Palm, Neanthe Bella Palm	Unopened inflorescences eaten raw or cooked	Haynes and Mclaughlin (2000)
Chamaedorea graminifolia H. Wendl.	Pacaya, Xiat Palm	Unopened flower clusters eaten in salads, folded into egg batter and fried or used as boiled vegetables in Central America	Uphof (1968), Tanaka (1976), Williams (1981), Facciola (1990)

Chamaedorea tepejilote Liebm.	Pacaya Palm, Tepejilote Palm	Selectively propagated plants are grown for the young male inflorescences called 'pacaya' eaten raw, boiled or fried in egg batter	Hedrick (1972), Williams (1981), Facciola (1990), Haynes and Mclaughlin (2000)
Cocos nucifera L.	Coconut	Sap from cut inflorescene stalk extracted to make palm sugar, jaggery, almost sap juice to make lightly fermented beverage, toddy, vinegar Yg infl enclosed in spathe eaten in lalab	Ochse and van den Brink (1980), Jones (1984)
Collinia elegans (Mart.) Liebm. ex Oerst. = *Chamaedorea elegans* Mart.	Parlour Palm, Neanthe Bella Palm,	Young unexpanded flower spikes eaten like asparagus	Uphof (1968), Hedrick (1972), Facciola (1990)
Copernicia cerifera (Arruda) Mart. = *Copercinia prunifera* (Mill.) H.E. Moore	Carnauba Wax Palm	Young inflorescence eaten	Tanaka (1976), Kunkel (1984), Facciola (1990)
Corypha utan Lam.	Gebang Palm, Ibus	Sap from inflorescence used to make wine and sugar	Haynes and Mclaughlin (2000)
Eugeissona utilis Becc.	Kadjatoa	Purple flower pollen used as condiment	Haynes and Mclaughlin (2000)
Guilielma gasipaes (Kunth) L.H. Bailey = *Bactris gasipaes* Kunth var. *gasipaes*	Peach Palm, Pejibaye	Flowers may be chopped and added to salads	Facciola (1990)
Hyphaene petersiana Klotzsch ex Mart.	African Ivory Nut Palm	Palm wine made by fermenting mesocarp pulp and from sap by tapping flower bud (nondestructive)	Haynes and Mclaughlin (2000)
Iriartea ventricosa Mart. = *Iriartea deltoidea* Ruiz and Pav.	Stilt Palm, Copa Palm, Barrigona Palm, Huacrapona	Flowers yield an ash used as a substitute for common salt in Guiana, Brazil	Tanaka (1976), Kunkel (1984), Facciola (1990)
Mauritia flexuosa L.f.	Buriti Palm, Wine Palm	Sap from the inflorescence is drunk or made into palm wine or sugar	Hedrick (1972), Cavalcante (1977), Facciola (1990)
Nannorrhops ritchiana (Griff.) Aitch.	Mazari Palm	Young inflorescences eaten	Watt (1908), Hedrick (1972), Tanaka (1976), Facciola (1990)
Nypa fruticans Wurmb	Mangrove Palm, Nipa, Nipa Palm, Nipah, Golpata (Bangladesh, India)	Inflorescences cooked in nipa syrup to produce an energy-giving sweetmeat	Hedrick (1972), Facciola (1990)
Oncosperma filamentosum (Kunth) Blume = *Oncosperma tigillarium* (Jack) Ridl.	Nibung, Nibong, Nibung Palm	Flowers used to flavour rice in Malysia	Burkill (1966), Hedrick (1972), Tanaka (1976), Facciola (1990)
Phoenix canariensis Chabaud	Canary Island Date Plam	Sap from cut inflorescence stalk extracted to make palm sugar	Jones (1984)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Phoenix dactylifera L.	Date Palm	Sap from cut inflorescence stalk extracted to make palm sugar, jaggery; male inflorescence eaten as delicacy	Jones (1984), Facciola (1990)
Phoenix reclinata Jacq.	Sengal Dat Eplam, Wild Date Palm; Wilde-Dadelboom (Afrikaans)	Sap from cut inflorescene stalk extracted to make palm sugar	Jones (1984)
Phoenix sylvestris (L.) Roxb.	Silver Date Palm, Toddy Palm, Wild Date Palm, India Date Palm, Date-Sugar Palm	Sap from cut inflorescene stalk extracted to make palm sugar	Jones (1984)
Raphia hookeri G. Mann and H. Wendl.	Raffia Palm, Wine Palm	Juice produced after removing immature inflorescence used to make wine	Hedrick (1972), Kunkel (1984), Facciola (1990), Haynes and Mclaughlin (2000)
Raphia vinifera P. Beauv.	Bamboo Palm; King Bamboo Palm	Juice produced after removing immature inflorescence used to make wine	Hedrick (1972), Kunkel (1984), Facciola (1990), Haynes and Mclaughlin (2000)
Rhopalostylis sapida (Sol. ex G. Forst.) H. Wendl. and Drude	Nika Palm, Nikau Palm	Young inflorescence eaten	Hedrick (1972), Facciola (1990)
Trachycarpus fortunei (Hook.) H. Wendl.	Chusan Palm, Chinese Windmill Palm	Unopened inflorescences eaten raw or cooked. The fresh flowers and terminal bud are also consumed	Hedrick (1972), Tanaka (1976), Stuart (1979), Facciola (1990), Haynes and Mclaughlin (2000)
Aristolochiaceae			
Aristolochia bracteata Retz.	Dutchman's Pipe, Worm Killer; Um-Glaigla (Arabic)	Flowers used as a tea substitute in southern Kordofan, Sudan	Abdelmuti (1991) (cited by Freedman 2013)
Asarum canadense L.	American Wild Ginger	Flowers used as flavouring, have fragrance and taste liken to ginger	Facciola (1990)
Asparagaceae			
Agave attenuata Salm-Dyck	Century Plant, Foxtail Agave	Young fat flower stalks roasted	King (2007)
Agave americana L.	Aguamiel, Century Plant, Maguey, American Aloe	The sweet sap from the flowering stem is drunk or fermented into an alcoholic beverage pulque which open distillation yields the spirit mescal. Kickapoo Indians baked the flower stalks on hot stones and made into 'quiote'	Facciola (1990), Deane (2007–2012a)
Agave angustifolia Haw.	Carribean Agave	Young fat flower stalks roasted	King (2007)
Agave atrovirens Karw.ex Salm-Dyck	Century Plant, Maguey	Flower stalks roasted and eaten	Facciola (1990), Deane (2007–2012a)

Agave cantala (Haw.) Roxb. ex Salm-Dyck	Cantala, Bombay Aloe, Cebu Maguey, Manila Maguey	Flower stalks roasted and eaten	Deane (2007–2012a)
Agave chrysantha Peebles	Golden-Flowered Agave	Flower stalks roasted and eaten	Deane (2007–2012a)
Agave complicata Trel. ex Ochot = *Agave americana* subsp. *americana*	Century Plant	Flower stalks roasted and eaten	Deane (2007–2012a)
Agave crassipina Trel = *Agave salmiana* subsp. *crassipina* (Trel.) Gentry	Giant Agave, Pulque Agave	Flower stalks roasted and eaten	Deane (2007–2012a)
Agave deserti Engelm.	Desert Agave, Mescal, Century Plant, Maguey	Flowers and buds are eaten. Young flower stalks are baked until they form a sweet, starchy cake called 'mescal'. Nectar from flowers consumed directly by Indians	Tanaka (1976), Clarke (1977), Facciola (1990)
Agave palmeri Engelm.		Flower stalks roasted and eaten	Deane (2007–2012a)
Agave parryi Engelm.	Century Plant, Parry's Agave	Young fat flower stalks roasted and eaten, nectar from the flowering stalk made into a sweet syrup	Facciola (1990), Deane (2007–2012a)
Agave salmiana Otto ex Salm-Dyck	Pulque Agave, Century Plant	Flower stalks cut for 'quiote' which is sold in the streets and chewed like sugarcane in southwestern America	Uphof (1968), Facciola (1990), Deane (2007–2012a)
Agave shawii Engelm.	Shaw's Agave, Century Plant	Sweet nectar is used in California	Yanovsky (1936)
Agave shrevei Gentry		Flower stalk eaten	Laferriere et al. (1991)
Agave sisalana Perrine	Century Plant	Flowers can be boiled or roasted. The stalks before they blossom in summer can also be roasted and taste like molasses. The sap obtained after removal of the stalk can be used to make tequila. Flower nectar can be used to make sauces or sugar and bottled	Deane (2007–2012a)
Agave spp.	Century Plant	Flowers edible	Stangland (2004), McCullough (2007)
Agave stricta Salm-Dyck	Century Plant, Needle Agave, Needle Leaf Agave, Globe Agave, Hedgehog Agave, Hedgehog Century Plant	Flowers lightly cooked and dipped in egg batter for frying	King (2007)
Agave tequilana F.A.C. Weber	Blue Agave, Century Plant	Flowers used as above	Deane (2007–2012a)
Agave utahensis Engelm.	Utah Agave, Century Plant	Flower stalks edible	Harrington (1974), Facciola (1990), Deane (2007–2012a)
Agave vivipara auct.non. = *Agave angustifolia* Haw.	Century Plant	Flowering stalks eaten in India	Watt (1908)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Aloe barteri Baker = *Aloe tenuifolia* Lam.	African Aloe	Blossoms used as a soup vegetable in West Africa	Irvine (1952), Uphof (1968)
Aloe candelabrum A. Berger = *Aloe ferox* Mill.	Bitter Aloe, Red Aloe; Bitteraalwyn, Bergaalwyn (Afrikaans); Inhlaba (Zulu); Ikhala (Xhosa)	Flowers sucked for nectar	Fox et al. (1982), Facciola (1990)
Aloe chabaudii Schönland		Flowers eaten as vegetables	Kunkel (1984), Facciola (1990)
Aloe ferox Mill	Cape Aloe, Bitter Aloe, Red Aloe (English); Bitteraalwyn, Bergaalwyn (Afrikaans); Inhlaba (Zulu); Ikhala (Xhosa)	Flowers sucked for sweet nectar, sippable blossoms	Fox et al. (1982), Facciola (1990), Deane (2007–2012u)
Aloe greatheadii Schönland	Spotted Aloe; Transvaalaalwyn, Grasaalwyn (Afrikaans); Kgopane (Tswana)	Flower buds are a delicacy after being boiled	Kunkel (1984), Facciola (1990), Deane (2007–2012u)
Aloe littoralis Baker	Mopane Aloe; Bergaalwyn, Windhoekaalwyn, Mopanie-Aalwyn (Afrikaans)	Flowers used as potherbs	Fox et al. (1982), Facciola (1990)
Aloe macrocarpa Tod.	Aloe	Flowers eaten as vegetable	Fox et al. (1982), Facciola (1990)
Aloe marlothii A. Berger	Mountain Aloe	Flowers with nectar that can be consumed, sippable blossoms	Fox et al. (1982), Facciola (1990), Deane (2007–2012u)
Aloe zebrina Baker	Zebra Leaf Aloe, Spotted Aloe	Edible flowers and buds after being boiled. In Angola, they are pressed into cakes	Fox et al. (1982), Facciola (1990), Deane (2007–2012u)
Aspidistra sutepensis K. Larsen	Lilao (Thai)	Steamed flowers eaten as vegetable	Pongpangan and Poobrasert (1985), Maisuthisakul et al. (2008), Maisuthisakul (2012)
Clistoyucca brevifolia (Engelm.) Rydb. = *Yucca brevifolia* Engelm.	Joshua Tree	Young flower buds roasted on hot coals	Yanovsky (1936)
Convallaria keiskei Miq.	Lily of the Valley, Susuran; Kimigage-So (Japanese)	The flowers and flower buds are preserved in salt or mixed with leaf tea and drunk	Tanaka (1976), Kunkel (1984), Facciola (1990)
Convallaria majalis L.	Lily of the Valley, Convall-Lily, Convallaria, Jacob's Ladder	In some parts of Germany, a wine is prepared from the flowers mixed with raisin	Grieve (1971), Facciola (1990)
Dasylirion texanum Scheele	Texas Sotol, Sotol	Central bud roasted in mescal pits and used as food by Indians or made into a beverage	Uphof (1968), Facciola (1990)
Dasylirion wheeleri S. Watson ex Rothr.	Common Sotol, Desert Spoon, Sotol	As above	Uphof (1968), Facciola (1990)

Dichelostemma pulchellum (Salisb.) Heller = *Dichelostemma congestum* (Sm.) Kunth.	Wild Hyacinth	Flowers eaten raw make a nice decoration in the salad bowl	Moerman (1998), Facciola (1990)
Dichopogon fimbriatus (R.Br.) J.F. Macbr.	Nodding Chocolate Lily	Flowers are edible	Steenbeeke (2001)
Dichopogon strictus (R.Br.) J.G. Baker	Chocolate Lily Grass Lily	Flowers eaten raw; chocolate scented	Cribb and Cribb (1987)
Hesperoyucca whipplei (Torr.) Trel.	Chaparral Yucca	Flowers boiled and eaten	Yanovsky (1936), Tanaka (1976), Facciola (1990)
Hosta spp.	Plantain Lily	Flowers are edible	Deane (2007–2012k, t)
Lomandra longifolia Labill.	Longleaf Mat-Rush	Flowers eaten raw. Tiny creamy flowers eaten taste like peas with flower fragrance, flowers soaked in lemon juice, strained and base juice used as a fruit drink	Cribb and Cribb (1987), Low (1989)
Lomandra spp.	Mat Rush	Tiny creamy flowers eaten	Low (1989)
Ornithogalum pyrenaicum L.	Prussian Asparagus	Young unexpanded inflorescence cooked and served like asparagus vegetables	Grieve (1971), Facciola (1990)
Ornithogalum umbellatum L.	Star of Bethlehem	Flowers eaten baked in bread	Fernald et al. (1958), Hedrick (1972), Facciola (1990)
Peliosanthes teta Andrews	China Lily; Cu Hua Qiu Zi Cao (Chinese)	The edible part is the inflorescence. This indigenous vegetable has become very popular and more cultivated in some rural areas of northern Thailand	Chaikla et al. (2011)
Polianthes tuberosa L.	Tuberose	Flowers eaten cooked; used in vegetable soups or added to the substrate of 'kecap', an Indonesian soy sauce. The flowers are the source of tuberosa-flower water	MacNicol (1967), Tanaka (1976), Facciola (1990), Roberts (2000)
Samuela carnerosana Trel. = *Yucca carnerosana* (Trel.) McKelvey	Palma Barreta	Young flower clusters eaten boiled or roasted in Mexico	Uphof (1968), Tate (1976), Facciola (1990)
Sansevieria gracilis N.E.Br.	Sansevieria	Flowers are edible	Kunkel (1984), Facciola (1990)
Thysanotus patersonii R.Br.	Fringed Lily	Flowers are edible	SERCUL (2011)
Veltheimia bracteata Harv.ex Baker	Winter Red Hot Poker, Forest Lily	Flowers eaten like spinach	Hedrick (1972), Kunkel (1984), Facciola (1990), Deane (2007–2012v)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Yucca aloifolia L.	Aloe Yucca, Spanish Bayonet	Flowers edible raw or cooked. They are delicious raw or can be dried, crushed and used as a flavouring. Flowering stem is peeled and boiled, used like asparagus	Morton (1977), Kunkel (1984), Facciola (1990)
Yucca angustissima Engelm. ex Trevir.	Narrowleaf Yucca	As above	Harrington (1974)
Yucca baccata Torr.	Banana Yucca, Datil Yucca, Spanish Bayonet	Flower buds edible cooked. The older flowers are best as they are rich in sugar. The flowers, harvested before the summer rains, have been used as a vegetable. Flowering peduncles eaten cooked	Yanovsky (1936), Hedrick (1972), Sweet (1962), Harrington (1974), Clarke (1977), Facciola (1990), Stangland (2004), Elias and Dykeman (2009)
Yucca brevifolia Engelm.	Joshua Tree	Flowers edible cooked. The flower buds, before opening, can be parboiled in salt water to remove the bitterness, drained and then cooked again and served like cauliflower. The opened flowers are rich in sugar and can be roasted and eaten as candy	Tanaka (1976), Tate (1976), Facciola (1990)
Yucca constricta Buckley	Buckley's Yucca	Flowers edible raw or cooked. Delicious raw, they can also be dried, crushed and used as a flavouring. Flowering stem eaten cooked and used like asparagus	Bird (1990)
Yucca elata (Engelm.) Engelm.	Soap Tree Yucca	As above	Tate (1976), Kunkel (1984), Bird (1990), Moerman (1998)
Yucca elephantipes Regel	Spineless Yucca, Soft-Tip Yucca	Petals edible after removal of bitter anthers, used in salad and fried in batter	Uphof (1968), Facciola (1990)
Yucca filamentosa L.	Spoonleaf Yucca, Adam's Needles, Eve's Thread	Blossoms are edible raw or boiled. Flowers also dried, crushed and used as a flavouring. Petals used as garnish and salad. One Mexican dish is sauteed yucca flowers with chipotle	Hedrick (1972), Kunkel (1984), Bird (1990), Belsinger (1990), Facciola (1990), Newman and O'Connor (2009), Deane (2007–2012e, 2007–2012zb)
Yucca filifera Chadaub	Palm China, China Palm	Flowers edible raw or cooked. Delicious raw, they can also be dried, crushed and used as a flavouring. Flowering stem cooked and used like asparagus	Bird (1990)
Yucca glauca Nutt.	Soapweed Yucca	Flowers eaten raw in salad or cooked as potherbs, flower stalk cooked and inner portion eaten	Yanovsky (1936), Harrington (1974), Facciola (1990)
Yucca gloriosa L.	Spanish Dagger	Flowers edible raw or cooked. They are delicious raw and can also be dried, crushed and used as a flavouring. Flowering stem cooked and used like asparagus	Bird (1990)

Yucca harrimaniae Trel.	Spanish Bayonet, Spanish Dagger	As above	Harrington (1974), Bird (1990)
Yucca mohavensis Sarg. = *Yucca schidigera* Roezl ex Ortgies	Mojave Yucca	Flowers boiled for food, flowers eaten raw or used in jellies	Yanovsky (1936), Tanaka (1976), Facciola (1990)
Yucca recurvifolia Salisb. = *Yucca gloriosa* var. *recurvifolia* (Salisb.) Engelm.	Curveleaf Yucca; Pendulous Yucca	Flowers eaten raw or cooked. They are delicious raw, and can also be dried, crushed and used as a flavouring. A crisp crunchy texture, the flowers are very substantial and need to be well chewed. Flowering stem cooked and used like asparagus	Fern (1992–2003), Wikipedia (2012)
Yucca rupicola Scheele	Twisted-Leaf Yucca	As above	Wikipedia (2012)
Yucca schidigera Roezl ex Ortgies	Mojave Yucca	Young flowering stems chopped and cooked like asparagus or baked like a sweet potato	Bird (1990), Facciola (1990)
Yucca smalliana Fernald = *Yucca flaccida* Haw.	Adam's Needle	Flowers eaten raw or cooked. They are delicious raw and can also be dried, crushed and used as a flavouring. Flowering stem cooked and used like asparagus	Bird (1990)
Yucca spp.	Yucca		
Yucca whipplei Torr. = *Hesperoyucca whipplei* (Torr.) Tre.	Our Lord's Candle	Flowers eaten raw or cooked	Uphof (1968), Usher (1974)
Asteraceae			
Achillea borealis Bong. = *Achillea millefoliu*m L. subsp. *borealis* (Bong.) Breitung	Milfoil	Flowers used as below	Schofield (2003)
Achillea millefolium L.	Common Yarrow, Sneezewort, Soldier's Friend, Thousand-Leaf	Flowers used in herbal teas and lemonade; flowers fried in butter sprinkled with sugar or orange juice. An essential oil derived from the flowering tops is used commercially for flavouring soft drinks and alcoholic drinks	Uphof (1968), Grieve (1971), Facciola (1990), Schofield (2003)
Achillea ptarmica (Willd.) Rupr. Ex Heimerl	Sneeze-Wort, Pearl Sneeze-Wort	Flowers used as above	Schofield (2003)
Achillea sibirica Ledeb. = *Achillea alpina* L.	Chinese Yarrow; Nokogiri-Sou (Japanese)	Flowers used as above	Schofield (2003)
Achyrocline satureioides (Lam.) DC.	Alecrim Da Parede, Macela, Marcala Do Campo (Brazil)	Flowers used for flavouring bitter spirits	Seidemann (2005)
Acmella oleracea (L.) R.K. Jansen	Para Cress, Toothache Plant, Szechuan Buttons	Flowers eaten	Wetwitayaklung et al. (2008), Ochse and van den Brink (1980), Deane (2007–2012p)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Actinea odorata (A. Gray) Kuntze = *Actinella odorata* (DC.) A. Gray	Bitterweed	Infusion of flowering tops used as beverage in Texas	Yanovsky (1936)
Ageratum conyzoides L.	Billygoat-Weed, Chick Weed, Goatweed, Whiteweed	Fragrant flowers and foliage used for scenting coconut oil in south eastern Polynesia	Facciola (1990), Brown (2011)
Anthemis nobile L. = *Chamaemelum nobile (Il.) All.*	Camomile, Chamomile, Roman Chamomile, English Chamomile, Low Chamomile	Flower used to flavour food and brewed into tea. Flowers have a sweet apple flavour	Newman and O'Connor (2009)
Arctium lappa L.	Great Burdock, Gobo	Pith of flower stalk eaten raw in tossed salads, boiled as potherb or made into confection	Facciola (1990), Roberts (2000)
Arctium minus (Hill.) Benth.	Lesser Burdock, Beggars Buttons	Pith of flower stalk eaten raw in tossed salads or cooked as asparagus	Harrington (1974), Facciola (1990), Roberts (2000)
Argyranthemum frutescens (L.) Sch. Bip.	Marguerite Daisy	Flowers edible	Rop et al. (2012)
Artemisia absinthium L.	Wormwood	Flowering tops used to counter grassiness of goose and duck dishes	Uphof (1968), Grieve (1971), Facciola (1990)
Artemisia ludoviciana Nutt.	Prairie Sage, White Sagewort, Gray Sagewort, White Sagebrush, Mountain Sagewort	The flower heads can be used as seasoning or to make a tea	Dean (2007–2012s)
Artemisia vulgaris L.	Mugwort	Flowering tops added to beer or steeped into tea	Fernaldet al. (1958), Grieve (1971), Facciola (1990)
Aster kantoensis Kitam.	Kawara-Nogiku (Japanese)	Flowers eaten	Kunkel (1984)
Aster koraiensis Nakai	Korean Starwort	Flowers eaten	Kunkel (1984)
Balsamorhiza deltoidea Nutt.	Puget Balsam Root, Deltoid Balsam Root	Flower stalk eaten as cooked vegetables	Dean (2007–2012s)
Balsamita major Desf. = *Tanacetum balsamita* L.	Costmary, Bible-Leaf, Alecost, Balsam Herb, Bible Leaf, Mint Geranium	Flower petals used for conserve	Grieve (1971), Larkcom (1980), Facciola (1990)
Balsamorhiza sagittata (Pursh) Nutt.	Arrowleaf Balsam Root, Oregon Sunflower	Young immature flower stalks peeled and inner pith eaten	Hedrick (1972), Facciola (1990)
Bellis perennis L.	Common Daisy, Common Lawn Daisy, Daisy, English Daisy, European Daisy, True Daisy, Bruisewort	Flowers eaten with lettuce or greens, salad, crystallized or petals garnish on cakes. Flower and petals eaten in salads, flower buds eaten in sandwiches, soups and salads, preserved in vinegar used as substitute for capers	Hedrick (1972), Cribb and Cribb (1987), Larkcom (1980), Facciola (1990), Barash (1997), Lauderdale and Evans (1999), Newman and O'Connor (2009)

Berlandiera lyrata Benth.	Chocolate Daisy, Chocolate Flower, Lyreleaf Greeneyes, Green-Eyed Lyre Leaf	Flowers used for seasoning foods	Yanovsky (1936), Facciola (1990)
Bidens alba (L.) DC.	Spanish Needles, Beggar's Tick, Butterfly Needles, Hairy Beggarticks	Blossoms excellent for salad, they hold their flavour while cooking and can be added to a variety of dishes	Deane (2007–2012d)
Bidens bigelovii A. Gray	Bigelow's Beggarticks	Infusion of flowering tops used as beverage in Texas	Yanovsky (1936)
Calendula arvensis (Vaill.) L.	Field Marigold	Flower heads pickled	Kunkel (1984), Facciola (1990)
Calendula officinalis L.	Calendula, Pot Marigold, English Marigold, Poet's Marigold	Flowers used in salad, soup, butter, sauce, drinks, cookie; fresh petals are chopped and added to salads. The dried petals have a more concentrated flavour and are used as a seasoning in soups, cakes, omelette, curry, custard, etc. An edible yellow dye is obtained from the petals and used as a saffron substitute to colour and flavour rice, soups, stews, cheese, cakes, puddings	Organ (1960), Uphof (1968), Facciola (1990), Garland (1993), Barash (1997), Lauderdale and Evans (1999), Roberts (2000), Lust (2001), Newman and O'Connor (2009), Mlcek and Rop (2011)
Carduus nutans L.	Musk Thistle, Nodding Thistle	Pith of flowering stem, boiled, salted and dressed. Dried flowers used in some countries as rennet to curdle milk	Fernald et al. (1958), Facciola (1990)
Carlina acanthifolia All.	Carline Thistle	Flowering head cooked; used as a globe artichoke substitute	Hedrick (1972), Tanaka (1976), Kunkel (1984), Facciola (1990)
Carlina acaulis L.	Stemless Carline Thistle	Flowers used as above	Kunkel (1984), Facciola (1990)
Carlina vulgaris L.	Carline Thistle	Flowers used as above	Hedrick (1972), Tanaka (1976), Kunkel (1984), Facciola (1990)
Carthamus tinctorius L.	Safflower, Dyer's Saffron False Saffron	Bitter flower petals used as saffron substitute for colouring bread, butter and liqueurs and also used in herbal tea	Yanovsky (1936), Uphof (1968), Grieve (1971), Tanaka (1976), Facciola (1990), Hu (2005), Newman and O'Connor (2009)
Centaurea cyanus L.	Cornflower, Bachelor's Button, Bluebottle, Boutonniere Flower, Hurtsickle, Cyani Flower	Flowers edible raw or cooked. The fresh florets can be used in salads, as a vegetable or a garnish. An edible blue dye is obtained from the flowers, used for colouring sugar, gelatin and confections. Flowers are ideal for mixing with other flowers to make attractive confetti for sprinkling over salads, omelettes and pasta dishes	Facciola (1990), Bown (1995), Lauderdale and Evans (1999), Roberts (2000), Newman and O'Connor (2009), Rop et al. (2012), Anonymous (2012a)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Centaurea nigra L.	Black Knapweed, Lesser Knapweed, Common Knapweed	Flower petals eaten raw, added to salads	Facciola (1990)
Chamaemelum nobile (L.) All.	Roman Camomile, Chamomile, Garden Camomile, Ground Apple, Low Chamomile	Fresh or dried flowers used to flavour sherry in Spain, used in herbal tea	Grieve (1971), Garland (1993), Barash (1997), Facciola (1990), Lauderdale and Evans (1999), Newman and O'Connor (2009)
Chamomilla aurea J. Gray = *Matricaria aurea* (Loefl.) Sch. Bip.	Golden Chamomile, Hungarian Chamomile	Dried flower heads brewed into an aromatic tea, also used for flavouring fine liqueurs of the French types viz. Benedictine and D.O.M., a source of essential oil for food industry	Uphof (1968), Morton (1976), Facciola (1990)
Chamomilla recutita (L.) Rauschert = *Matricaria chamomilla* L.	German Chamomile, Camomile, Scented Mayweed, Wild Chamomile, Hungarian Chamomile	Flowers used in herbal teas	Garland (1993), Burnie and Fenton-Smith (1996)
Chrysanthemum coronarium L.	Garland Chrysanthemum, Chrysanthemum Coronarium Greens, Edible Chrysanthemum Coronarium, Chop-Suey Greens, Crown Daisy	Flowers petals are used fresh, blanched briefly and added to salads, soups or pickles and eaten with fish, or dried and used in teas. A fragrant pickle known as 'kikumi' is made from the petals in Japan	Harrington (1974), Tanaka (1976), Facciola (1990), Dasuki and van den Bergh (1994), Lauderdale and Evans (1999), Woodward (2000), Roberts (2000), Newman and O'Connor (2009)
Chrysanthemum frutescens L. = *Argyranthemum frutescens* (L.) Sch. Bip.	Marguerite Daisy	Flowers edible	Rop et al. (2012)
Chrysanthemum indicum L.	Mother Chrysanthemum, Mother Daisy, Winter Aster, Ground Apple, Whig Plant; Manzanilla (Spanish)	Flower heads pickled in vinegar	Tanaka (1976), Facciola (1990)
Chrysanthemum leucanthum L. = *Chrysanthemum vulgare* (Vaill.) Lam.	Oxeye Daisy	Unopened flowers can be marinated and used like capers. They are also used in salad and as condiment with fish or stuffed in a chicken breast	Newman and O'Connor (2009), Anonymous (2012c)
Chrysanthemum morifolium Ramat.	Chrysanthemum, Florist Chrysanthemum, Hardy Garden Mum	Edible leaves and flower heads boiled served as salads with fish and tofu and seasoned with vinegar and soy sauce. Flowers also prepared as tempura, pickled, dried or added to soups. Flower petals brewed into 'tangu', an aromatic tea	Tanaka (1976), Clarke (1977), Facciola (1990), Lauderdale and Evans (1999)
Chrysanthemum parthenium (L.) Pers. = *Tanacetum parthenium* (L.) Sch. Bip.	Feverfew	Flowers edible	Rop et al. (2012)

Chrysanthemum sinense Sabine = *Chrysanthemum morifolium* Ramat.	See *Chrysanthemum morifolium*	In China leaves and flowers eaten in soups	Read (1946)
Chrysanthemum spatiosum L.H. Bailey = *Chrysanthemum coronarium* L.	See *Chrysanthemum coronarium*	Used as for Florist Chrysanthemum	Facciola (1990), Dasuki and van den Bergh (1994), Woodward (2000)
Chrysothamnus confinis Greene = *Ericameria nauseosa* subsp. *consimilis* (Greene) G.L. Nesom and G.I. Baird	Douglas Rabbitbrush	Flower buds eaten with salt in New Mexico	Yanovsky (1936)
Cichorium intybus L.	Chicory, Raddichio, Endive, Succory	Blue flowers crystallized and used to decorate cakes and puddings; flowers can be used in salads, fresh or pickled. The fresh flowers have a mild lettuce flavour and make a decorative addition to salads, while flower buds can be pickled. Picked blooms look attractive frozen in ice cubes and added to drinks	Fernald et al. (1958), Larkcom (1980), Facciola (1990), Burnie and Fenton-Smith (1996), Lauderdale and Evans (1999), Roberts (2000), McCullough (2007), Newman and O'Connor (2009)
Cirsium arvense (L.) Scop	Canadian Thistle	Flower stalk boiled and eaten as vegetables	Uphof (1968), Launert (1981), Facciola (1990)
Cirsium eriophorum (L.) Scop.	Wooly Thistle	Flower buds cooked used as a globe artichoke substitute	Hedrick (1972), Kunkel (1984), Facciola (1990)
Cirsium oligophyllum (Franch. & Sav.) Matsum.	Nohara Azami (Japanese)	The flower heads are fried or used in salads	Facciola (1990)
Cirsium palustre (L.) Coss.ex Scop.	Marsh Thistle, European Swamp Thistle	Flower stalks eaten in salad or boiled as vegetables	Fernand et al. (1958), Grieve (1971), Harrington (1974), Facciola (1990)
Cirsium tanakae (Franch. & Sav.) Matsum. = *Cirsium oligophyllum* (Franch. & Sav.) Matsum.	Nohara Azami (Japanese)	Flower heads fried or used in salad in East Asia	Tanaka (1976), Facciola (1990)
Cirsium vulgare (Savi.) Ten.	Spear Thistle, Common Thistle	Unopened flower heads eaten, receptacle cooked and served like artichoke, young flower stalks eaten, dried flower used as substitute for rennet in curdling milk for cheese making	Fernald et al. (1958), Harrington (1974), Clarke (1977), Kunkel (1984), Cribb and Cribb (1987), Facciola (1990)
Cnicus benedictus L.	Blessed Thistle	Flower heads, harvested before the flowers open, have been used as a globe artichoke substitute	Stuart (1987)
Cosmos bipinnatus Cav.	Garden Cosmos, Mexican Aster	Petals source of carotenoids for the food industry	Tinoi et al. (2006)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Cosmos sulphureus Cav.	Cosmos, Sulphur Cosmos, Yellow Cosmos, Orange Cosmos, Klondike Cosmos	Flowers used in salad	Kaisoon et al. (2011, 2012)
Crotalaria juncea L.	Brown Hemp, Indian Hemp, Sunn Hemp; O-Hawaii Maton (Manipur)	Young shoots and inflorescences eaten in Manipur India	Yumnum and Tripathi (2012)
Cynara cardunculus L.	Cardoon, Artichoke Thistle, Cardone, Cardoni, Carduni, Cardi	Flower bases steamed, cooked; fleshy receptacle of unopened flower head, dried flowers used as substitute for rennet in making Serra cheese in Portugal. Some dishes included pickled artichokes, artichoke with mint and yoghurt, artichoke dip	Hedrick (1972), Cribb and Cribb (1987), Low (1989), Facciola (1990), Van den Bergh (1994a, b), Roberts (2000), Newman and O'Connor (2009)
Cynara humilis L.	Wild Artichoke, Artichoke Thistle; Alcachofra-Brava (Portuguese); Alcachofa, Alcachofa De Campo (Spanish)	Flower receptacle used in preparation of a popular tangine stew. In Morocco, the dreid flowers used as rennet in coagulating rape, a kind of sweetened junket	Wolfert (1973), Facciola (1990)
Cynara scolymus L. = *Cynara cardunculus* subsp. *flavescens* Wiklund	Globe Artichoke, Bur Artichoke, Artichoke Thistle	Flower buds steamed, basal fleshy portion of phyllaries (involucral bracts) of the capitula and young receptacle used as vegetables. Fleshy receptacle of unopened flower head used as substitute for rennet	Van den Bergh (1994a, b), Low (1989), Hu (2005)
Dahlia juarezii Van der Berg = *Dahlia coccinea* Cav.	Dahlia, Cactus Dahalia, Single-Flowered Dahlia	Flowers used in salads, cream, cheese, dahlia dip, sundried tomato and dahlia bread	Roberts (2000)
Dahlia pinnata Cav.	Dahlia, Garden Dahlia	The flower petals are used in salads	Kunkel (1984), Facciola (1990)
Dahlia rosea Cav. = *Dahlia pinnata* Cav.	See *Dahlia pinnata*	Flowers used in salads, cream, cheese and dahlia dip, sundried tomato and dahlia bread	Hedrick (1972), Roberts (2000)
Dahlia spp.	Dahlia	Used as above	Roberts (2000)
Dendranthema grandiflorum (Ramat.) Kitam.	Chrysanthemum, Garden Mum, Hardy Mum, Cushion Mum	The flower heads or petals are parboiled and served as a salad with tofu and seasoned with vinegar or soya sauce. They can also be prepared as tempura, pickled, dried or added to soups	Read (1946), Uphof (1968), Facciola (1990), Newman and O'Connor (2009)
Dendranthema indicum (L.) Des Moul.	Chrysanthemum, Winteraster	The flower heads are pickled in vinegar	Uphof (1968), Kunkel (1984), Facciola (1990)
Dendranthema vestitum (Hemsl.) Ling = *Chrysanthemum vestitum* (Hemsl.) Stapf.	Ju-Hua (Chinese)	Dried flowers used in herbal teas	Hu (2005)

Dendranthema morifolium (Ramat.) Tzvel.	Florists Chrysanthemum, Hardy Garden Mum; Ju Hau (Chinese)	Ligulate florets used for special Chinese delcicacy, dried flortes used for chryasnathemum tea, in Korea rice wine flavoured with chrysanthemum flowers is called 'gukwaju', florets mix with a thick snake meat soup	Hu (2005), Wikipedia (2012)
Dicoria brandegeei A. Gray = *Dicoria canescens* A. Gray	Desert Twinbugs	Flowers and seeds ground for food in Arizona	Yanovsky (1936)
Echinacea purpurea (L.) Moench	Eastern Purple Coneflower, Purple Coneflower, Echinacea, Snakeroot	Some dishes include Echinacea Pane bagno (bathed bread) decorated with fresh echinacea petals and a wedge of lemon; American Indian savoury Echinacea spread, Echinacea and melon fruit salad	Roberts (2000)
Emilia sonchifolia (L.) DC.ex DC.	Lilac Tasselflower, Red Tassel Flower, Cupid's Shaving Brush, Emilia, Purple Sow Thistle, Flora's Paintbrush	The whole plant, including the unopened flowers, can be eaten raw or cooked	Cribb and Cribb (1987)
Erechtites hieracifolia (L.) Raf.	American Burnweed, Fireweed, Pilewort	Young inflorescence head, flowering top eaten raw or steamed and served with rice	Rifai (1994)
Erechtites valerianifolia (Link ex Wolf) Less ex DC.	Brazilian Fireweed, Tropical Burnweed, Ceylon Thistle, Fireweed, Fireweed Daisy	Young inflorescence head, flowering top eaten raw or steamed and served with rice	Burkill (1966), Ochse and van den Brink (1980), Cribb and Cribb (1987), Facciola (1990), Rifai (1994)
Galactites tomentosa Moench	Purple Milk Thistle	Tender flower stalk eaten	Hedrick (1972), Facciola (1990)
Galinsoga parviflora Cav.	Gallant Soldier, Potato Weed, Yellow Weed, Galinsoga	The leaves, stem and flowering shoots eaten raw or cooked and eaten as a potherb, or added to soups and stews	Fernald et al. (1958), Harrington (1974), Cribb and Cribb (1987), Facciola (1990), Elias and Dykeman (2009)
Gundelia tournefortii L.	Galgal, Tumbleweed, Tumble Thistle	The thick flowering stem, with the young and still undeveloped flower buds, is sold in the local markets in Jerusalem. It is a sought after vegetable, cooked like globe artichokes	Hedrick (1972), Kunkel (1984), Wright (2001)
Gynura nepalensis DC.	Cholesterol Spinach; Tera Paibi (Manipur)	Young shoots and inflorescences are eaten	Yumnum and Tripathi (2012)
Helianthus annuus L.	Common Sunflower, Sunflower, Mirasol	Young flower buds are steamed and served like globe artichokes with butter and vinegar; petals of openend flowers can be used	Hedrick (1972), Harrington (1974), Facciola (1990), Garland (1993), Barash (1997), Lauderdale and Evans (1999), Roberts (2000)
Helianthus tuberosus L.	Jerusalem Artichoke, Sunroot, Sunchoke, Earth Apple, Topinambour	Flower reported edible	King (2007)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Helichrysum italicum (Roth) G. Don	Curry Plant, Immortelle	Flower heads used for tea; also a source of essential oil used to enhance fruit flavours in candy, ice cream, baked goods, soft drinks and chewing gum	Morton (1976), Facciola (1990)
Lactuca serriola L.	Prickly Lettuce	Unopened flower heads can be used as a green (raw or cooked); they are very bitter	Harden (1992)
Leucanthemum vulgare (Vaill.) Lam.	Ox-Eye Daisy	Flower heads used like dandelion in home wine making	Fernald et al. (1958), Launert (1981), Facciola (1990)
Matricaria matricarioides (Less.) Porter	Pineapple Weed, Wild Chamomile, Disc Mayweed	Flower heads eaten raw or cooked, a tasty nibble. Fresh or dried flowers are used to make herbal teas—golden pineapple scented tea when steeped in hot water	Facciola (1990), Schofield (2003)
Matricaria recutita L. = *Matricaria chamomilla* L.	German Chamomile, Chamomile, Blue Chamomile, Wild Chamomile, Hungarian Chamomile, Scented Mayweed	Flower heads eaten raw, added to salad, vegetable casseroles and stir-fries. Flowers used to flavour tea	Garland (1993), Brotonegora (2000), Schofield (2003)
Melampodium divaricatum (Rich.) DC.	Butter Daisy, Million Gold Melampodium	Petals source of carotenoids for the food industry	Tinoi et al. (2006)
Onopordum acanthium L.	Scotch Thistle, Heraldic Thistle	Green base of flower head cooked and eaten like artichokes; floral parts used as an adulterant of saffron	Fernald et al. (1958), Grieve (1971), Hedrick (1972), Cribb and Cribb (1987), Facciola (1990)
Onopordum illyricum L.	Illyrian Cotton Thistle	Flower buds eaten cooked, used as a globe artichoke	Facciola (1990)
Pectis papposa Harv. and A. Gray	Field Marigold, Chickweed, Manybristle Cinchweed	Flowers used for seasoning meat by Indians in New Mexico	Yanovsky (1936), Uphof (1968), Facciola (1990)
Petasites frigidus (L.) Fries	Sweet Coltsfoot, Arctic Butterbur, Arctic Sweet Coltsfoot	Flower heads eaten cooked, steamed, dressed with garlic butter or cheese sauce. Flowers battered and fried as floral fritters or chopped and added to casseroles and soups	Uphof (1968), Kunkle (1984), Facciola (1990), Schofield (2003)
Petasites hyperboreus Rydb.	Arctic Sweet Coltsfoot, Northern Coltsfoot	Used as above	Schofield (2003)
Petasites japonicus var. *giganteus* F. Schmidt ex Makino = *Petasites japonicas* subsp. *giganteus* F. Schmidt ex Kitam.	Giant Sweet Coltsfoot	Flower buds eaten as vegetable or used as a condiment	Tanaka (1976), Facciola (1990)

Petasites japonicus (Siebold. & Zucc.) Maxim.	Sweet Coltsfoot, Butterbur	Flower heads eaten cooked, steamed and dressed with garlic butter or cheese sauce. Flowers battered and fried as floral fritters or chopped and added to casseroles and soups. Flower buds have a slightly bitter but agreeable taste and are prized as a vegetable and condiment in Japan	Uphof (1968), Tanaka (1976), Douglas (1978), Facciola (1990), Van den Bergh (1994a, b)
Petasites palmatus (Aiton) A. Gray	Palmate Butter, Butterbur	Flowering stems and flower buds are boiled, steamed and dressed with garlic butter or cheese sauce. Flowers battered and fried as floral fritters or chopped and added to casseroles and soups	Tanaka (1976), Kunkel (1984), Facciola (1990), Schofield (2003)
Petasites sagittatus (Pursh.) A. Gray	Arrowleaf Sweet Coltsfoot	Flowers used as above	Schofield (2003)
Pluchea indica (L.) Less	Indian Fleabane, Indian Camphorweed, Indian Pluchea	Young leaves, shoot tips and young inflorescences eaten raw in salad, cooked or steamed	Martin and Ruberté (1975), Ochse and van den Brink (1980), Facciola (1990)
Ratibida columnifera (Nutt.) Wooton and Standl.	Cone Flower, Mexican Hat	Flower heads brewed into tea	Yanovsky (1936), Facciola (1990)
Scolymus hispanicus L.	Spanish Salsify, Golden Thistle, Scorzonera, Spanish Oyster Plant	Flowers used to adulterate saffron. Flower buds eaten raw, added to salads. Also used in French omelette	Uphof (1968), Hedrick (1972), Kunkel (1984), Facciola (1990)
Scorzonera mollis M. Bieb	Skorzonerë Butloshe (Albanian)	Flowers eaten raw. The flowers have a scent of chocolate	Uphof (1968), Usher (1974), Tanaka (1976), Kunkel (1984)
Scorzonera mongolica Maxim.	Mongolian Viper's Grass Meng Gu Ya Cong (Chinese)	Flowers eaten raw	Kunkel (1984)
Scorzonera papposa DC.	Oriental Viper's Grass	Flowers eaten raw	Kunkel (1984)
Scorzonera undulata Vahl	L-Giz, Talma (Morocco)	Capitula (chocolate taste) eaten raw by children and shepherds	Usher (1974), Kunkel (1984), Bellakhdar (1997)
Scorzonera undulata subsp. *deliciosa* (DC.) Maire	Scorzonera Zuccherina (Italian)	Flowers eaten raw	Usher (1974), Kunkel (1984)
Sigesbeckia orientalis L.	Sticky Weed, Siegesbeckia Herb, Yellow Crown Beard; Xi Xian Xao (Chinese); Colle Colle (Creole); Tuskushi-Me-Namomi (Japanese)	Fragrant flowers used for scenting coconut oil	Brown (1954), Facciola (1990)
Silphium laciniatum L.	Compass Flower, Compass Plant, Rosinweed	Flower stalks used as chewing gum	Fernald et al. (1958), Facciola (1990)
Silybum marianum (L.) Gaertn.	Blessed Milk Thistle, Variegated Thistle	Flowers buds steamed, eaten cookedor steamed like globe artichoke	Low (1989), Facciola (1990), Bown (1995)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Solidago canadensis L.	Canada Golden Rod, Rock Goldenrod	Flower steeped for beverage or added to herbal tea blends. Blossoms can be added to pancakes and fritter batters, bread and biscuit doughs. Goldenrods edible raw, can be used for decoration and making tea	Roberts (2000), Schofield (2003)
Solidago lepida DC.	Western Canada Golden Rod	Flowers used as above	Schofield (2003)
Solidago odora Aiton	Sweet Golden Rod, Fragrant Golden Rod	Fully expanded flowers and leaves used to brew tea	Fernald et al. (1958), Facciola (1990)
Solidago spathulata DC.	Coast Golden Rod	Flowers used as for Canadian Goldenrod flowers	Schofield (2003)
Solidago virgaurea L.	Golden Rod, Aaron's Rod, European Goldenrod, Goldrute,	Goldenrods edible raw, can be used for decoration and making tea	Roberts (2000)
Spilanthes acmella (L.) Murray = *Blainvillea acmella* (L.) Philipson	Toothache Plant, Paracress	Young leaves and flower heads are eaten raw, boiled. Flowers chewed	Ochse and van den Brink (1980), Roemantyo (1994), Wetwitayaklung et al. (2008)
Spilanthes iabadicensis A.H. Moore = *Acmella uliginosa* (Sw. Cass)	Legetan; Zhao Sheng Jin Niu Kou (Chinese)	Young leaves and flower heads are eaten raw or boiled	Roemantyo (1994)
Spilanthes paniculata Wall. ex DC. = *Acmella paniculata* (Wall. ex DC.) R.K. Jansen	Daisy Cress, Panicled Spot Flower; Jin Niu Kou (Chinese); Raan, Phak Khraat (Thai); Yari Sennichimodoki (Japanese)	Young leaves and flower heads are eaten raw, boiled or added to curry	Roemantyo (1994), Jircas (2010)
Tagetes tenuifolia L.	Lemon Marigold, Signet, Signet Marigold	Flowers used sparingly as garnish, in salads and sandwiches, or added to desserts and wines and made into herbal tea	Facciola (1990), Barash (1997), Newman and O'Connor (2009), Deane (2007–2012g)
Tagetes erecta L.	African Marigold, Aztec Marigold, Mexican Marigold; Daao Rueang (Thai)	Flowers used in salad, herbal tea and garnish or fried in light curry. Food colourant lutein extracted from the flowers	Cantrill (2004), Newman and O'Connor (2009), Kaisoon et al. (2011, 2012), Deane (2007–2012g)
Tagetes lucida Cav.	Mexican Marigold, Pericón, Mexican Mint Marigold, Mexican Tarragon, Spanish Tarragon, Cempaxóchitl, Texas Tarragon, Sweet Mace	Salad, herbal tea, garnish, flowering heads brewed into anise-flavoured tea; used in salad garnish	Hedrick (1972), Facciola (1990), Brown (2011), Deane (2007–2012g)
Tagetes patula L.	French Marigold, Dwarf Marigold, Marigold; Amarillo (Spanish, Tagalog)	Flowers used in refreshing drink, salad, herbal tea, garnish; dried flowers served as adulterant of saffron or as colouring for butter and cheese	Kunkel (1984), Morton (1976), Facciola (1990), Lauderdale and Evans (1999), Rop et al. (2012), Deane (2007–2012g)

Tagetes signata Bartl. = *Tagetes tenuifolia* L.	Signet Marigold	Flowers used in salad, herbal tea, garnish, marigold butter and muffins	Barash (1997), Lauderdale and Evans (1999)
Tanacetum parthenium (L.) Sch. Bip.	Feverfew, Featherfew, Featherfoil, Flirtwort	Dried flowers used in tea, in wine and certain pastries	Uphof (1968), Facciola (1990)
Tanacetum vulgare L.	Tansy, Bitter Buttons	The flowers have a unique flavour and are eaten or used as a garnish. A bitter, somewhat lemon-flavoured tea is made from the leaves and flowering tops	Fernaldet al. (1958), MacNicol (1967), Grieve (1971), Facciola (1990)
Taraxacum albidum Dahlst.	White Dandelion; Shirobana-Tanpopo (Japanese)	Flowers eaten after parboiled	Tanaka (1976), Facciola (1990)
Taraxacum bessarabicum (Hornem.) Hand-Mazz.	Pissenlit De Bessarabie (French)	Flowers eaten raw or cooked. A pleasant tea is made from the flowers	Fern (1992–2003)
Taraxacum formosanum Kitam.	Formosan Dandelion	The unopened flower buds can be used in fritters and tea	Fern (1992–2003)
Taraxacum heterolepis Nakai and Koidz ex Kitag.		Flowers eaten raw or cooked. The unopened flower buds can be used in fritters. A pleasant tea is made from the flowers	Fern (1992–2003)
Taraxacum hondoense Nakai and Koidz	Kanto Tanpopo (Japanese)	The unopened flower buds can be used in fritters	Fern (1992–2003)
Taraxacum hybernum Steven		Flowers used as above	Fern (1992–2003)
Taraxacum japonicum Koidz.	Japanese Dandelion, Daiho-Kwanseitampopo (Japanese)	Flowers used as above	Fern (1992–2003)
Taraxacum kok-saghyz L.E. Rodin	Rubber Dandelion, Russian Dandelion	Flowers used as above	Fern (1992–2003)
Taraxacum laevigatum (Willd.) DC.	Red-Seed Dandelion	Flowers used as above	Fern (1992–2003)
Taraxacum magellanicum Comm. ex Sch. Bip.	Native Dandelion; Tohetaka, Tohetake, Tohetea (Maori)	Flowers used as above	Fern (1992–2003)
Taraxacum megalorrhizon Hand.-Mazz.	Cyprus Dandelion, Big-Root Dandelion; Pentaramia, Agrioradiko (Crete)	Flowers used as above	Fern (1992–2003)
Taraxacum mongolicum Hand.-Mazz.	Chinese Dandelion	Flowers used as above	Fern (1992–2003)
Taraxacum obovatum (Willd.) DC.	Pissenlit À Feuilles Obovales, Pissenlit Obovale	Flowers eaten raw or cooked. The unopened flower buds can be used in fritters	Fern (1992–2003)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Taraxacum officinale Webb	Dandelion, Blowball, Lion's Tooth, Cankerwort, Milk-Witch, Yellow-Gowan, Irish Daisy, Monks-Head, Priest's-Crown and Puff-Ball, Faceclock, Pee-A-Bed, Wet-A-Bed, Canker-Wort, Swine's Snout	Young leaves, flowers and buds are edible. Dandelion buds make good pickles. Dandelion flowers rolled in flour and fried in butters taste much like morel mushrooms. Flowers eaten in pancakes, omelletes, fritters, salads, e.g. dandelion and bacon salad. Flowers used in dandelion wine. Flowers can be crystallized. Flowers used as an ingredient in the Arabic cake 'yublo'	Harrington (1974), Garland (1993), Van den Bergh (1994a, b), Barash (1997), Facciola (1990), Lauderdale and Evans (1999), Roberts (2000), Schofield (2003), Newman and O'Connor (2009)
Taraxacum platycarpum Dahlst.	Tanpopo (Japanese)	The unopened flower buds can be used in fritters and tea	Fern (1992–2003)
Taraxacum sinicum Kitag.	Jian Di Pu Gong Ying (Chinese)	Flowers edible raw or cooked. The unopened flower buds can be used in fritters	Fern (1992–2003)
Thelesperma filifolium (HooK.) A. Gray	Showy Navajo Tea	Flowers used for tea substitute	Facciola (1990)
Thelesperma gracile (Torr.) A. Gray = *Thelesperma megapotanicum* (Spreng.) Kuntze	Cota, Indian Tea, Hopi Tea, Navajo Tea, Zuni Tea, Greenthread	Flower buds eaten. A tea is made from the leaves and dried flowers	Usher (1974), Kunkel (1984), Facciola (1990)
Thelesperma megapotanicum (Spreng.) Kuntze	Cota, Indian Tea, Hopi Tea, Navajo Tea, Zuni Tea, Greenthread	Flower buds eaten. A tea is made from the fresh or dried leaves and flowering stems, imparts a delicious hint of mint in its aftertaste	Facciola (1990), Moerman (1998)
Tragopogon porrifolius L.	Salsify, Purple Salsify, Common Salsify, Oyster Plant, Vegetable Oyster, Jerusalem Star, Goatsbeard	Flowers eaten raw, added to salads or as garnish. Flowers also pickled. Flower stalks cooked and dressed like asparagus	Uphof (1968), Grieve (1971), Hedrick (1972), Facciola (1990), Anonymous (2012a)
Tragopogon pratensis L.	Meadow Salsify, Showy Goat's-Beard, Jack-Go-To-Bed-At-Noon	Flowering stems and buds cooked served like asparagus	Fernald et al. (1958), Launert (1981), Facciola (1990)
Tussilago farfara L.	Coltsfoot, Assfoot,British Tobacco, Bull's-Foot, Clayweed, Cleats, Colt-Herb, Coltsfoot, Coughwort, Dove-Dock, Dummyweed, Foalfoot, Ginger, Gingerroot, Gowan, Hoofs, Horsefoot, Horsehoof, Kuan Dong, Sowfoot, Tussilage; Pas- D'âne (French)	Flower buds and young flowers eaten raw or cooked in soups or potherbs have a pleasant aniseed flavour imparting a distinctive aromatic flavour to salads. A wine can be made from the blossoms; Fresh and dried flowers can be used to brew an aromatic tea	Uphof (1968), Lauernert (1981), Facciola (1990), Deane (2007–2012t)

Youngia chelidoniifolia (Makino.) Kitam. = *Paraixeris chelidoniifolia* (Makino) Nakai	None	Flowers eaten cooked	Tanaka (1976), Kunkel (1984)
Youngia japonica (L.) DC.	Japanese Hawkweed	Shoot and flowers used as 'liangcha'	Hu (2005)
Balsaminaceae			
Impatiens balsamina L.	Garden Balsam, Rose Balsam, Touch Me Not	Flowers made into 'kofta' fritters or used to flavour tea	Paul (2011)
Impatiens walleriana Hook.f.	Garden Balsam, Impatiens, Busy Lizzie	Petals or whole flowers come in many colours and look attractive, used as a garnish in salads or floated in cold drinks	Ropp et al. (2012), Anonymous (2012a)
Basellaceae			
Basella alba L.	Indian Spinach, Malabar Spinach	Young shoots and flowers eaten after steaming or blanching and serve with chilli sauce or add in curry	Jircas (2010)
Basella rubra Roxb. = *Basella alba* L.	Indian Spinach, Malabar Spinach	Flowers and young stem used as vegetable	Pongpangan and Poobarasert (1985)
Begoniacea			
Begonia boliviensis	Bolivian Begonia	Flowers edible	Rop et al. (2012)
Begonia cucullata Willd.	Wax Begonia	Flowers edible	Deane (2007–2012b)
Begonia elatior	Begonia	Flowers edible	Friedman et al. (2007)
Begonia semperflorens Hook. = *Begonia cucullata* var. *hookeri* (A.DC.) L.B.SM and Schub.	Wax Begonia	Flower used in fruit salad, crystallized, or as garnish, used to prepare Begonia spread	Friedman et al. (2007), Deane (2007–2012b, e)
Begonia × *tuberhybrida* Voss	Tuberous Begonia. Hybrid Tuberous Begonia	The brightly coloured flowers have a delicious light, lemon taste and a crisp texture. Use snipped petals as a garnish in salads and sandwiches or dip whole petals in flavoured yogurt and serve as an appetizer	Newman and O'Connor (2009), Deane (2007–2012b), Anonymous (2012a)
Berberidaceae			
Berberis aristata DC.	Chitra, Indian Barberry, Tree Turmeric	Flower buds added to sauces	Kunkel (1984), Facciola (1990)
Berberis canadensis Mill.	Allegheny Barberry	Flowers edible	Kavasch (2005)
Mahonia aquifolium (Pursh.) Nutt. = *Berberis aquifolium* Pursh.	Oregon Holly Grape	Flowers edible raw. They can also be used to make a lemonade-like drink	Hedrick (1972), Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Betulaceae			
Alnus oregona	Oregon Alder	Catkins eaten raw or cooked have a bitter flavour; added to soups, dried and powdered as a spice, or nibbled raw	Schofield (2003)
Alnus rhombifolia Nutt.	White Alder	Flowers used as above	Schofield (2003)
Alnus rubra Ong.	Red Alder	Flowers used as above	Schofield (2003)
Alnus sinuata (Regel.) Rydb.	Sitka Alder	Flowers used as above	Schofield (2003)
Alnus tenuifolia Nutt.	Mountain Alder	Flowers used as above	Schofield (2003)
Alnus viridis crispa (Aiton.) Turrill.	American Green Alder	Flowers used as above	Schofield (2003)
Betula glandulosa Michx.	Scrub Birch	Flowers used as above	Schofield (2003)
Betula kenaica W.H. Evans	Kenai Birch	Flowers used as above	Schofield (2003)
Betula nana L.	Dwarf Birch	Flowers used as above	Schofield (2003)
Betula occidentalis Hook.	Water Birch	Flowers used as above	Schofield (2003)
Betula papyrifera Marshall	Paper Birch	Flowers used as above	Schofield (2003), Facciola (1990)
Betula pendula Roth.	Silver Birch	Young catkins eaten	Bryan and Castle (1975), Schofield (2003)
Betula pubescens Ehrh.	White Birch	Young catkins eaten	Bryan and Castle (1975), Scholfield (2003)
Bignoniaceae			
Catalpa bungei C.A. Meyer	North China Catalpa; Qiu Shu (Chinese)	Unopened buds pickled, flowers stir-fried	Hu (2005)
Catalpa kaempferi Sieb. and Zucc. = *Catalpa ovata* G. Don	Chinese Catalpa	In China, fresh or dried flowers washed, thoroughly boiled and eaten with oil and salt	Read (1946)
Catalpa ovata G. Don	Chinese Catalpa	Flowers and young pods eaten cooked	Facciola (1990)
Chilopsis linearis (Cav.) Sweet	Desert Willow	The blossoms used for food	Moerman (1998)
Dolichandrone rheedii (Spreng.) Seem. = *Dolichandrone spathacea* (L.f.) Schum.	Mangrove Trumpet Tree; Thakut (Burmese)	Flowers eaten in Myanmar	Tanaka (1976)
Dolichandrone serrulata (Wall. DC.) Seem.	Khae Khao (Thai); Thakut (Burmese)	Flowers eaten	Wetwitayaklung et al. (2008), Maisuthisakul et al. (2008), Maisuthisakul (2012)

Dolichandrone stipulata (Wall.) Benth. and Hook.f. = *Markhamia stipulata* (Wall. Seem.	Mahlwa (Burmese); Xi Nan Mao Wei Mu (Chinese)	Flowers eaten in Myanmar	Hedrick (1972), Facciola (1990)
Heterophragma adenophyllum (Wall. Ex G. Don) Seem. Ex Benth. and Hook. f. = *Haplophragma adenophyllum* (Wall. Ex G. Don.) Dop	Karenwood; Khae Khon (Thai)	Flowers, young fruit, slightly bitter, cooked as vegetables	Pongpangan and Poobarasert (1985)
Markhamia stipulata (Wall.) Seem. ex K. Schum.	Khae Hang Kang (Thai)	Flowers, young fruit cooked as vegetables	Pongpangan and Poobarasert (1985)
Millingtonia hortensis L.f.	Indian Cork Tree, Tree Jasmine	Flowers edible	Wongwattanasathien et al. (2010)
Oroxylum indicum (L.) Kurz.	Broken Bones Plant, Indian Trumpet Flower, Midday Marvel, Tree of Damocles; Kotodu,Boongli (Assamese)	In Andhra Pradesh and Assam, the flowers are cooked and eaten as vegetables. In Java, the young leaves, flowers and the bark of the trunk are eaten uncooked with rice usually prepared as 'sambal pepeh'	Ochse and van den Brink (1980), Patiri and Borah (2007), Reddy et al. (2007), Medhi and Borthakur (2012)
Spathodea campanulata Beauv.	African Tulip Tree, Fire Bell	Flowers eaten in Thailand	Wetitayaklung et al. (2008)
Bixaceae			
Cochlospermum fraseri Planch.	Kapok Bush	Flowers eaten in salad	Low (1991)
Boraginaceae			
Anchusa azurea Mill.	Anchusa, Italian Bugloss, Alkanet, Wild Bugloss	Flowers eaten raw, make an excellent and decorative addition to the salad bowl, or used as a garnish	Larkcom (1980), Facciola (1990)
Anchusa capensis Thunb.	Cape Forget-Me-Not	Prized blue flowers eaten in salads, including seafood, fruit, potato, vegetable and tossed green salads, also used in cold drinks, pasta, puddings, custards, icing and hot and cold soups	Kunkel (1984), Facciola (1990)
Anchusa officinalis L.	Alkanet, Common Bugloss, Common Alkanet, Common Anchusa, Alkanet, Bee Bread, Ox's Tongue, Starflower, Common Borage, Orchanet, Spanish Bugloss, Enchusa, Lingua Bovina, Blue Bugloss	Flowers eaten raw. An excellent and decorative addition to the salad bowl, or used as a garnish	Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Borago officinalis L.	Borage, Starflower	Flowers used in vegetable and fruit salads or used to garnish soups or to decorate desserts, cakes and pudding. Flowers impart flavour to summer fruit drinks (punch, compote), beer, cider and wine. Flower petals used to colour vinegar blue. Flowers make an excellent choice for freezing in ice cubes and floating on iced tea. Petals have a cucumber taste and the stamens add a hint of sweetness	Hedrick (1972), Launert (1981), Chiej (1984), Facciola (1990), Garland (1993), Barash (1997), Lauderdale and Evans (1999), Roberts (2000), Newman and O'Connor (2009)
Cordia dichotoma G. Forst.	Fragrant Manjack, Snotty Gobbles, Glue Berry, Pink Pearl, Bird Lime Tree, Indian Cherry, Clammy Cherry	Flowers are eaten	Cribb and Cribb (1987), Tanaka (1976), Facciola (1990)
Cordia myxa L.	Assyrian Plum, Sebasten, Large Sebesten, Lasora (Hindi), Uddhala (Tamil), Sleshmataka (Sanskrit)	Flowers eaten as vegetables	Dalziel (1937), Hedrick (1972), Facciola (1990)
Echium vulgare L.	Blue Devil, Blue Echium, Blue Thistle, Blue Weed, Blueweed, Common Viper's Bugloss, Common Vipersbugloss, Viper's Bugloss	Flowers are candied and added to salads	Deane (2007–2012t)
Mertensia bella Piper	Beautiful Bluebells, Oregon Lungwort	Flowers eaten raw as snacks or added to salad	Schofield (2003)
Mertensia ciliata (James ex Torr.) G. Don	Mountain Bell, Tall Fringed Bluebells, Streamside Bluebells	Flowers used as above	Schofield (2003), Wikipedia (2012)
Mertensia longiflora Greene	Mall Bluebells, Long Bluebells	Flowers used as above	Schofield (2003)
Mertensia maritima (L.) Gray	Oysterleaf, Oysterplant, Sea Bluebells	Flowers used as above	Schofield (2003)
Mertensia oblongifolia (Nutt.) G. Don = *Cerinthodes oblongifolia* (Nutt.) Kuntze	Oblongleaf Bluebells, Sagebrush Bluebells	Flowers used as above	Schofield (2003)
Mertensia paniculata (Aiton) G. Don = *Cerinthodes paniculatum* Kuntze	Tall Lungwort, Tall Bluebell	Flowers used as above	Schofield (2003)
Myosotis sylvatica Ehrh.ex Hoffm.	Forget-Me-Not, Wood Forget-Me-Not	Blossoms are added to salads, used as a garnish, and make excellent candied blossoms	Deane (2007–2012o)
Pentaglottis sempervirens (L.) Tausch.	Evergreen Alkanet, Green Alkanet, Evergreen Bugloss, Alkanet	Flowers edible raw, have a mild flavour and mucilaginous texture and are mainly used as an ornament in fruit drinks and salads	Larkcom (1980), Launert (1981), Facciola (1990)

Brassicaceae			
Alliaria petiolata (M. Bieb.) Cavara and Grande	Garlic Mustard	Flowers eaten raw	Elias and Dykeman (2009)
Arabis alpina L.	Alpine Rock Cress	Flowers eaten raw or cooked and have a cress-like flavour	Tanaka (1976), Kunkel (1984), Facciola (1990), Deane (2007–2012u, x)
Arabis lyrata L. = *Arabidopsis lyrata* (L.) O'Kane and Al-Shehbaz	Kamchatka Rockcress	Buds are used as salad garnish or boiled in water and served with butter and parmesan cheese	Schofield (2003)
Argula sp.	Rocket, Roquette	Light yellow flowers are sprinkled on salads or put afloat in soups to add a bit of pepper	Deane (2007–2012d)
Armoracia rusticana P. Gaertn., B. Mey. and Scherb.	Horseradish	Flowers edible sprinkle onto salad	Deane (2007–2012p)
Barbarea orthoceras Ledeb.	American Yellowrocket, American Wintercress	Flower buds used as salad garnish or boiled and eaten with butter and parmesan cheese	Schofield (2003)
Barbarea vulgaris R. Br.	Bittercress, Yellow Rocketcress	Flowering stems are harvested before the flowers open and cooked like broccoli	Fernald et al. (1958), Facciola (1990)
Brassica alboglabra L.H. Bailey = *Brassica oleracea* (Alboglabra Group); *Brassica oleracea* L. cv. group Chinese Kale	Chinese Kale, Kai Lan	Open and unopened flowers, stalks and shoots eaten	Larkcom (1980), Sagwansupyakorn (1994), Woodward (2000)
Brassica campestris L. = *Brassica rapa* L.	Field Mustard; Hangam (Manipur)	In Northeast India, the flowers are a delicacy; they are used to make a vegetable soup. The flowers are cleaned and boiled without any herbs, not even salt, and the soup is consumed in a mug along with meals. It is slightly bitter	Hauzel (2012)
Brassica carinata A. Braun	Abyssinian Cabbage	Immature flowering stems cooked; used like broccoli	Larkcom (1980), Facciola (1990)
Brassica chinensis L. = *Brassica rapa* L. cv. group Pak Choi	Chinese Cabbage, Pak Choi	Flowers eaten	Larkcom (1980), Tay and Toxopeus (1994)
Brassica cretica Lam. = *Brassica oleracea* var. *botrytis* L., *Brassica oleracea* L. cv. group Cauliflower	Cauliflower	Immature flowering head eaten raw or cooked	Uphof (1968), Simons (1975), Hu (2005), Newman and O'Connor (2009)
Brassica juncea var. *crispifolia* L.H. Bailey = *Brassica juncea* subsp. *juncea*	Curled Mustard	Flowers and young flowering stems eaten raw or cooked	Larkcom (1980)
Brassica juncea var. *foliosa* L.H. Bailey = *Brassica juncea* subsp. *juncea*	Plain-Leaved Mustard; Da Wang Jie (Chinese); Setsuriko (Japanese)	Flowers used as above	Larkcom (1980)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Brassica juncea var. *multiceps* N. Tsen and S.N. Lee = *Brassica juncea* subsp. *juncea*	Nine-Headed Mustard, Red in Snow, Serrated-Leaved Mustard, Multishoot Mustard	Flowers used as above	Larkcom (1980)
Brassica juncea var. *napiformis* (Paillieux & Bois) Kitam = *Brassica juncea* subsp. *juncea*	Turnip-Rooted Mustard	Flowers used as above	Larkcom (1980)
Brassica juncea var. *tumida* N. Tsen and S.N. Lee = *Brassica juncea* L. Czern	Sichuan Pickled Mustard, Sichuan Swollen Stem Mustard, Big Stem Mustard, Yangtze River Mustard	Flowers used as above	Larkcom (1980)
Brassica juncea (L.) Czern.	Brown Mustard	Flowers used as above	Larkcom (1980)
Brassica juncea var. *rugosa* (Roxb.) Kitam. = *Brassica juncea* subsp. *juncea*	Cabbage Leaf Mustard, Heading Leaf Mustard, Broad-Leaved Mustard, Swatow Mustard	Flowers used as above	Larkcom (1980)
Brassica napus L.	Rape, Oilseed Rape	Inflorescences used like broccoli	Uphof (1968), Tanaka (1976), Facciola (1990)
Brassica nigra (L.) K. Koch	Black Mustard	Young flower clusters used like broccoli	Uphof (1968), Grieve (1971), Facciola (1990)
Brassica oleracea (Acephala Group) = *Brassica oleracea* L. cv. group Kale	Kale, Collard, Flowering Kale	Unopened flower clusters called broccolini used like broccoli	Facciola (1990), Kraft and Kraft (1977)
Brassica oleracea (Alboglabra Group) = *Brassica oleracea* L. cv. group Chinese Kale	Chinese Broccoli, Chinese Kale, Kai Lan	Leaves, flowers, flower stalks and young inflorescences steamed, stir-fried, cooked with oyster sauce or used in 'sukiyaki'. Florets cut from stems dipped in tempura batter and deep fried	Herklots (1972), Tanaka (1976), Kraft and Kraft (1977), Facciola (1990), Larkcom (1991), Sagwansupyakorn (1994)
Brassica oleracea (Botrytis Group) = *Brassica oleracea* L. cv. group Cauliflower	Cauliflower; Kobi Yhamchet (Manipur)	Immature flower heads eaten raw in salads, boiled, steamed, braised, fried, used in soups and casseroles and prepared as tempura, etc.; flower stalks make excellent eating, made into soups	Tanaka (1976), Larkcom (1980), Facciola (1990), Van der Vossen (1994), Newman and O'Connor (2009), Yumnum and Tripathi (2012)
Brassica oleracea (Italica Group) = *Brassica oleracea* L. cv. group Broccoli	Broccoli, Cape Broccoli Sprouting Broccoli	Immature flower heads eaten raw in salads, boiled, steamed, sauteed, prepared as tempura, marinated, serve as au gratin or with a cream sauce	Facciola (1990), Van der Vossen (1994), Lauderdale and Evans (1999), Newman and O'Connor (2009)
Brassica oleracea var. *palmifolia* DC. = *Brassica oleracea* (Palmifolia Group)	Jersey Kale	Young flowering shoots eaten raw or cooked	Fern (1992–2003)

Brassica oleracea var. *asparagoides* DC. = *Brassica oleracea* L.	Nine-Star Perennial Broccoli	Flowering shoots used as above	Fern (1992–2003)
Brassica oleracea var. *italica* Plenck = *Brassica oleracea* (Italica Group), *Brassica oleracea* L. cv. group Broccoli	Broccoli, Calabrese; Ye-Hua (Chinese)	As for broccoli	Van der Vossen (1994), Hu (2005), Newman and O'Connor (2009)
Brassica oleracea var. *viridis* L. = *Brassica oleracea* (Viridis Group)	Collards, Cow Cabbage, Kale, Tall Kale, Tree Kale, Fodder Kale	Young flowering shoots eaten raw or cooked	Fern (1992–2003)
Brassica parachinensis Bailey = *B. rapa* L. cv. group Caisin	Caisin, Choi Sum	Young flowering shoots – raw or cooked	Larkcom (1980, 1991), Opeña and Tay (1994)
Brassica pekinensis (Lour.) Rupr. = *Brassica rapa* (Pekinensis Group), *Brassica rapa* L. cv. group Chinese Cabbage	Chinese Cabbage, Celery Cabbage, Peking Cabbage, Petsai	Young flowering shoots eaten raw or cooked	Larkcom (1980), Kuo and Toxopeus (1994)
Brassica perviridis (L.H. Bailey) L.H. Bailey = *Brassica rapa* (Perviridis Group)	Mustard Spinach, Komatsuna	Young flowering shoots eaten raw or cooked	Larkcom (1980, 1991)
Brassica rapa Ruvo Group	Broccoli Raab, Runip Broccoli, Rapini	Flowering stem and leaves pleasantly bitter taste, eaten boiled, steamed, braised, sautéed or served with pasta, potatoes, Italian sausages, etc.	Kraft and Kraft (1977), Halpin (1978), Facciola (1990)
Brassica rapa Sarson Group	Sarson, Toria	Flower cluster used for culinary purposes, flower stalks cooked as vegetables	Tanaka (1976), Facciola (1990)
Brassica rapa var. *parachinensis* (L.H. Bailey.) Hanelt. = *Brassica rapa* (Caisin Group)	Choysum, Caixin, False Pakchoi	Mature inflorescence, flowers and flowering shoots and leaves eaten cooked, steamed or stir-fried	Opeña and Tay (1994)
Brassica rapa L.	Field Mustard, Wild Turnip, Turnip Mustard, Turnip Rape	Immature flower clusters served like broccoli	Crowhurst (1972), Tanaka (1976)
Brassica rapa var. *campestris* (L.) Peterm. = *Brassica rapa* L.	Oil Rape Shoot; Yoi-Cai-Tia (Chinese)	Flowering shoots eaten	Hu (2005)
Brassica rapa var. *nipposinica* L.H. Bailey = *Brassica rapa* (Nipposinica Group)	Potherb Mustard, Mibuna Salad Green, Kyoto Salad Green Japanese Salad Green; Mizuna, Mibuna (Japanese)	Immature flowering shoots and leaves cooked like broccoli	Larkcom (1980, 1991)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Brassica rapa var. *parachinensis* (L.H. Bailey) Hanelt = *Brassica rapa* (Caisin Group)	False Pak Choi, Choysum, Caixin, Caisin	Immature flowering shoots and leaves cooked like broccoli	Larkcom (1980, 1991), Woodward (2000), Hu (2005)
Brassica rapa var. *purpurea* (L.H. Bailey) Kitam. = *Brassica rapa* L.	Red Oil Rape, Purple-Stem Mustard; Hon Tsai Tai (Chinese)	Flowering shoots and leaves eaten	Larkcom (1991), Hu (2005)
Brassica rapa var. *rosularis* (Tsen & Lee) Hanelt = *Brassica rapa* L. subsp. *chinensis* (L.) Hanelt	Flat Cabbage, Flat Pak Choi, Rosette Pakchoi, Spoon Mustard, Tatsoi	Flowering shoots and leaves eaten	Larkcom (1991)
Brassica spp.	Wild Mustard	Flower buds used as salad garnish or boiled and eaten with butter and parmesan cheese	Schofield (2003), Newman and O'Connor (2009)
Bunias orientalis L.	Turkish Warty Cabbage, Turkish Rocket, Hill Mustard	Flower buds and flowering stems eaten raw or cooked	Phillipsand Rix (1998)
Cakile edentula (Bigelow) Hook.	American Sea Rocket	Flower buds combined with milder greens used as potherb	Fernad et al. (1958), Facciola (1990)
Cakile maritima Scop.	Sea Rocket, European Searocket	Leaves, stems, flower buds and immature seedpods eaten raw or cooked	Grieve (1971), Hedrick (1972), Facciola (1990)
Cardamine heptaphylla (Vill.) O.E. Schulz.	Seven-Leaf Toothwort, Pinnate Coral Root	Flowers eaten raw	Fern (1992–2003)
Cardamine hirsuta L.	Hairy Bittercress, Nursery Weed, Common Bitter Cress, Splitting Jenny, Flickweed	Leaves and flowers eaten raw or cooked, mainly used as a garnish or flavouring in salads etc., but are also sometimes used as a potherb	Hedrick (1972), Tanaka (1976), Larkcom (1980), Facciola (1990)
Cardamine kitaibelii Bech.	Kitaibel's Bittercress	Flowers eaten raw	Fern (1992–2003)
Cardamine pentaphyllos (L.) Crantz	Showy Toothwort	Flowers eaten raw	Fern (1992–2003)
Cardamine pratensis L.	Lady's Smock, Cuckoo Flower	Flowers and flower buds with a pungent cress-like flavour eaten raw as a pleasant nibble and also add a delicious flavour to salads	Facciola (1990), Fern (1992–2003)
Cochlearia anglica L.	English Scurvy Grass	Flower heads eaten raw in salads and sandwiches	Facciola (1990)
Crambe maritima L.	Sea Kale	The flowering shoots used like sprouting broccoli; they are quite nice raw and delicious when lightly steamed	Fern (1992–2003)
Crambe orientalis L.	Oriental Sea Kale	Flower stalks prepared like broccoli	Hedrick (1972), Facciola (1990)

Diplotaxis muralis (L.) DC.	Annual Wall Rocket, Stinking Wall-Rocket, Stink-Weed, Cross-Weed, Sand-Rocket, Wall-Mustard	The flowers and the leaves have a spicy, peppery flavour and are delicious added to a salad and rice or sprinkled over cooked French beans. Whole flowers added to 'taramasalata' and serve with brown toast	Anonymous (2012a)
Eruca sativa Mill. = *Eruca vesicaria* (L.) Cav.	Rocket Salad, Arugula, Roquette	Flowers are used as a garnish; the flowers and the leaves have a spicy, peppery flavour and are delicious added to a salad and rice or sprinkled over cooked French beans. Add whole flowers to 'taramasalata' and serve with brown toast	Kraft and Kraft (1977), Halpin (1978), Facciola (1990), Lauderdale and Evans (1999), Newman and O'Connor (2009), Anonymous (2012a)
Eruca vesicaria var. *sativa* (Mill.) Thell. = *Eruca vesicaria* (L.) Cav.	Rocket Arugula	Flowers eaten raw (make a nice garnish on the salad bowl)	Larkcom (1980), Facciola (1990), Lauderdale and Evans (1999)
Eutrema wasabi (Sieb.) Max. = *Eutrema japonicum* (Miq.) Koidz.	Japanese Horse Radish, Wasabi	Flowers soaked in salt water mixed with sake lees to make a popular pickle called 'wasabi-zuke'	Tanaka (1976), Faciola (1990)
Hesperis matronalis L.	Sweet Rocket, Dame's Violet	Flowers add spicy flavour to salads and fruit dishes. It combines well with chicken dishes and many fish recipes. Flowers can also be made into a flavoursome hot tea	Deane (2007–2012n), Anonymous (2012a), McVicar (2003)
Lepidium densiflorum Schrad.	Common Pepperweed, Prairie Peppergrass, Peppercress	Flower buds used as salad, garnish, or boiled and eaten with butter and parmesan cheese	Schofield (2003)
Lobularia maritima (L.) Desv.	Sweet alyssum	Flowers can be used as flavouring herb in salads or other dishes	Facciola (1990), Deane (2007–2012o, x)
Matthiola incana (L.) R.Br.	Stock	Flowers eaten as a vegetable or used as salad, garnish especially with sweet desserts	Tanaka (1976), Facciola (1990)
Peltaria alliacea Jacq.	Garlic Cress	Flowers eaten raw; make a very tasty addition to summer salads	Fern (1992–2003)
Raphanus landra Moretti ex DC. = *Raphanus raphanistrum* subsp. *landra* (Moretti ex DC.) Bonnier and Layens	Radish	Flowers used as above	Fern (1992–2003)
Raphanus maritimus Don = *Raphanus raphanistrum* subsp. *landra* (Moretti ex DC.) Bonnier and Layens	Sea Radish	Flowers used as above	Fern (1992–2003)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Raphanus raphanistrum L.	Wild Radish	Flowers eaten raw, a nice addition to salads. The flower buds are lightly steamed and used as a broccoli substitute	Launert (1981)
Raphanus sativus L.	Radish, European Radish, Jointed Charlock; Lobak (Chinese)	Flower heads eaten as cooked vegetables. Young inflorescences and leaves serve as a vegetable or sepan	Tanaka (1976), Ochse and Van Den Brink (1980), Larkcom (1980), Facciola (1990), Woodward (2000), Newman and O'Connor (2009), Brown (2011)
		Flowers add colour to the top of a salad or sprinkle over cooked vegetables to add a little spice	
Raphanus sativus var. caudatus (L.f) H. Vilm. = *Raphanus sativus* var. *mougri* H.W.J. Helm	Radish (English), Hatsuka Daikon (Japanese) Rat-Tail; Radish Phak Khee Huut (Thai)	In Thailand, inflorescences and young fruits are eaten with 'nam phrik' or cooked in the mixed vegetable curry, 'kaeng kae'. Flowers eaten raw, a nice spicy addition to salads	Uphof (1968), Grieve (1971), Tanaka (1976), Larkcom (1980), Facciola (1990), Jircas (2010), Anonymous (2012a)
Raphanus sativus var. *niger* J. Kern = *Raphanus sativus* var. *sativus*	Oriental Radish	Young flower clusters eaten raw or cooked. Flowers have a spicy flavour with a crisp pleasant texture; they make a nice addition to salads or can be used as a broccoli substitute	Launert (1981), Facciola (1990), Fern (1992–2003)
Raphanus sativus var. *oleiformis* Pers.	Fodder Radish	Flowers used as above	Launert (1981), Facciola (1990), Fern (1992–2003)
Rhynchosinapis wrightii (O.E. Schulz.) Dandy = *Coincya wrightii* (O.E. Schultz) Stace	Lundy Cabbage	Flowers and young flowering stems eaten raw or cooked	Fern (1992–2003)
Sinapis arvensis L.	Charlock, Wild Mustard, Wild Turnip	Young inflorescence and flowering stems—cooked. A pleasant, cabbage/radish flavour, they can be used as a broccoli substitute	Hedrick (1972), Launert (1981), Facciola (1990), Steenbeeke (2001), Komarov (2004)
Sisymbrium irio L.	London Rocket, Londonrocket, Rocket Mustard	Flowers eaten raw in salad	Bailey (1949), Kunkel (1984), Facciola (1990)
Thlaspi arvense L.	Field Pennycress	Flower buds used as salad garnish, or boiled and eaten with butter and parmesan cheese	Schofield (2003)
Bromeliaceae			
Bromelia pinguin	Wild Pineapple, Wild Pine, Pinguin, Bayonette	Fried inflorescence eaten in El Savador	Uphof (1968), Williams (1981), Facciola (1990)
Karatas plumeiri E. Morren = *Bromelia karatas* L.	Karatas, Monkey Banana, Pingouin, Pinguin, Pingwing, Plumier Pingwing, Wild Pin	Young inflorescences cooked or used with eggs	Williams (1981)
Tillandsia erubscens Schlecht.	Flor De Encino	Inflorescences eaten reputed to be sweet	Laferriere et al. (1991)

Tillandsia recurvata L.		Inflorescences eaten	Laferriere et al. (1991)
Burseraceae			
Boswellia serrata Roxb. ex Colebr.	Indian Olibanum Tree, Olibanum, Luban, Gond	In India, flowers and seeds eaten by the Bhils peoples	Watt (1908)
Cactaceae			
Epiphyllum oxypetalum (DC.) Haw.	Dutchman Pipe Cactus, Night Queen, Orchid Cactus, Jungle Cactus, Night Blooming Cereus; Tan Hua (Chinese)	Dried open flowers used for making soups	Hu (2005)
Ferocactus acanthodes (Lem.) Britton and Rose	Barrel Cactus	Flower buds eaten cooked	Clarke (1977), Facciola (1990)
Ferocactus viridescens (Nutt. ex Torr. & A. Gary) Britton and Rose	Coast Barrel Cactus	Flower buds edible	Hedrick (1972), Tate (1976), Facciola (1990)
Ferocactus wislizenii (Engelm.) Britton and Rose	Arizona Barrel Cactus	Flower buds eaten cooked	Hedrick (1972), Tate (1976), Facciola (1990)
Hamatocactus hamatacanthus (Muehlenpf.) F.M. Knuth	Turks Head, Lemon Cactus	Unopened flowers soaked overnight in water and boiled or fried	Tate (1976), Uphof (1968), Facciola (1990)
Hylocereus megalanthus (K. Schum. ex Vaupel) Ralf Bauer	Yellow Pitahaya, Midnight Cactus.	Flowers used as below	Lim (2012a)
Hylocereus polyrhizus (F.A.C. Weber) Britton and Rose = *Hylocereus lemairei* (Hook.) Britton and Rose	Red Pitaya, Red Pitahaya, Dragonfruit, Night Blooming Cereus, Strawberry Pear, Belle Of The Night, Conderella Plant	Unopened flower buds are cooked and eaten as vegetable. The flowers are harvested before anthesis and dried for subsequent use as vegetable in soups	Lim (2012a)
Hylocereus undatus (Haw.) Britton and Rose	Pitahaya, Dragonfruit, Night Blooming Cereus, Strawberry Pear, Belle Of The Night, Conderella Plant; Ba Wang (Chinese)	Flowers used as above vegetable in soups	Morton (1987), Facciola (1990), Hu (2005), Lim (2012a)
Marshallocerues thurberi (Engelm.) Backeb. = *Stenocereus thurberi* subsp. *thurberi*	Organ Pipe Cactus	Petals are eaten in southwestern America	Yanovsky (1936), Tate (1976), Facciola (1990)
Myrtillocactus geometrizans (Mart. ex Pfeiff.) Console	Blue Candle, Whortleberry Cactus, Garambulla Cactus, Garambullo, Bilberry Cactus, Blue Flame, Blue Candle, Blue Myrtle Cactus	Flowers eaten raw in salads or cooked with eggs	Facciola (1990)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Opuntia basilaris Engelm. and J.M. Bigelow	Bakersfield Beavertail, Beavertail, Branching Beavertail, Elongated Beavertail, Kern Beavertail, Short-Joint Beavertail, Trelease Beavertail, Trealease's Beavertail, Woodbury Beavertail	Flowers and flowerbuds eaten cooked	Yanosky (1936), Facciola (1990)
Opuntia ficus-indica (L.) Mill.	Prickly Pear, Indian Fig, Tuna Cactus, Barbary Fig, Cactus Pear, Christian Fig,	Among all the Opuntia, the Prickly Pear Cactus flower is the most often eaten, not raw but cooked, usually boiled. Their flavour leans towards tart. The blossoms also make a good wine	Deane (2007–2012i), Roberts (2000)
Calycanthaceae			
Chimonanthus praecox (L.) Link	Wintersweet, Japanese Allspice; La Mei Hua (Chinese)	In China, the flowers are thoroughly boiled and eaten with oil and salt. The flower petals are used to flavour and scent tea	Read (1946), Tanaka (1976), Kunkel (1984), Facciola (1990)
Campanulaceae			
Campanula alliariifolia Willd.	Cornish Bellflower	Flowers—a pleasant taste and texture with a slight sweetness	Thomas (1977)
Campanula carpatica var. *turbinata* (Schott, Nyman and Kotschy) Nyman = *Campanula carpatica* Jacq.	Carpathian Bellflower, Tussock Bellflower	Flowers—raw or cooked. Slightly sweet, they make a very pleasant and decorative addition to the salad bowl[K]	Fern (1992–2003)
Campanula carpatica Jacq.	Carpathian Bellflower, Tussock Bellflower	Flowers and leaves, flowers used in salads	Fern (1992–2003)
Campanula cochleariifolia Lam	Fairies' Thimbles, Earleaf Bellflower	Flowers added to salad. Flowers eaten raw, added to salad, imparting a pleasant sweetness and a very attractive decoration to a salad	Fern (1992–2003)
Campanula fenestrellata Feer	Adriatic Bellflower	Flowers used as above added to salad	Fern (1992–2003)
Campanula garganica Ten.	Adriatic Bellflower	Flowers used as above	Fern (1992–2003)
Campanula glomerata L.	Crown Of Snow, Snow Crown	Flowers used as above	Fern (1992–2003), Deane (2007–2012q)
Campanula lactiflora M. Bieb.	Milky Bellflower	Flowers used as above	Fern (1992–2003)
Campanula latifolia L.	Giant Campanula, Large Campanula	Flowers used as above	Fern (1992–2003)
Campanula latiloba A. DC. = *Campanula grandis* subsp. *grandis*	Latiloba Campanula, Great Bellflower	Flowers used as above	Fern (1992–2003)
Campanula medium L.	Canterbury Bells, Bellflower	Flowers used as above	Fern (1992–2003)

Campanula persicifolia L.	Peach-Leaved Bellflower, Harebell, Willow Bell	Flowers used as above	Fern (1992–2003)
Campanula portenschlagiana Schult.	Dalmation Bellflower	Flowers used as above	Fern (1992–2003)
Campanula poscharskyana Degen	Serbian Bellflower, Trailing Bellflower	Flowers used as above	Fern (1992–2003)
Campanula punctata Lam.	Spotted Bellflower	Flowers and leaves cooked as potherb. The flowers make a decorative and tasty addition to the salad bowl	Read (1946), Tanaka (1976), Kunkel (1984), Facciola (1990), Fern (1992–2003), Dean (2007–2012q)
Campanula pyramidalis L.	Chimney Bellflower	Flowers eaten raw. A nice decorative addition to salads, the flowers have a pleasant sweet flavour	Fern (1992–2003)
Campanula takesimana Nakai = *Campanula punctata* var. *punctata*	Korean Bellflower	Flowers used as above	Fern (1992–2003)
Campanula versicolor Andrews	Bellflower	Flowers used as above	Fern (1992–2003), Dean (2007–2012q)
Platycodon grandiflorus (Jacq.) A.DC.	Balloon Flower, Japanese Bellflower, Common Balloon Flower	Blossoms sweet, used in salads, stuffed, candied or dipped in butter	Deane (2007–2012o)
Wahlenbergia ceracea Lothian	Alpine Bluebell, Waxy Bluebells	Flowers may be eaten, making a colourful (albeit tasteless) addition to a salad	Harden (1992), Steenbeeke (2001)
Wahlenbergia communis Carolin = *Wahlenbergia capillaris* (Lodd.) G. Don.	Tufted Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia fluminalis (J.M. Black) E. Wimm. ex H. Eichler	River Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia gracilenta Lothian	Annual Bluebell, Hairy Annual Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia gracilis (G. Forst.) A.DC	Australian Bluebell	Flowers edible	Harden (1992), King (2007)
Wahlenbergia graniticola Carolin	Granite Bluebell	Flowers may be eaten, making a colourful (albeit tasteless) addition to a salad	Harden (1992), Steenbeeke (2001)
Wahlenbergia littoricola P.J. Sm.	Coast Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia luteola P.J. Sm.	Bronze Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia multicaulis Benth.	Tadgell's Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia planiflora P.J. Sm.	Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Wahlenbergia queenslandica Carolin ex P.J. Sm.	Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Wahlenbergia sp.	Native Blue Bells	Flowers used in salads	Cribb and Cribb (1987), Low (1991), Symmons and Symmons (1994)
Wahlenbergia stricta (R.Br.) Sweet	Austral Bluebell, Tall Bluebell, Austral Bluebell	The flowers of Wahlenbergia may be eaten, making a colourful (albeit tasteless) addition to a salad	Harden (1992), Steenbeeke (2001)
Wahlenbergia tumidifructa P.J. Sm.	Mallee Annual-Bluebell	Flowers used as above	Harden (1992), Steenbeeke (2001)
Cannabaceae			
Humulus lupulus L.	Hops, Common Hop; Pi-Jua-Hua (Chinese)	Pistillate inflorescence used for flavouring beer; buds eaten; dried flower heads used to flavour beer and liquor also used to leaven bread, used in tea, used in aperitif	Garland (1993), Hu (2005)
Capparaceae			
Boscia albitrunca (Burch.) Gilg and Benedict	Shepherd's Tree, Witgatboom, Matoppie	Flower buds pickled and used as caper substitute	Uphof (1968), Fox et al. (1982), Facciola (1990)
Capparis arborea (F. Muell.) Maiden	Native Pomegranate, Wild Lime, Wild Lemon, Brush Caper Berry	Edible flower buds pickled	Cribb and Cribb (1987), Low (1991), Symmons and Symmons (1994)
Capparis decidua (Forssk.) Edgew.	Caper, Karil; Kursan, Murkheit, Sodad, Tundub (Arabic); Meringa (Somali)	Flower bud eaten as potherb or pickled in India, Floral nectar also eaten in Rajasthan, India	Hedrick (1972), Bhandari (1974), Tanaka (1976), Saxena (1979), Facciola (1990)
Capparis ovata Desf. = *Capparis spinosa* L.	Caper, Caper Berry, Caper Bush	Flower buds can be pickled and used like capers	Kunkle (1984), Facciola (1990)
Capparis sarmentosa A. Cunn. ex Benth.	Climbing Caper	Edible flower buds pickled	Cribb and Cribb (1987), Low (1991), Symmons and Symmons (1994)
Capparis sepiaria L.	Indian Capers, Wild Caper Bush, Hedge Caper Bush	Flower buds can be pickled and used like capers	Tanaka (1976), Facciola (1990)
Capparis spinosa L.	Caper, Caper Berry, Caper Bush	Flower buds pickled and used to flavour sauces, butter, salads, stuffing, fish, meat, cheese and hors d'oeuvres	Hedrick (1972), Facciola (1990)
Capparis spinosa L. *var.mariana* (Jacq.) K. Schumann = *Capparis mariana* Jacq.	Caper, Caper Berry, Caper Bush	Pickled flower buds used to complement salty or oily foods, olives, salted meat and fish and to flavour casseroles	Garland (1993), Ong and Siemonsma (1999)
Capparis velutina P.I. Forst.	Kin Kin Scrub, Native Pomegranate	Edible flower buds pickled	Cribb and Cribb (1987), Low (1991), Symmons and Symmons (1994)

Crateva adansonii DC.	Garlic Pear Tree, Three-Leaf Caper, Obtuse Leaf Crateva; Kumbok (Thai)	Flowers consumed as food	Wetitayaklung et al. (2008)
Crateva magna (Lour.) DC. = *Crateva religiosa* G. Forst.	Spider Tree, Sacred Garlic Pear, Three-Leaved Caper; Kum Nam (Thai)	Flowers consumed as food	Wetitayaklung et al. (2008)
Crateva religiosa G. Forst.	Spider Tree, Sacred Garlic Pear, Three-Leaved Caper; Kum Nam (Thai)	In Myanmar, the flowers are pickled and eaten for their digestive action	Hedrick (1972), Uphof (1968), Tanaka (1976), Facciola (1990)
Caprifoliaceae			
Centranthus macrosiphon Boiss	Long-Spurred Valerian, Pretty Betsy, Spur Valerian	Flowers eaten raw	Tanaka (1976)
Lonicera affinis Hook. and Arn.	Wild Honeysuckle, Coastal Honeysuckle; Hama-Nindou (Japanese)	Flowers used as a flavouring in drinks	Kunkel (1984)
Lonicera caprifolium L.	Goat-Leaf Honeysuckle, Italian Honeysuckle, Perfoliate Honeysuckle, Pefoliate Woodbine	Flowers eaten	McVicar (2003)
Lonicera henryi Hemsley = *Lonicera acuminata* var. *acuminata*	Central China Honeysuckle; Xi Ye Ren Dong (Chinese)	Flowering shoots and flowers used for tea	Tanaka (1976), Facciola (1990), Hu (2005)
Lonicera japonica Thunb.	Japanese Honeysuckle; Jin Yin Hua, Er Hua, Shuang Hua (Chinese); Suikazura (Japanese)	Flower and buds used as ingredient in five-flower tea 'wu-hua cha' use in wine in China and beverage in Japan. The petals have also been used for making sorbet dessert. Flowers sucked for their sweet nectar and used as vegetable or made into syrup and puddings	Crowhurst (1972), Tanaka (1976), Facciola (1990), Barash (1997), Lauderdale and Evans (1999), Roberts (2000), Hu (2005)
Patrinia scabiosifolia Fisch. ex Trevir.	Yellow Patrinia, Golden Lace; Omina-Eshi (Japanese)	Flower buds eaten steamed, fried, oil-roasted, preserved, in soups, or parboiled and dried for later use	Tanaka (1976), Facciola (1990)
Patrinia villosa (Thunb.) Juss.	Patrinia; Bai Jiang Cao (Chinese), Otoko-Eshi (Japanese)	Flower buds eaten, fried, preserved or as potherb	Tanaka (1976), Facciola (1990)
Sambucus australasica (Lindl.) Fritsch	Yellow Elderberry	Flowers eaten raw or cooked	Cribb and Cribb (1987), Low (1991)
Valeriana officinalis L.	Valerian, Garden Valerian, Valerian Root	Flowers edible	McVicar (2003)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Valerianella locusta (L.) Laterr.	Corn Salad, Lamb's Lettuce, Lewiston Cornsalad	Inconspicuous flowers edible and flowering stems eaten raw	Larkcom (1980), Facciola (1990)
Caricaceae			
Carica papaya L.	Papaya	Inflorescence and flowers steamed, eaten with rice or added to soups and stews. In Indonesia, flowers are candied	Ochse and van den Brink (1980), Facciola (1990), Lim (2012a)
Caryophyllaceae			
Dianthus barbatus L.	Sweet William	The flowers can be crystallized. They have a mild flavour and are used as a garnish for vegetable and in fruit salads, cakes, desserts, cold drinks, lemonades butter and lemonade. The petals of Sweet Williams will add zest to ice cream, sorbets, salads, fruit salad, dessert sauces, seafood and stir-fries. It is advisable to remove the white heel at the base of the petal as this has a bitter taste	Facciola (1990), Lauderdale and Evans (1999), Anonymous (2012a)
Dianthus caryophyllus L.	Carnation, Pinks, Chinese Pink, Clove Pink	Flowers can be crystallized. The flower petals have a strong smell of cloves and are candied, used as a garnish in salads, for flavouring fruit, fruit salads, butter, lemonade, etc. They can also be used as a substitute for rose petals in making syrup. Petals preserved in sugar, syrup or vinegar and added to cordial, used to flavour food and drink, wine, tea, marmalade and sorbet. The petals should be removed from the calyx and their bitter white base should be removed	Morton (1976), Facciola (1990), Garland (1993), Barash (1997), Lauderdale and Evans (1999), Anonymous (2012a), Rop et al. (2012)
Dianthus chinensis L.	Dianthus, Pinks, Chinese Pinks	Most dianthus have a pleasant spicy, floral, clove-like taste, especially the more fragrant varieties, and are ideal for decorating or adding to cakes. They also make a colourful garnish to soups, salads and the punch bowl	Lauderdale and Evans (1999), Anonymous (2012a)
Dianthus deltoides L.	Maiden Pinks	Flowers used as above	Barash (1997), Lauderdale and Evans (1999), Anonymous (2012a)
Dianthus plumarius L.	Pink, Modern Border Pink	The petals are used in making cordials, syrups, sauces, salads, vinegars, lemonade and butter. They can be crystallized and used as garnish. Children suck the flowers for their sweet edible nectar	Tanaka (1976), Kunkel (1984), Facciola (1990), Anonymous (2012a)

Dianthus spp.	Carantions, Pinks	Flowers used as above	Lauderdale and Evans (1999), Newman and O'Connor (2009)
Dianthus superbus L.	Fringed Pink	Children suck the flowers for their sweet edible nectar	Tanaka (1976), Kunkel (1984), Facciola (1990), Lauderdale and Evans (1999), Anonymous (2012a)
Paronychia argentea Lam.	Algerian Tea, Silver Nailroot, Silvery Whitlow Wort	Infusion of flower used as tea	Uphof (1968), Facciola (1990)
Paronychia capitata (L.) Lam.	Algerian Tea, Whitlow Wort	Flowers used as substitute for tea	Uphof (1968), Facciola (1990)
Petrorhagia prolifera (L.) P.W. Ball and Heywood	Childing Pink, Proliferous Pink	Flowers used as tea	Uphof (1968), Facciola (1990)
Stellaria media (L.) Vill.	Chickweed, Five-Petaled Chickweed, Chickenwort, Craches, Maruns, Winterweed	Flowering top used as vegetable or garnish	Cribb and Cribb (1987), Clarke (1977), Facciola (1990)
Celastraceae			
Celastrus dependens Wall. = *Celastrus paniculatus* subsp. *multiflorus* (Roxb.) D. Hou.	Black Ipecac, Black Oil Plant, Black Oil Tree, Celastrus Dependens, Climbing Staff Plant, Climbing Staff Tree, Dhimarbel, Intellect Tree	The young flowers are used as a vegetable	Facciola (1990)
Celastrus paniculatus Willd.	Shrubby Bittersweet, Black Ipecac, Black Oil Plant, Black Oil Tree, Celastrus Dependens, Climbing Staff Plant, Climbing Staff Tree, Dhimarbel, Intellect Tree	Young flowers used as vegetable	Kunkel (1984)
Cleomaceae			
Cleome gynandra L.	African Spider Flower, Spider Flower, Shone Cabbage; Phak Sian (Thai)	Young shoots and young inflorescences are fermented in salt water and served with 'nam phrik'. The leaves are also eaten in soup with spareribs	Jircas (2010)
Cleome integrifolia Torr. and A. Gray = *Cleome serrulata* Pursh.	Rocky Mountain Beeplant, Bee Spider-Flower	Flowers boiled, eaten as potherb	Uphof (1968), Harrington (1974), Facciola (1990)
Cleome monophylla L.	Single-Leaved Cleome	Flowers eaten	Fox et al. (1982), Facciola (1990)
Cleome serrulata Pursh	Rocky Mountain Beeplant, Bee Spider-Flower	Young shoots, leaves and flowers are cooked and used as potherbs. Flowers used in New Mexico and Arizona	Yanovsky (1936), Uphof (1968), Tanaka (1976), Facciola (1990)
Clusiaceae			

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Mammea americana L.	Mammee Apple, Mamey	A liqueur called 'Eau de Créole', or 'Crème de Créole', is distilled from the fragrant white flowers	Morton (1987), Facciola (1990)
Mesua ferrea L.	Ceylon Ironwood, Indian Rose Chestnut, Cobra's Saffron, Mesua	Flowers eaten	Wessapan et al. (2007), Wetitayaklung et al. (2008)
Combretaceae			
Combretum grandiflorum G. Don	Ohwiremnini (Ghana – Akan-Asante); Fu Yayos (Gambia—Diola)	Flowers sucked for the nectar	Dalziel (1937), Facciola (1990)
Combretum paniculatum Vent.	Burning Bush, Forest Flame-Creeper (English); Bambagwena, Mupfurura (Zimbabwe—Shona)	Flowers sucked for the nectar	Dalziel (1937), Facciola (1990)
Combretum platypterum (Welw.) ex M.A. Lawson	Kyeramoa, O-Hwirɛmo Σpaka (Ghana—Akan—Asante)	Flowers sucked for the nectar	Dalziel (1937), Facciola (1990)
Quisqualis indica L. = *Combretum imdicum* (L.) DeFilipps	Chinese Honeysuckle, Drunken Sailor, Quisqualis, Rangoon Creeper, Red Jasmine	Flowers eaten in Thailand	Wetitayaklung et al. (2008)
Commelinaceae			
Commelina africana L.	Yellow Commelina	Flowers eaten cooked	Deane (2007–2012n)
Commelina communis L.	Asiatic Dayflower	Leaves, flowers and young shoots eaten raw or cooked	Hedrick (1972), Tanaka (1976), Facciola (1990)
Commelina cyanea R.Br.	Native Wandering Jew, Wandering Sailor, Scurvy Weed	Flowers edible	King (2007)
Rhoeo spathacea Sw = *Tradescantia spathacea* Sw.	Oyster Plant, Moses-in-the-Cradle, Boat Lily, Moses-in-a-Boat; Bang Hua (Chinese)	Leafy shoots and flowers eaten in China	Hu (2005)
Tradescantia virginiana L.	Spiderwort, Indian Paint, Moses in the Bulrushes	Flowers eaten raw. They make an attractive edible garnish and can be made into candy	Fernald et al. (1958), Peterson (1977), Facciola (1990)
Convolvulaceae			
Calonyction aculeatum (L. House) = *Ipomea alba* L.	Moonflower, Moonlight Flower, Prickly Ipomoea, Giant Moon Flower; Yue Guang Hua (Chinese); Terulak (Indonesian)	Leafy shoots and fleshy sepals eaten as potherb, dried flowers used for soup and also in pastries in Yunnan. In Indonesia, flowers used fresh or dried in 'kimlo' (a vegetable soup)	Ochse and van den Brink (1980), Hu (2005), Ng (2011)
Calonyction album (L. House) = *Ipomea alba* L.	Moonflower, Moonlight Flower, Prickly Ipomoea, Giant Moon Flower; Yue Guang Hua (Chinese); Terulak (Indonesian)	As above	Burkill (1966), Martin and Ruberté (1975), Ochse and van den Brink (1980), Facciola (1990), Ng (2011)

Ipomoea alba L.	Moonflower, Moonlight Flower, Prickly Ipomoea, Giant Moon Flower; Yue Guang Hua (Chinese); Terulak (Indonesian)	As above	Hu (2005), Ng (2011)
Costaceae			
Cheilocostus speciosus (J. Koenig) C.D. Specht	Cane-Reed, Crape Ginger, Crepe Ginger, Elegant Costus, Malay Ginger, Spiral Flag, Spiral Ginger, Wild Ginger	Flowers edible in salad or as garnish	Carle (1995), Chan (1998)
Costus barbatus Suess.	Spiral Ginger, Red Tower Ginger	Flowers used as above	Carle (1995), King (2007)
Costus erythrophyllus Loes.	Blood Red Spiral Costus, Oxblood Ginger, Violet Spiral Flag	Flowers used as above	Carle (1995), King (2007)
Costus productus Gleason ex Maas	Costus Ginger, Dwarf Orange Ginger, Orange Tulip Ginger, Spiral Ginger	Flowers used as above	Carle (1995), Campbell (2006), NTBG (2013)
Costus spp.	Spiral Gingers	Many species, each with distinct citrus flavours—added to salads	Carle (1995), King (2007)
Cucurbitaceae			
Benincasa hispida (Thunberg ex Murray) Cogniaux cv-group Fuzzy Gourd Group	Fuzzy Gourd, Fuzzy Melon, Hairy Gourd, Hairy Melon	Young leaves and flower buds are steamed and eaten as a vegetable or are added as a flavouring to soups. Young shoots, flowers and fruits are consumed as vegetable in various parts of Thailand and Indonesia	Facciola (1990), Huxley et al. (1992), Jircas (2010), Lim (2012b)
Benincasa hispida (Thunberg ex Murray) Cogniaux cv-group Wax Gourd Group	Wax Gourd, Chinese Winter Melon, Wax Gourd; Fak, Fang (Thai)	As above	Jircas (2010), Lim (2012b)
Benincasa hispida Thunb.	Hairy Melon, Hairy Wax Gourd	Flowers, fruits and leaves relished as vegetables	Ochse and Bakhuizen van den Brink (1980), Facciola (1990), Woodward (2000), Lim (2012b)
Cucurbita argyrosperma C. Huber.	Cushaw, Green-Stripe Cushaw, Japanese Pie Pumpkin, White Cushaw, Silver Seed Gourd,	Flowers eaten cooked	Facciola (1990)
Cucurbita filicifolia Bouché	Siam Pumpkin, Thin Vermicelli Pumpkin, Asian Pumpkin, Fig Leaf Gourd, Pie Melon, Malabar Gourd, Thai Marrow	Flowers are eaten	Widjaja and Sukprakarn (1994), Lim (2012b)
Cucurbita foetidissima Kunth	Buffalo Gourd	Flowers said to be edible after preparation	Facciola (1990)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Cucurbita maxima Duchesne ex Lam.	Squash, Pumpkin, Buttercup Squash	Flowers, fruits and leaves relished as vegetables	Widjaja and Sukprakarn (1994), Newman and O'Connor (2009), Lim (2012b)
Cucurbita mixta Pangalo = *Cucurbita argyrosperma* Huber.	Cushaw Pumpkin, Squash	Flowers edible	Widjaja and Sukprakarn (1994)
Cucurbita moschata (Duchesne ex Lam.) Duchesne ex Poiret	Squash, Pumpkin, Butternut Squash, Long Island Cheese Pumpkin; Fak Thong (Thai), Kabocha (Japanese)	Young leaves unopened flower Mature fruit is commonly used as ingredient of various kinds of spicy vegetable soups. Young shoots, flowers and fruits are also eaten	Herklots (1972), Ochse and van den Brink (1980), Facciola (1990), Widjaja and Sukprakarn (1994), Newman and O'Connor (2009), Jircas (2010), Lim (2012b)
Cucurbita pepo L.	Squash, Gourd, Pumpkin, Vegetable Marrow, Zucchini, Calabashes, Acorn Squash, Summer Pumkin, Autumn Pumpkin	Flowers, fruits and leaves relished as vegetables	Widjaja and Sukprakarn (1994), Barash (1997), Lauderdale and Evans (1999), Newman and O'Connor (2009), Lim (2012b)
Cucurbita spp.	Pumpkin, Squash, Vegetable Marrow, Zucchini, Calabashes, Acorn Squash	Flowers used in desserts and puddings	Barash (1997), Newman and O'Connor (2009), Dean (2007–2012a)
Lagenaria siceraria (Molina) Standley	Bottle Gourd, Calabash Gourd	Young tender fruits, young shoots, leaves and flower buds of non-bitter varieties eaten as vegetables in Asia and Africa	Lim (2012b)
Luffa aegyptiaca P. Miller	Bath Sponge, Smooth Luffa, Dish Cloth Gourd, Sponge Gourd	Flowers, buds, young fruits and leaves relished as vegetables	Lim (2012b)
Luffa acutangula (L.) Roxb.	Angled Luffa	Flowers, buds, young fruits and leaves relished as vegetables	Herklots (1972), Facciola (1990), Jansen et al. (1994), Woodward (2000), Lim (2012b)
Luffa cylindrica (L.) M. Roem. = *Luffa aegyptiaca* P. Miller	Bath Sponge, Smooth Luffa, Dish Cloth Gourd, Sponge Gourd	Flowers, buds, young fruits and leaves relished as vegetables	Herklots (1972), Ochse and van den Brink (1980), Facciola (1990), Jansen et al. (1994), Lim (2012b)
Momordica charantia	Bitter Gourd, Bitter Melon	Fragrant yellow blossoms can be used for flavouring	Reyes et al. (1994), Lim (2012a, b)
Momordica cochinchinensis Loureiro	Giant Spine Gourd (English), Nanban Kikarasuuri (Japanese), Fak Khao (Thai), Gac (Vietnamese)	In Thailand, young fruits, shoots and flowers are ingredient of curry. After boiling, they are eaten with chilli sauces and rice. Young shoots are fried with oyster sauce with pork or shrimp	Jircas (2010), Lim (2012b)

Cycadaceae			
Cycas siamensis Miq.	Silver Cycas, Thai Silver Cycas; Prong (Thai)	Core of young conical flower bud eaten after prolonged cooking	Pongpangan and Poobarasert (1985)
Cyperaceae			
Scirpus lacustris L. = *Schoenoplectus lacustris* (L.) Palla.	Great Bulrush	Pollen mixed with meal for making bread	Harrington (1974), Facciola (1990)
Scirpus paludosus A. Nelson = *Bolboschoenus maritimus* subsp. *paludosus* (A. Nelson) T. Koyama	Alkali Bulrush	Pollen mixed with meal for making bread by Indian tribes	Fernand et al. (1958), Upholf (1968), Facciola (1990)
Scirpus validus Vahl = *Schoenoplectus tabernaemontani* (C.C. Gmel.) Palla	Tall Bulrush, Great American Bulrush	Pollen used in soups and bread	Fernand et al. (1958), Tanaka (1976), Facciola (1990)
Dilleniaceae			
Dillenia indica L.	Chulta, Dillenia, Elephant-Apple, Hondapare Tree, Indian Catmon; San Plao, Matad (Thai)	In India (Deccan and Garhwal Himalayas) innermost sepals used to flavour food and eaten. A syrup is made from the flower sepals	Pongpangan and Poobrasert (1985), Watt (1908), Patiri and Borah (2007), Lim (2012b)
Dillenia pentagyna Roxb.	Karmal, Dog Teak, Dillenia, Nepali Elephant Apple; Agachi (Garo); Dieng Soh Karbam (Khasi)	Flowers India (Bombay Presidency): flowers especially the fleshy calyces and fruits eaten as vegetable in Assam. Flower buds have a pleasant acid flavour, eaten raw or cooked in Oudh and Central India	Gamie (1902), Seal, (2012), Patiri and Borah (2007)
Dillenia philippinensis Rolfe	Philippine Catmon, Philippine Dillenia	Flowers used as flavouring for sour fish soup	Lim (2012b)
Dillenia serrata Thunb.	Dengen, Dongi Bolusu, Songi (Borneo)	Yellow carpels eaten	Lim (2012b)
Dioscoreaceae			
Dioscorea pentaphylla L.	Five-Leaved Yam	Flowers eaten in the Deccan, India	Watt (1908)
Dipterocarpaceae			
Dipterocarpus obtusifolius Teijsm. ex Miq.	Hiang (Thai); Mai Xat (Laotian)	Flowers sour, edible raw	Pongpangan and Poobarasert (1985)
Shorea talura Roxb.	Lac Tree, Lac Tree Of South India; Payom (Thai)	Flowers eaten cooked	Pongpangan and Poobarasert (1985)
Doryanthaceae			
Doryanthes excelsa Corrêa	Gymea Lily, Flame Lily	Flower stalk, young flower heads were eaten after steaming as a traditional aboriginal food	Low (1989), Kapitany (2012)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Ericaceae			
Acrotriche attenuata F. Muell.	Trailing Ground-Berry	Abundant flower nectar sucked by children	Cribb and Cribb (1987)
Acrotriche prostrata	Trailing Ground-Berry	Abundant flower nectar sucked by children	Cribb and Cribb (1987)
Acrotriche serrulata (Labill.) R.Br.	Honeypots, Heath	Tiny flowers eaten	Low (1989)
Agapetes variegata (Roxb.) D. Don ex G. Don	Agapetes	Flowers cooked eaten with rice in India	Altschul (1973), Facciola (1990)
Arctostaphylos glauca Lindl.	Bigberry Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Arctostaphylos manzanita Parry	Common Manzanita, Whiteleaf Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Arctostaphylos nevadensis A. Gray	Pinemat Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Arctostaphylos parryana Lemmon	Parry Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Arctostaphylos patula Greene	Greenleaf Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Arctostaphylos pungens Kunth	Pointleaf Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Arctostaphylos tomentosa (Pursh.) Lindl.	Downy Manzanita	Blossom eaten as nibbles	Deane (2007–2012q)
Azalea indica L.	Pink Azalea	Flowers edible	Tanaka (1976)
Azalea oldhamii (Maxim.) Mast. = *Rhododendron oldhamii* Maxim.	Rhodendron, Azalea	Flower petals sometimes eaten	Tanaka (1976)
Calluna vulgaris (L.) Hull	Common Heather, Heather	Dried flower heads made a good tea	Hedrick (1972), Facciola (1990)
Erica cerinthoides L.	Fire Erica, Fire Heath, Red Hairy Heath	Flowers sucked for nectar	Kunkel (1984)
Gaultheria appressa A.W. Hill	White Waxberry	The swollen calyx of the flower is succulent, surrounding the seed at maturity. It is somewhat bitter and has little to recommend it as a food	Harden (1992), Steenbeeke (2001)
Gaultheria viridicarpa I. Telfor and J.B. Williams	Waxberry	As above	Harden (1992), Steenbeeke (2001)
Ledum columbianum Piper = *Rhododendron columbianum* (Piper) Harmaja.	Pacific Labrador Tea	Light delicate beverage made by boiling over leaves and or flowers	Schofield (2003)
Ledum glandulosum Nutt.	Western Labrador Tea	As above	Schofield (2003)
Ledum palustre ssp. *decumbens* (Aiton) Hultén = *Ledum palustre* var. *decumbens* Aiton	Labrador Tea	As above	Schofield (2003)

Ledum palustre ssp. *groenlandicum* (Oeder) Hultén = *Rhododendron groenlandicum* (Oeder) Kron and Judd.	Labrador Tea	As above	Schofield (2003)
Melichrus procumbens (Cav.) Druce	Honeypot, Jam-Pot Jam-Tart Heath	Small blossoms make sweet tea and have an abundant nectar	Cribb and Cribb (1987), Low (1989)
Melichrus urceolatus R.Br.	Urn-Heath	Abundant nectar	Cribb and Cribb (1987)
Rhododendron arboreum Sm	Red Rhodendron; Lali Gurans (Nepali); Burans (Garhwali); Eras (Kumaoni); Adrawal (Punjabi); Billi (Tamil); Pu (Kannada); Kattupoo Varasu (Malayalam)	The fresh and dried flowers have a sweet and sour taste and are used in the preparation of squash, jams, jellies and local pleasant brew drank daily as refreshing appetizer and also to prevent high-altitude sickness. Fresh petals are used to prepare a chutney known as 'barah ki chutney'	Gupta (1962), Hedrick (1972), Tanaka (1976), Pradhan and Lachungpa (1990), Facciola (1990), Namrata et al. (2011), Srivastava (2012)
Rhododendron indicum (L.) Sweet	Rhododendron, Southern Indica Hybrid Azaleas; Otakumi Tutuji (Japanese)	Flowers eaten raw or cooked	Tanaka (1976), Kunkel (1984), Facciola (1990)
Rhododendron kaempferi Planch.	Torch Azalea, Kaempferi Azalea	Flowers eaten raw or cooked	Tanaka (1976), Kunkel (1984), Facciola (1990)
Rhododendron lapponicum (L.) Wahlenb.	Lapland Rosebay	Flower tops used as substitute for tea	Hedrick (1972)
Rhododendron mucronulatum Turcz.	Korean Rhodendron; Ying Hong Du Juan (Chinese); Jindallae (Korean)	Flower petals used in Hwajeon flower glutinous rice cake	Tanaka (1976), Wikipedia (2012)
Richea scoparia Hooker f.	Scoparia, Alpine Richea	Flowers sucked for nectar	Schaeffer and Fletcher (2012)
Styphelia sp.	Five Corners	Flower sucked for nectar	Low (1989)
Vaccinium myrtilloides Michx.	Bilberry, Bulberry, Whortleberry, Huckleberry, Hurtleberry, Blueberry, Trackleberry, Whinberry, Bleaberry, Airelle, Fraughan	The flowers can be eaten raw or used to make preserves	Moerman (1998)
Vaccinium vacciniaceum (Roxb.) Sleumer.	Tu Guan Xiao Lun Ye Yue Ju (Chinese)	The acid-tasting flowers are used in curries	Kunkel (1984)
Epigaea repens L.	Mayflower, Trailing Arbutus	Flowers have a spicy slightly acid flavour; they are eaten as a wayside nibble or are added to salads as a thirst quencher	Tanaka (1976), Kunkel (1984), Facciola (1990)
Euphorbiaceae			
Chrozophora plicata (Vahl) A. Juss. ex Spreng.	Giradol	Petals provide a red and blue dye used for colouring liqueurs, wine, pastries and Dutch cheeses	Uphof (1968), Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Croton corymbulosus Engelm. = *Croton pottsii* var. *pottsii* (Klotzsch) Müll. Arg.	Leatherweed	Infusion of flowering tops used as beverage in Texas	Yanovsky (1936)
Euphorbia hirta L.	Common Spurge, Asthma Weed, Hairy Spurge, Garden Spurge; Pakhang Leiton (Manipur)	Young shoots and inflorescences eaten	Yumnum and Tripathi, (2012)
Euphorbia pulcherrima Willd. ex Klotzsch	Poinsettia, Christmas Star, Christmas Flower, Painted Leaf, Lobster Plant, Mexican Flameleaf, Crown of the Andes	Young shoot, inflorescence and leaves steamed or stewed	Ochse and van den Brink (1980)
Euphorbia tetragona Haw.	Naboom	Flowers rich in nectar sometimes used n confectionary	Facciola (1990)
Ricinus communis L.	African Coffee Tree, Castor, Castor Bean, Castor Oil, Castor Oil Plant	Young inflorescences boiled	Uphof (1968), Hedrick (1972), Facciola (1990)
Fabaceae			
Acacia aneura F. Muell. ex Benth.	Mulga Acacia	Flowers cooked, often in fritters	Cribb and Cribb (1987)
Acacia concinna (Willd.) DC.	Soap Pod	Flowers used as vegetable	Hedrick (1972), Altschul (1973), Facciola (1990)
Acacia coriacea DC.	Wiry Wattle, Wire Wood	Flowers edible	Wikipedia (2012)
Acacia cultriformis A. Cunn. ex G. Don.	Knife-Leaf Wattle	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia dealbata Link	Mimosa	Flowers used as above	Cribb and Cribb (1987)
Acacia decurrens Willd.	Acacia Bark, Early Black Wattle, Green Wattle, Sydney Wattle, Wattle Bark, Tan Wattle, Golden Teak, Brazilian Teak	Flowers used as above	Cribb and Cribb (1987)
Acacia farnesiana (L.) Willd.	Farnese Wattle, Mimosa Wattle, Cassie Flower	Flowers edible	Stangland (2004), McCullough (2007), Department of the Army (2009)
Acacia longifolia (Andrews) Willd.	Long-Leaved Wattle, Acacia Trinervis, Aroma Doble, Golden Wattle, Coast Wattle, Sallow Wattle, Sydney Golden Wattle	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia macradenia Benth.	Zig-Zag Wattle	Flowers edible	King (2007)
Acacia melanoxylon R.Br.	Blackwood, Hickory, Sally Wattle, Tasmanian Blackwood, Mudgerabah	Flowers cooked, often used in fritters	Cribb and Cribb (1987)

Acacia mucronata Wendl.	Narrow-Leaf Wattle	Flowers used as above	Cribb and Cribb (1987), Fern (1992–2003)
Acacia nilotica (L.) Delile	Egyptian Mimosa, Egyptian Thorn	Flowers used as above	MacNicol (1967), Tanaka (1976), Facciola (1990)
Acacia oshanesii F. Muell. and Maiden	Irish Wattle	Wattle flowers steeped in liqueur, coated with sugar and batter before deep frying	Deane (2007–2012w)
Acacia paradoxa DC.	Kangaroo Thorn, Prickly Wattle, Hedge Wattle, Paradox Acacia	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia podalyriifolia Cunn. ex Don	Silver Wattle, Mt Morgan Wattle	Wattle flowers steeped in liqueur, coated with sugar and batter before deep frying	Cribb and Cribb (1987), Facciola (1990), Deane (2007–2012w)
Acacia pycnantha Benth.	Golden Wattle Broad-Leaved Wattle, Witch	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia retinodes Schldl.	Retinodes Water Wattle, Swamp Wattle, Wirilda, Ever-Blooming Wattle, Silver Wattle	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia saligna (Labill.) H.L. Wendl.	Coojong, Golden-Wreath Wattle, Orange Wattle, Blue-Leafed Wattle, Port Jackson Willow	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia sophorae (Labill.) R.Br.	Boobyalla, Coast Wattle, Coastal Wattle, False Boobyalla, Sallow Wattle	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Acacia spectabilis A. Cunn. ex Benth.	Mudgee Wattle, Glory Wattle, Pilliga Wattle, Golden Wattle	Wattle flowers steeped in liqueur, coated with sugar and batter before deep frying or mixed into the batter of pikelets and pancakes	Cribb and Cribb (1987), Facciola (1990), Deane (2007–2012w)
Acacia verticillata (L'Hér.) Willd.	Prickly Moses, Prickly Mimosa	Flowers cooked, often used in fritters	Cribb and Cribb (1987)
Aeschynomene aspera L.	Sola, Sola Pith Plant, Pith Plant; Chigonglei (Manipur)	Flowers used extensively in cooking during Cheiraoba, the New Year of the Meitei community in Manipur, India	Hauzel (2012)
Albizia julibrissin Durazz	Mimosa, Persian Silk Tree, Pink Siris, Lenkortan Acacia, Bastard Tamarind	Flowers eaten as a cooked vegetable or crystallized	Kunkel (1984), Facciola (1990)
Arachis pintoi Krapov. and W.C. Gregory	Pinto Peanut, Perennial Peanut, Golden Glory	Yellow flowers are edible	Wallace (2009)
Astragalus multiceps Benth.	Kandiara	The calyx of the flower is eaten and has a sweetish flavour	Kunkel (1984)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Bauhinia acuminata L.	Dwarf White Bauhinia, White Orchid-Tree, Snowy Orchid-Tree; Mati Kotora (Assamese)	Flowers eaten fried in Assam	Patiri and Borah (2007)
Bauhinia carronii F. Muell.	Queensland Ebony, Northern Beantree	Aborigines sucked copious nectar from the white flowers	Cribb and Cribb (1987), Facciola (1990)
Bauhinia hookeri F. Muell.	White Bauhinia, Bauhinia, Pegunny, Mountain Ebony, Queensland Ebony, Hooker's Bauhinia	Copious nectar sucked from the flowers	Cribb and Cribb (1987), Facciola (1990)
Bauhinia malabarica Roxb.	Lilac Bauhinia; Malabar Bauhinia; Kotra, Tenga Kotra (Assamese)	Flowers eaten cooked in Assam	Patiri and Borah (2007)
Bauhinia purpurea L.	Hong Kong Orchid Tree, Purple Camel's Foot, Hawaiian Orchid Tree; Kanchanam (Garhwal); Sieo Dok Daeng (Thai)	Flower buds eaten as vegetables, cooked and pickled in Andhra Pradesh, India (Garhwal Himalayas). Young terminal leaves, stems and flowers eaten raw or cooked, flowers and buds cooked eaten as potherb and in curries in Asia	Gupta (1962), Martin and Ruberté (1975), Tanaka (1976), Pongpangan and Poobarasert (1985), Facciola (1990), Reddy et al. (2007), Patiri and Borah (2007), Namrata et al. (2011), Deane (2007–2012h)
Bauhinia racemosa Lam.	Bidi Leaf Tree; Katmauli (Hindi); Bardoli (India—Deccan)	Flowers eaten in India (Deccan)	Gammie (1902), Watt (1908)
Bauhinia retusa Roxb. = *Bauhinia semla* Wunderlin	Sehra (Madhya Pradesh)	Buds and flowers cooked, and pickled in India (Garhwal Himalayas)	Gupta (1962)
Bauhinia variegata L.	Indian Orchid Tree, Bauhinia, Butterfly Ash, Butterfly Tree, Camel's Foot, Camel's Foot Tree, Mountain Ebony, Orchid Tree, Orchidtree, Poor Man's Orchid, Pink Orchid Tree, Purple Orchid Tree, Variegated Orchid Tree, Variegated Orchid-Tree, White Bauhinia, White Camel's Foot, White Variegated Orchid Tree; Yang- Ti Jia (Chinese)	Young flower buds, young leaves and pods eaten in curries in India (Garhwal Himalayas) and salad. Young leaves, flower buds, flowers and young fruits used as vegetables in Hainan island. Flowers used for their nectar; buds and flowers cooked and pickled	Darlington and Ammal (1945), Gupta (1962), Hedrick (1972), Tanaka (1976), Kunkel (1984), Facciola (1990), Hu (2005), Patiri and Borah (2007), Namrata et al. (2011), Deane (2007–2012h)
Caesalpinia gillesii (Hook.) D. Dietr.	Bird-of-Paradise Shrub, Yellow Bird of Pradise Tree	Flower stamens used to adulterate saffron	Facciola (1990)
Caesalpinia pulcherrima (L.) Sw.	Peacock Flower, Pride Of Barbados, Dwarf Poinciana, Barbados Flower-Fence, Red Bird-of-Paradise	Flowers lightly cooked and eaten	Tanaka (1976), Pongpangan and Poobrasert (1985), Facciola (1990), King (2007)
Callistemon spp.	Bottle Brushes	Flower spikes steeped in warm water for the nectar	Schaeffer and Fletcher (2012)

Canavalia ensiformis (L.) DC.	Common Jack Bean, Ensiform Bean	Young leaves, flowers eaten steamed as 'lalab'	Ochse and van den Brink (1980)
Canavalia gladiata (Jacq.) DC.	Sword Bean; Thua Phraa, Thua Daap, Thua Faa (Thai); Natamame (Japanese)	The young shoots, young pods and flowers of the sword bean are served blanched with nam 'phrik'. The sour-tasting leaves are put in tom yam soup or eaten blanched with vermicelli and peanut curry. The young pods can be used in curries or fried	Kooi (1994), Saidin (2000), Jircas (2010), Lim (2012b)
Canavalia maritima (Aubl.) Urb. = *Canavalia rosea (Sw.) DC.*	Beach Bean, Bay Bean, Seaside Jack-Bean, Coastal Jack-Bean, Mackenzie Bean, Wonder Bean	In Malaysia, flowers eaten as flavouring	Burkill (1966), Facciola (1990)
Caragana ambigua Stocks	Pea Shrub	Flowers eaten raw or cooked	Hedrick (1972), Tanaka (1976)
Caragana sinica (Buc'hoz.) Rehder.	Chinese Pea Shrub	Flowers eaten raw or cooked	Uphof (1968), Tanaka (1976), Kunkel (1984)
Cassia auriculata L. = *Senna auriculata* (L.) Roxb.	Avarm Senna; Ranawara, Avaram (Telugu); Tangedu (Andhra Pradesh)	Flowers eaten as vegetable in Andhra Pradesh, India. Dried flowers used as coffee substitute	Watt (1908), Facciola (1990), Rahmansyah (1992), Reddy et al. (2007)
Cassia fistula L.	Cascara, Golden Shower, Indian Laburnum. Pudding Pipe Tree; Raela (Andhra Pradesh); Sonaru (Assamese)	Flowers eaten in Andhra Pradesh, India; flowers eaten by Santal people; flowers and buds eaten cooked in Assam	Watt (1908), Facciola (1990) Reddy et al. (2007), Patiri and Borah (2007), Lim (2012b)
Cassia garrettiana Craib = *Senna garrettiana* (Craib) H.S. Irwin and Barneby	Manatapat; Ki Lek Maeng, Khi Lek San, Khi Lek Kao, Samae Sarn (Thai)	Young leaves, flowers bitter cooked as food	Pongpangan and Poobarasert (1985)
Cassia hookeriana Hook. = *Senna birostris* var. *hookeriana* (Hook.) H.S. Irwin and Barneby	Mutuy (Quechua)	Flowers boiled and eaten in Peru (Vilcanota Valley)	Gade (1975)
Cassia latopetiolata Vogel = *Senna versicolor* (Vogel) H.S. Irwin and Barneby	Mutuy (Quechua)	Flowers boiled and eaten in Peru (Vilcanota Valley)	Gade (1975)
Cassia occidentalis = *Senna occidentalis* (L.) Link	Coffee Senna, Negro Coffee, Coffee Weed, Stinking Weed; Khi Lek Phi, Chum Het Lek (Thai)	Flowers eaten as steamed vegetables	Fernand et al. (1958), Ochse and van den Brink (1980), Facciola (1990)
Cassia siamea Lam. = *Senna siamea* (Lam.) H.S. Irwin and Barneby	Khi Lek Yai (Thai)	Flowers cooked as vegetables by Garos in Lower Assam; flowers cooked in curries in Thailand	Maisuthisakul et al. (2008), Maisuthisakul (2012), Kusamaran et al. (1998), Rojanpo and Tepsuwan (1992, 1993), Patiri and Borah (2007), Kaisoon et al. (2011)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Cassia sophera (L.) Wall. = *Senna sophera* (L.) Roxb.	African Senna, Pepper Leaved Senna; Kasaunda (Hindi); Phak Wan Ban, Phak Khet, Phak Khlet (Thai)	Flowers eaten in China	Read (1946)
Cassia timoriensis DC = *Senna timoriensis* (DC.) H.S. Irwin and Barneby	Wild Cassia; Khi Lek Lueat, Khi Lek Pa, Khi Lek Daeng (Thai)	Young leaves, flowers bitter cooked as food	Pongpangan and Poobarasert (1985)
Cassia tomentosa L.f. = *Senna multiglandulosa* (Jacq.) H.S. Irwin and Barneby	Mutuy (Quechua)	Flowers boiled and eaten in Peru (Vilcanota Valley)	Gade (1975), Facciola (1990)
Cercis canadensis L.	Eastern Redbud, Judas Tree, Redbud Red Bud Tree	Flowers eaten raw in salad, cooked or pickled; unopened buds pickled used as caper substitute	Uphof (1968), Hedrick (1972), Usher (1974), Tanaka (1976), Facciola (1990), Roberts (2000), Newman and O'Connor (2009)
Cercis occidentalis A. Gray	Western Redbud, Californian Redbud	Flowers eaten raw, added to salads, buds pickled	Yanovsky (1936), Facciola (1990)
Cercis siliquastrum L.	Judas Tree, Love Tree	Flowers eaten raw, have a sweetish-acid taste and make a nice addition to the salad bowl	Hedrick (1972), Tanaka (1976), Facciola (1990), Roberts (2000)
Clianthus puniceus (G. Don.) Lindl.	Parrot's Beak, Kaka-Beak Parrot's Bill, Lobster Claw	Flowers have a crisp and leafy taste	D'Cruz (1998)
Clitorea ternatea L.	Butterfly Pea, Blue-Pea and Cordofan-Pea	Flowers used as a food colourant; used in salad, dessert and as vegetable	Hedrick (1972), Burkill (1966), Wetitayaklung et al. (2008), Kaisoon et al. (2011)
Crotalaria glauca Willd.	Grass-Leaved Crotalaria	Flowers eaten as potherb	Hedrick (1972)
Crotalaria longirostrata Hook. and Arn.	Chepil, Chepilin, Chipilin, Longbeak Rattlebox	Flowers eaten	Uphof (1968), Williams (1981), Facciola (1990)
Crotalaria ochroleuca G. Don	Slender Leaf Rattlebox	Flowers eaten	Kunkel (1984), Facciola (1990)
Cytisus scoparius (L.) Link	Scotch Broom, Broom, Hogweed	The flower buds are pickled and used as a substitute for capers. Young buds and flowering tops used in cooking, bitter buds eaten as salad, fresh or pickled, and in herbal tea	Uphof (1968), Grieve (1971), Facciola (1990), Phillips and Foy (1992), Garland (1993)
Diphysa robinioides Millsp. = *Diphysa carthagenensis* Jacq.	Macano, Palo Amarillo	Yellow flowers becomes mucilaginous when steamed and added to beans or tortilla	Facciola (1990)
Dolichos lablab L. = *Lablab purpureus* (L.) Sweet	Hyacinth Bean, Lablab Bean, Field Bean, Pig-Ears, Rongai Dolichos, Lab-Lab Bean, Poor Man's Bean, Tonga Bean; Kwao-Nam (Thai)	Flowers cooked as vegetables in spicy stir-fry or eaten dipped in spicy chilli sauce	Pongpangan and Poobarasert (1985), Saidin (2000)

Dolichos malosanus Baker = *Dolichos kilimandscharicus* subsp. *kilimandscharicus* Taub.	Veld Lupin	Flowers consumed as vegetables by natives	Uphof (1968), Facciola (1990)
Erythrina americana Mill.	American Coral Tree, Naked Coral Tree, Flor De Colorin	In Mexico, the flowers and immature inflorescences are eaten especially in tamales at Easter time	Kunkel (1984), Facciola (1990)
Erythrina berteroana Urb.	Coral Bean, Pito Coral Tree	Flowers and immature inflorescences are eaten with meat, in stews and in egg dishes	Martin and Ruberté (1975), Tanaka (1976), Facciola (1990)
Erythrina flabelliformis Kearney	Coralbean, Southwestern Coral Bean	Flowers reported edible and relished in Mexico	Deane (Deane 2007c)
Erythrina glauca Willd. = *Erythrina fusca* Lour.	Purple Coraltree, Gallito, Bois Immortelle, Bucayo	Flowers folded into batter, cooked and eaten	Williams (1981), Facciola (1990)
Erythrina herbacea L.	Eastern Coral Bean, Cardinal Spear	Flowers eaten cooked	Facciola (1990), Deane (2007–2012c)
Erythrina rubrinervia Kunth	Gallito, Palo De Pito, Palo Santo, Pernilla De Casa, Peronil	Flowers and flower buds eaten like string beans in El Savador and Guatemala	Altschul (1973), Uphof (1968), Facciola (1990)
Erythrina variegata L.	Variegated Coral Tree, Indian Coral Bean, Tigers-Claw, Variegated Coralbean, Variegated Coraltree, Indian Coraltree, Indian Wiliwili	The flowers and young leaves are edible and cooked like string beans in water	Deane (2007–2012c)
Gliricidia sepium (Jacq.) Walp.	Madre De Cacao, Gliricidia, Mexican Lilac, Mother of Cocoa, Nicaraguan Cacao Shade, Quick Stick, St. Vincent Plum, Tree of Iron	Flowers cooked in egg batter and fried or cooked as potherbs	Williams (1981), Facciola (1990)
Hardenbergia violacea (Schneev.) Stearn	Native Sarsaparilla, False Sarsaparilla Vine	Purple flowers eaten raw	Haslam (2011)
Indigofera pulchella Roxb. = *Indigofera cassioides* DC.	Cassia Indigo	Flowers occasionally eaten as vegetables	Watt (1908), Tanaka (1976)
Indigofera cassioides DC.	Cassia Indigo	The flowers are occasionally eaten as a vegetable	Kunkel (1984), Facciola (1990)
Indigofera dosua D. Don	Kathewat, Kati, Theot (Hawaiian)	Flowers eaten as potherb in India	Watt (1908)
Indigofera gerardiana Baker = *Indigofera heterantha* Brandis.	Himalayan Indigo, Gerard's Indigo	Flowers eaten in India (Garhwal Himalayas)	Gupta (1962)
Indigofera hebepetala Baker	Fuzzy Petal Indigo	The flowers and tender immature pods are cooked as a vegetable or pickled	Manandhar (1991)
Indigofera heterantha Brandis	Himalayan Indigo, Indigo Bush	The flowers are boiled and pickled	Manandhar (1991)
Indigofera pseudotinctoria Matsum.	False Indigo	The leaves and flowers are boiled and eaten in China	Read (1946), Tanaka (1976), Kunkel (1984), Facciola (1990)

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Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Kennedia prostrata R.Br.	Running Postman, Scarlett Runner	Flowers eaten for sweet source of nectar and tea. Flowers can be used as colourful garnish for salad	SERCUL (2011), Schaeffer and Fletcher (2012)
Kraunhia floribunda (Willd.) Taub. = *Wisteria floribunda* (Willd.) DC.	Japanese Wisteria	Flowers thoroughly boiled, washed and eaten with oil and salt in China	Read (1946), Deane (2007–2012l)
Lablab purpureus (L.) Sweet	Hyacinth Bean, Lablab Bean, Field Bean, Pig-Ears, Rongai Dolichos, Lab-Lab Bean, Poor Man's Bean, Tonga Bean; Kwao-Nam (Thai)	Flowers eaten raw or steamed, or added to soups and stews	Fernald et al. (1958), Hedrick (1972), Pongpangan and Poobrasert (1985), Facciola (1990), Tanaka and Nguyen (2007)
Lathyrus davidii Hance	Chin Yin Hua, Da Shan Li Dou, Jiang Mang Shan Li Dou, Jiang Mang Xiang Wan Dou, Shan Jiang Dou, Shan Chiang Tou (Chinese); Itachi Sasage (Japanese)	Young plant, including the inflorescence is cooked and used as a potherb or added to soups	Tanaka (1976), Kunkel (1984), Facciola (1990)
Lespedeza bicolor Trucz.	Tartary Bush Clover; Hu Zhi Zi (Chinese); Yama-Hagi (Japanese),	Young leafy shoot and flower buds used as tea in China. Flowers eaten boiled or fried in Japan	Tanaka (1976), Kunkel (1984), Hu (2005)
Lespedeza davurica (Laxm.) Schindl.	Ox-Bush Clover, Mongolian Lespedeza; Niu Zhi Zi (Chinese); Daguur Khoshoonbut (Mongolian)	Flowers and leaves used for tea in China	Hu (2005)
Leucaena leucocephala (Lam.) de Wit	White Leadtree, Lead Tree, Koa Haole, Ekoa, Leucaena, Horse Tamarind, Jumbie Bean, White Popinac, Jumbay	Flowers eaten in Thailand	Kaisoon et al. (2011)
Leucaena glauca (Willd.) Benth. = *Leucana leucocephala* (Lam.) de Wit	White Leadtree, Lead Tree, Koa Haole, Ekoa, Leucaena, Horse Tamarind, Jumbie Bean, White Popinac, Jumbay	Flower buds eaten in salad and cooked as vegetable	Ochse and van den Brink (1980)
Lysiphyllum carronii (F. Muell.) Pedley	Red Bauhinia, Queensland Ebony, Northern Beantree, Carrons Bauhinia	Nectar sucked from flowers	Cribb and Cribb (1987)
Lysiphyllum gilvum (Bailey) Pedley	Bauhinia Tree, Queensland Bean Tree, Bohemia	Flower pounded, mixed with honey and fermented to make an intoxicating drink. Nectar sucked from flowers or soaked in water to make drinks	Low (1991)
Lysiphyllum hookeri (F. Muell.) Pedley	Bauhinia, White; Bauhinia; Pegunny; Ebony, Mountain; Ebony, Queensland; Hooker's Bauhinia; Mountain Ebony; White Bauhinia; Queensland Ebony; Bauhinia	Nectar sucked from flowers	Cribb and Cribb (1987)

Medicago polymorpha L.	California Burclover, Toothed Bur Clover, Toothed Medick, Burr Medic	Flowers eaten raw in salad or cooked as potherb, stir-fried or used in soups	Tanaka (1976), Facciola (1990)
Medicago sativa L.	Alfalfa, Spanish Clover, California Clover, Buffalo Herb, Lucerne, Purple Medic	Flower heads blended with red clover and spearmint or peppermint and brewed into tea	Clarke (1977), Facciola (1990)
Melilotus alba Ledeb. = *Melilotus officinalis* subsp. *alba* (Medik.) H. Ohashi and Tateishi	White Melilot, White Sweet Clover	Flowers eaten raw or cooked and used as a vanilla-like flavouring	Kunkel (1984), Facciola (1990)
Melilotus officinalis (L.) Pall.	Melilot, Yellow Sweet Clover, Yellow Melilot, Ribbed Melilot, Common Melilot	Flowers eaten raw or cooked. The flowers and seeds are used as a flavouring. Flower tops are dried and used to scent and flavour sausages and stuffings like rabbit, marinades and beers	Hedrick (1972), Schofield (2003), Garland (1993)
Mimosa pudica L.	Sensitive Plant, Touch-Me-Not, Humble Plant, Shameful Plant; Sleeping Grass, Ant Plant	Flowers crystallized or used for the preparation of distilled flower water	Crowhurst (1972), Facciola (1990)
Mucuna pruriens (L.) DC.	Velvet Bean, Cowitch, Cowhage, Kapikachu		King (2007)
Ononis spinosa L.	Spiny Rest Harrow, Rest Harrow	Flowers eaten raw and used as a decoration on salads	Chiej (1984)
Parkia timoriana (DC.) Merr.	Tree Bean; Yongchak (Manipur)	Young inflorescences and pods eaten	Yumnum and Tripathi (2012)
Phaseolus coccineus L.	Scarlet Runner Bean, Runner Bean, Dutch Runner Bean, Case Knife Bean, Seven Year Bean	Flowers can be eaten raw in salads, adding a mild bean flavour with a hint of nectar, or added to cooked runner bean dishes for decoration	Kunkel (1984), Facciola (1990), Lauderdale and Evans (1999), Newman and O'Connor (2009), Anonymous (2012a), Deane (2007–2012j)
Phaseolus vulgaris L.	Green Beans, Common Bean, Kidney Bean, String Bean, Garden Bean, Field Bean, Haricot	Flowers are edible	King (2007)
Pisum sativum L.	Garden Pea, English Pea, Green Pea, Snap Pea, Sweet Pea, Snow Pea	Flowers are edible raw in salad and have a fresh pea taste	Newman and O'Connor (2009), Deane (2007–2012m)
Psophocarpus tetragonolobus (L.) DC.	Four-Angled Bean, Goa Bean Winged Bean, Princess Bean	Flowers and buds eaten in salads, steamed or batter-fried like tempura, spicy stir-fry or dip in a sambal (spicy chilli) paste	Ochse and van den Brink (1980), Facciola (1990), Khan (1994), Woodward (2000), Saidin (2000)
Pterocarpus indicus Willd.	Rosewood, Angsana, Sena, Narra, New Guine Rosewood	Flowers used in salad and other dishes	King (2007)
Pterocarpus marsupium Roxb.	Indian Kino Tree, Malabar Kino, Kino	Seeds and flowers eaten in India (Deccan)	Watt (1908)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Pueraria lobata (Willd.) Ohwi = *Pueraria montana* (Lour.) Merr. var. *lobata* (Willd.) Maesen and S.M. Almeida	Kudzu, Kudzu Vine; Ge Gen (Chinese)	Flower and buds used as ingredient in five-flower tea 'wu-hua cha'. Flowers used as vegetables cooked or made into jellies or pickles	Hu (2005), Groen et al. 1996, Fernald et al. (1958), Facciola (1990), Deane (2007–2012k, z)
Robinia hispida L.	Rose Acacia, Britsly Locust, Rose Locust	Flowers edible	McVicar (2003)
Robinia luxurians (Dieck.) Schneid.		Flowers edible raw	Tanaka (1976)
Robinia neomexicana A. Gray	New Mexican Locust	Pink flowers eaten raw without preparation or cooked	Yanovsky (1936), Tanaka (1976), Facciola (1990), Moerman (1998)
Robinia pseudoacacia L.	Black Locust, Foreign Pagoda Tree; Yang Huai (Chinese)	Washed flower mixed with flour, steamed, seasoned and eaten in northern China. Flowers dipped into egg batter and fried, added to pancake batter or made into a pleasant drink	Fernald et al. (1958), Crowhurst (1972), Facciola (1990), Hu (2005)
Saraca bijuga Prain = *Saraca indica* L.	Ashoka Tree; Sok Nam (Thai); Gapis, Tengalan (Malay)	Flowers are sour and used as potherb	Burkill (1966), Tanaka (1976), Pongpangan and Poobarasert (1985), Facciola (1990), Wessapan et al. (2007)
Saraca indica L.	Ashoka Tree; Sok Nam (Thai); Gapis, Tengalan (Malay)	Flowers eaten in Thailand	Van den Bergh (1994b), Wetitayaklung et al. (2008)
Sarothamnus scoparius (L.) W.D.J. Koch = *Cytisus scoparius* (L.) Link	Broom, Genista, Irish Broom, Scotch Broom	Flower buds are added to salads, made into wine or pickled in vinegar and used like capers	Grieve (1971), Hedrick (1972), Facciola (1990)
Schotia capitata Bolle	Dwarf Boer-Bean	Flower nectar sucked	Facciola (1990)
Senna siamea (Lam.) Irwin and Barneby	Bombay Blackwood, Kassod Tree	Flowers eaten as food	Wetitayaklung et al. (2008)
Sesbania aegyptiaca Poir. = *Sesbania sesban* (L.) Merr.	Common Sesban, Egyptian Rattle Pod, Frother, River Bean, Sesban, Sesbania, Egyptian Sesban	Flowers of a wild and sometimes cultivated species eaten in West Africa. Flowers eaten fried with pounded rice or gram	Irvine (1952), Patiri and Borah (2007)
Sesbania bispinosa (Jacq.) W. Wright	Prickly Sesban, Spiny Sesbania	Flowers edible	Burkill (1966), Tananka (1976), Facciola (1990)

Sesbania grandiflora (L.) Pers.	Scarlet Wisteria Tree, Vegetable Humming Bird Vegetable Hummingbird (English), Shiro Gocho (Japanese)	Flowers, young fruits, young leaves and pods cooked as vegetables. Pistil removed first In Thailand, the shoots and young leaves are blanched and eaten with 'nam phrik', as are the flowers after the removal of the bitter stamens. The flowers can also be used in 'kaeng som' (sweet and sour curry), fried with pork or prawns or mixed with flour and fried. In Assam, flowers are fried and eaten with pounded rice or gram	Ochse and van den Brink (1980), Pongpangan and Poobarasert (1985), Facciola (1990), Rojanpo and Tepsuwan (1992), Kusamaran et al. (1998), Woodward (2000), Wetitayaklung et al. (2008), Hu (2005), Tanaka and Nguyen (2007), Patiri and Borah (2007), Jircas (2010)
Sesbania javanica Miq.	Sesbania-Pea; Sano Kin Dok, Phak Hong Haeng, Si Pree Laa, Sano Hin (Thai)	The young shoots are cooked and eaten with 'nam phrik'. The flowers are eaten either raw, blanched, fried with egg or fermented and are served with nam 'phrik kapi'. Because the flowers contain a carotenoid substance, they are used to give a yellow colour to various desserts such as 'kanom bua loi', which are coloured balls of sticky rice flour cooked in sweetened coconut milk	Tanaka and Nguyen (2007), Wetitayaklung et al. (2008), Jircas (2010)
Sesbania roxburghii Merr. = *Sesbania javanica* (Miq.)	Sesbania-Pea; Sano Kin Dok, Phak Hong Haeng, Si Pree Laa, Sano Hin, Sa No (Thai)	Flowers eaten raw or cooked	Pongpangan and Poobarasert (1985)
Sesbania sesban (L.). Merr.	Common Sesban, Egyptian Rattle Pod, Frother, River Bean, Sesban, Sesbania, Egyptian Sesban	In Nigeria (northern Kano State), flowers and fruits eaten. In Assam, flowers fried and eaten with pounded rice or gram	Dalziel (1937), Tanaka (1976), Mortimore (1989), Facciola (1990), Patiri and Borah (2007)
Sophora viciifolia Hance = *Sophora davidii* (Franch.) Pavol.	Shrub Pagoda Tree, David's Mountain Laurel; Lang Ya Ci (Chinese)	Flowers eaten in China	Hu (2005)
Sophora davidii (Franch.) Pavol.	Shrub Pagoda Tree, David's Mountain Laurel	Flowers eaten in China	Altschul (1973), Tanaka (1976), Facciola (1990)
Sophora japonica L. = *Styphnolobium japonicum* (L.) Schott.	Japanese Pagoda Tree, Pagoda Tree, Chinese Scholar Tree Yellow Berry, Pagoda Tree	Flower and buds used as ingredient in five-flower tea called 'wu-hua cha' in China and also eaten as food	Read (1946), Altschul (1973), Tanaka (1976), Facciola (1990), Hu (2005)
Tamarindus indica L.	Tamarind	Tree usually grown for its fruit. Young shoots and flowers are eaten as vegetable. The sour taste enhances the taste of many kinds of curries. In western Rajasthan, the leaves, fruits and flowers are eaten. In Nigeria (Kano State, northern), the pods, leaves, fruits, seeds and flowers eaten raw in salads or cooked	Gammie (1902), Tanaka (1976), Ochse and van den Brink (1980), Morton (1987), Mortimore (1989), Facciola (1990), Woodward (2000), Jircas (2010), Lim (2012b)

(continued)

Table 1 (continued)

Scientific name	English/common vernacular name	Flower edible uses	References
Trifolium agrarium L. = *Trifolium aureum* Pollich	Large Hop Trefoil, Large Trefoil Large Hop Clover, Golden Clover,R Hop Clover, Yellow Clover	Dried flower heads used as substitute for tea	Peterson (1977), Facciola (1990)
Trifolium cyathiferum Lindl.	Cup Clover, Bowl Clover	Flowers eaten as food	Moerman (1998)
Trifolium fucatum Lindl.	Sour Clover, Bull Clover, Puff Clover	Flowers and young seedpods eaten raw or cooked	Moerman (1998)
Trifolium hybridum L.	Alsike Clover, Hybrid Clover	Flowers sucked for nectar, added to soup, dip in batter and fry as fritters. Flower heads dried make into tea	Peterson (1977), Facciola (1990), Schofield (2003)
Trifolium incarnatum L.	Crimson Clover, Italian Clover, French Clover	Flower heads steep for brew and tea	Peterson (1977), Facciola (1990)
Trifolium involucratum Orteg. = *Trifolium mucronatum* subsp. *mucronatum* Willd. ex Spreng.	Cusp Clover	Flowers eaten in California	Yanovsky (1936)
Trifolium pratense L.	Red Clover, Beebread, Cow Clover, Cow Grass, Meadow. Clover, Purple Clover, Wild Clover.	Flower heads steep for brew, wines and pickles; young flowers used as sandwich filling; flowers sucked for nectar, added to soup, dip in batter and fry as fritters; flower head dried, powdered and sprinkled on boiled rice	Tanaka (1976), Cribb and Cribb (1987), Low (1989), Barash (1997), Lauderdale and Evans (1999), Facciola (1990), Roberts (2000), Schofield (2003), Newman and O'Connor (2009)
Trifolium repens L.	White Clover, Dutch White Clover	Flower heads steeped for brew, wines and pickles; young flowers used as sandwich filling; flowers sucked for nectar	Fernald et al. (1958), Hedrick (1972), Cribb and Cribb (1987), Low (1989), Facciola (1990), Schofield (2003)
Trifolium variegatum Nutt.	Whitetip Clover	Flowers eaten raw and have a sweet flavour	Moerman (1998)
Trifolium virescens Greene = *Trifolium fucatum* Lindl.	Sour Clover, Bull Clover, Puff Clover	Flowers eaten in California	Yanovsky (1936)
Ulex europaeus L.	Furze, Gorse, Common Gorse	Buds pickled in vinegar and eaten in salads	Low (1989), Deane (2007–2012y), Grieve (1971), Facciola (1990)
		Flowers are a trailside nibble. They can be added to salads, made into tea or used to flavour wine. Oddly, the blossoms smell slightly of coconut but taste like almonds. The bright flowers have also been used for dye, Easter eggs to clothes	
Vicia cracca L.	Tufted Vetch, Cow Vetch, Bird Vetch, Boreal Vetch, Shao Cai (Chinese)	Young shoot including flower buds cooked fresh or dried for winter use in China	Hu (2005)
Vigna luteola (Jacq.) Benth.	Hairy Cowpea, Hairypod Cowpea, Dalrymple Vigna, Deer Pea	Flowers edible cooked	Deane (2007–2012r)

Vigna umbellata (Thunb.) Ohwi and H. Ohashi	Rice Bean, Red Rice Bean	Flowers eaten	King (2007)
Vigna unguiculata subsp. *sesquipedalis* (L.) Verdc.	Snake Bean, Long Bean Yardlong Bean	Flowers used in spicy stir-fry or cooked in creamy coconut	Saidin (2000)
Wisteria floribunda (Willd.) DC.	Japanese Wisteria	Flowers cooked as food in parts of China	Tanka (1976), Kunkel (1984), Facciola (1990), Deane (2007–2012l)
Wisteria frutescens (L.) Poir	American Wisteria	The fresh flowers are eaten in tossed green salads. Flowers also excellent when dipped in batter and fried in oil as fritters	Fernand et al. (1958), Peterson (1977), Facciola (1990)
Wisteria sinensis (Sims) Sweet	Wisteria, Chinese Wisteria; Zi Teng Hua (Chinese)	Flowers and buds washed, mixed with flour, steamed, seasoned and eaten in northern China. Flowers also thoroughly boiled and eaten with oil and salt. The flowers are a common addition to cakes around Peking. Flowers folded into egg batter and made into fritters. Flowers also used for preserves or brewed into wine	Read (1946), MacNicol (1967), Tanaka (1976), Facciola (1990), Hu (2005), Deane (2007–2012l)
Wisteria villosa Rehder	Wooly Wisteria	Flowers edible	Tanaka (1976), Kunkel (1984)
Fagaceae			
Castanopsis hystrix Miquel = *Castanopsis purpurella* subsp. *purpurella*	Hong Zhui (Chinese)	Catkins eaten	Kunkel (1984)
Fagus grandifolia Ehrh.	American Beech, Beech, Carolina Beech, Gray Beech, Red Beech, Ridge Beech, Stone Beech, White Beech, Winter Beech	Swelling flower buds used for food	Yanovsky (1936)

species dealt with in this volume include both lesser-known, wild and underutilized plants and also common and widely grown ornamentals.

As in the preceding 6 volumes, topics covered include the following: taxonomy (botanical name and synonyms), common English and vernacular names, origin and distribution, agroecological requirements, edible plant part and uses, plant botany, nutritive and medicinal/pharmacological properties with up-to-date research findings and traditional medicinal uses, other nonedible uses and selected/cited references for further reading.

Use of Edible Flowers

Since antiquity right through the Middle Ages and the seventeenth century, flowers have been featured as an integral part of human nutrition in Europe—ancient Rome, medieval France, Victorian England, Middle East—and in Asia particularly in China, India, Thailand and Japan. Flowers have long been used as decorations in food prepared for the nobility. Today, consumption of edible flowers is increasing worldwide (Mlcek and Rop 2011; Rop et al. 2012). Edible flowers are becoming more popular as evidenced by the profusion of edible flower cookbooks, culinary magazine articles, scientific papers on edible flowers and television shows. Flowers are consumed in various forms, colours and flavours to enhance the nutritional and sensory qualities of foods. Its qualities, freshness and safety depend on the care taken in its harvesting and storage. Many of the lesser-known edible flowers are harvested in the wild from plants in the forest, wasteland, disturbed sites, near waterways and roadside often occurring as weeds (*Limnocharis*, milkweeds, beggarticks, dandelion, *Acacia* spp.). In contrast many of the commonly known edible flowers (e.g. roses, chrysanthemums, carnations, marigolds, daylilies, cornflower) are harvested from cultivated garden ornamentals or culinary herb garden (e.g. chives, *Mentha* spp. borage, rosemary, chamomile).

Edible flowers can be used raw or fresh as a garnish or as an integral part of a dish, such as a vegetable or fruit salad. Today, many restaurant chefs and innovative home cooks garnish their entrees with flower blossoms for a touch of elegance. Many flowers can be fried in light batter or cornmeal, e.g. squash, zucchini flowers or in fritters (e.g. Acacia blossoms). Some flowers can be steamed, boiled, grilled or used in soups and curries. Some flowers can be stuffed or used in stir-fry dishes. Edible flowers can be crystallized, candied; frozen in ice cubes and added to beverages; made into jellies and jams; used to make teas or wines; to flavour liquors, vinegar, oil, honey and scented sugars; added to punch, cocktail and other beverages; and minced and added to cheese spreads, herbal butters, pancakes, crepes and waffles. Many flowers can be used to make vinegars for cooking, marinades or dressings for salads.

Some important rules on the use of edible flowers:

- Flowers have to be accurately identified before eating.
- Do not eat flowers from florists, nurseries, garden centres, fruit orchards or flowers from plants found on the side of the road and in murky waterways because of possible contamination from pesticide sprays, vehicle carbon emissions and industrial and effluent run-off.
- Harvest/pick flowers that are free from diseases, insects, insect damage and soil particles.
- Pick young fresh flowers and buds on dry mornings, before the sun becomes too strong, to retain the bright colours and intense flavours.
- Use flowers immediately for best results or refrigerate in a plastic bag for a few days. Dried, frozen or freeze-dried flowers are best used in infusions or cooked.
- For medium and large flowers like hollyhocks, roses, lilies, calendula, chrysanthemum, lavender, rose, tulip, yucca, hibiscus, lavender, tulip and marigolds, use only the petals and discard stamens, pistil and calyx. The bitter 'heel' at the base of the petal should be removed.
- Eat edible flowers in moderation.
- People with hay fever, asthma or allergies should best avoid eating flowers since many allergies are due to sensitivity to pollen of specific plants.

Nutrients and Bioactive Phytochemicals in Flowers

Nutrients and phytochemicals contained in flowers are not markedly different from those found in other plant organs (leaves, stem fruit). Several thousands of compounds have been identified in flowers including nutrients (proteins, carbohydrates, lipids, fibre, minerals, fatty acids, vitamins and essential amino acids), flavonoids, carotenoids, anthocyanins and other phenolic compounds, waxes, resins in the floral parts (petals, sepals, pollens, etc.), in the floral nectar, as fragrance volatiles, and essential oil components monoterpenes, sesquiterpenes esters, alcohols (monoterpene and sesquiterpene alcohols), aldehydes, ketones, phenols, alkanes, esters, lactones, coumarins, ether, oxides, fatty acids, fatty acid derivatives, benzenoids, phenylpropanoids, isoprenoids and nitrogen- and sulphur-containing compounds (Mookherjee et al. 1990; Knudsen et al. 1993; Dobson et al. 1997; Kim et al. 2000; Falzari and Menary 2003; Kaisoon et al. 2011; Mlcek and Rop 2011; Rop et al. 2012; Diraz et al. 2012). The concentrations of these compounds vary throughout the development and maturation of the flower and also during storage after harvesting. Health benefits attributable to antioxidant capacity have been shown to be highly correlated with phenolic compounds (Kaisoon et al. 2011; Rop et al. 2012).

Flower Pollen

The composition of pollen changes from floral species to species, variation in absolute amounts of the different compounds can be very high. The major components of pollens are proteins and amino acid, lipids (fats, oils or their derivatives) (Manning 2001), and sugars (Crane 1990); the nutrient profile in dried bee-collected pollen and dried hand-collected pollen are as follows: water, 11 %, 10 %; crude protein, 21 %, 20 %; ash, 3 %, 4 %; crude fats, 5 %, 5 %; reducing sugars, 26 %, 3 %; nonreducing sugars, 3 %, 8 %; starch, 3 %, 8 %; and undetermined components, 29 %, 43 %, respectively. The minor components of bee-collected pollens are more diverse (Crane 1990): flavonoids at least 8; carotenoids (at least 11); vitamins C, E B complex (including, niacin, biotin, pantothenic acid, riboflavin (B_2) and pyridoxine (B_6)); minerals—macro-elements (K, Na, Ca, Mg, P, S) and micro-elements (Al, B, Cl, Cu, I, Fe, Mn, Ni, Si, Ti and Zn); all free amino acids; terpenes; nucleic acids DNA, RNA and others; enzymes >100; growth regulators auxins, brassins, gibberellins and kinins; and growth inhibitors. All amino acids essential to humans (phenylalanine, leucine, valine, isoleucine, arginine, histidine, lysine, methionine, threonine and tryptophan) can be found in pollen and most others as well, with proline being the most abundant. Most simple sugars in pollen comprise fructose, glucose and sucrose come from the nectar or honey of the field forager. The polysaccharides like callose, pectin, cellulose, lignin, sporopollenin and others are predominantly pollen components. Protein contents of above 40 % have been reported, but the typical range is 7.5–35 %: typical sugar content ranges from 15 to 50 %, and starch content is very high (up to 18 %) in some wind-pollinated grasses (Schmidt and Buchmann 1992). Low lipid levels (0.6–1.9 % dry mass) are found in bee-collected pollen of eucalypts (Bell et al. 1983; Manning and Harvey 2002), whereas an high level of 32 % dry mass is found for canola pollen by Evans et al. 1987. Pollen has been added to diets for domestic animals and laboratory insects resulting in improvements of health, growth and food conversion rates (Crane 1990; Schmidt and Buchmann 1992).

Floral Nectar

The nectar is a liquid with a sweet taste, comprising sugars, amino acids, nonprotein amino acids, proteins, minerals, lipids, organic acids, phenolic compounds, alkaloids, coumarins, saponins, terpenoids, etc. (Nicolson and Thornburg 2007). The major sugars in nectar are the disaccharide sucrose and the hexose monosaccharides glucose and fructose (Baker 1975; Baker and Baker 1983). Bernadello et al. (1999) found that the floral nectar of 29 species native to Argentinian Patagonia to be hexose dominant (72.41 %) or

hexose rich (17.24 %); a few were sucrose dominant (10.34 %). Though a large majority of floral nectars is dominated by sucrose, glucose and fructose, the pentose sugar xylose is a major nectar sugar in *Protea* and *Faurea*, two related genera of the Proteaceae (Nicolson and van Wyk 1998). Other minor sugars present in trace amounts in nectar include monosaccharides (e.g. mannose, arabinose, xylose), disaccharides (maltose, melibiose) or, more rarely, oligosaccharides (raffinose, melezitose, stachyose) (Baker and Baker 1982a, 1983; Nicolson and Thornburg 2007). Sorbitol is also a frequent constituent of Mediterranean nectars (Petanidou 2005). Minerals have been found in floral nectar (Hiebert and Calder 1983; Heinrich 1989). Potassium was found to be the dominant ion with 35–74 % in nectars; the other cations can be listed up according to their decreasing amounts: Na, Ca, Mg, Al, Fe and Mn (Heinrich 1989). Although all ten essential amino acids are commonly present in floral nectars as free amino acids, some nonessential amino acids such as asparagine and glutamine can occur in much higher concentrations (Nicolson and Thornburg 2007). The presence of amino acids in floral nectars was first reported by Ziegler (1956), later by Lüttge (1961, 1962) and Baker and Baker (1973, 1977, 1986) In *Erythrina* species pollinated by passerine birds, the total amino acid concentrations are far higher than in hummingbird-pollinated species (Baker and Baker 1982b). Few of the nontoxic nonprotein amino acids, including β-alanine, ornithine, homoserine and γ-aminobutyric acid (GABA), are known to accumulate in nectar (Nicolson and Thornburg 2007). The existence of proteins in nectar has been reported long ago (Pryce-Jones 1944; Lüttge 1961). The first enzymatic activity to be identified in nectar was invertase, found in the floral nectar of *Tilia* sp. (Beutler 1935). Other proteins identified in various floral nectars included the following: *trans*-glucosidase in *Robinia pseudoacacia* (Zimmerman 1953); *trans*-fructosidase in *Impatiens holstii* (Zimmerman 1954); phosphatase (Cotti 1962); tyrosinase in *Lathraea clandestina* (Lüttge 1961); mannose-binding lectin and alliinase in *Allium porrum* (Peumans et al. 1997); and nectarin IV (Naqvi et al. 2005) and nectarin I, II, II and V in *Nicotiana* sp. (Carter and Thornburg 2000; 2004a, b).

The presence of lipids has been reported in numerous floral nectars (Vogel 1971; Baker and Baker 1975; Bernardello et al. 1999). Some major lipids found in floral nectars of *Calceolaria* species (Scrophulariaceae) and in the rhattanys (*Krameria* species, Zygophyllaceae) included β-acetoxy fatty acids of varying chain length between C16 and C20 (Vogel 1971; Seigler et al. 1978). Ascorbic acid (vitamin C) is well known as an antioxidant in floral nectar (Baker and Baker 1975). Phenolic substances are quite widespread in nectars (Baker and Baker 1982a; Gil et al. 1995; Ferreres et al. 1996). European *Eucalyptus* honeys were found to have the following flavonoids: myricetin, quercetin, tricetin, luteolin and kaempferol (Martos et al. 2000) and *Robinia pseudoacacia* flowers to have nectar flavonol rhamnosides as floral markers (Truchado et al. 2008). Alkaloids and allelochemicals have been detected in the nectar of a large number of plants (Hazslinsky 1956; Baker and Baker 1975; Galetto and Bernardello 1992; Detzel and Wink 1993; Adler and Wink 2001). Recently, Singaravelan et al. (2005) reported four secondary alkaloid compounds occurring naturally in floral nectar: nicotine, anabasine, caffeine and amygdalin in many plants including *Nicotiana* spp. and *Tilia cordata* (Singaravelan et al. 2006). While terpenoids do occur in plant nectars (Detzel and Wink 1993), most are produced by cells with specialized metabolic potential that are dispersed throughout the flower (Bergström et al. 1995; Dudareva et al. 1998; McTavish et al. 2000).

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Tulbaghia violacea

Scientific Name

***Tulbaghia violacea* Harv.**

Synonyms

Omentaria cepacea (L.f.) Salisb. (inval.), *Omentaria violacea* (Harv.) Kuntze, *Tulbaghia cepacea* var. *maritima* Vosa, *Tulbaghia cepacea* var. *robustior* Kunth, *Tulbaghia violacea* var. *minor* Baker, *Tulbaghia violacea* var. *obtusa* Baker, *Tulbaghia violacea* var. *robustior* (Kunth) R.B. Burb

Family

Amaryllidaceae, also placed in Alliaceae, Liliaceae

Common/English Names

Pink Agapanthus, Society Garlic, Sweet Garlic, Wild Garlic

Vernacular Names

Afrikaans: Wildeknoflok, Wilde Knoffel
Swedish: Tulbaghia
Xhosa: Itswele Lomlambo
Zulu: Isihaqa

Origin/Distribution

Society Garlic is native to Natal, Transvaal and the Eastern Cape region in South Africa where it grows in rocky grasslands.

Agroecology

Society Garlic grows best in full sun in a light, well-drained and well-aerated sandy or sandy-loam soils. It tolerates light shade but may not flower much. It requires frequent watering during the growing season but less so during flowering and in the winter months. In winter the root ball should be kept moist with reduced watering. Established plants can survive extended droughts and moderate frosts and light freezes down to −6.7 °C.

Edible Plant Parts and Uses

Both the leaves and flowers can be used in salads and other dishes (Facciola 1990; Van Wyk and Gericke 2000; Harris 2004). The edible bulb and leaves have a taste of garlic without the nasty side effect of bad breath. Chopped leaves are used in sauces, soups and salads and as a garnish. The flower buds steeped in vinegar give it a mild garlic flavour and can also be used as a garnish. The Zulus use the leaves and flowers as spinach and as a hot, peppery seasoning with meat and potatoes.

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Botany

Society Garlic is a clump-forming herbaceous perennial, 60 cm high by 60 wide (Plates 1 and 2). Its rootstock is an ovoid corm with rhizomatous base, 1.5–2.7 cm long and 1–1.5 cm in diameter. Leaves 8–10, greyish-green, linear, 17–50 cm long, 0.35–0.7 cm wide; apex obtuse; base sheathing grows straight up out of the corm. Scape 39–70 cm long grows up from the centre of the rosette of leaves. Atop the scape sits a large umbel with 8–20 sweet-scented lilac-pink flowers on; pedicels 10–20 mm long arise from the same point (Plates 2 and 3). Flower with a cylindrical perianth tube, 8–10 mm long expanding to six elliptic lobes 6–7 mm long, 1.5–2.8 mm wide, apex acute with slightly in-rolled margin. Corona of three distinct oblong lobes, 2.5–3 mm long, 1–1.5 mm wide with retuse apex; stamens included in perianth tube, upper series 2–2.5 mm below mouth, lower series ±6 mm from base; anthers 1 mm long; ovary oblong to obovoid, 2.5 mm long, 1.5 mm in diameter; ovules numerous; style 1 mm long, 0.4 mm in diameter; stigma capitate, small. The fruit, triangular capsules, are grouped into a head, and when ripe, they split to release the flattened, hard black seeds.

Plate 1 Society Garlic foliage

Plate 2 Flowering Society Garlic plant

Plate 3 Society Garlic flowers

Nutritive/Medicinal Properties

Jacobsen et al. (1968) reported the presence of an alkylcysteine sulfoxide lyase and three unidentified S-substituted cysteine sulfoxide derivatives, whereas Burton and Kaye (1992) isolated 2,4,5,7-tetrathiaoctane-2,2-dioxide and 2,4,5,7-tetrathiaoctane from the leaves of *T. violacea*. The amino acid (RSRC)-*S*-(methylthiomethyl) cysteine-4-oxide was isolated from rhizomes of *Tulbaghia violacea* (Kubek et al. 2002). Its content varied in different parts of the plant (rhizomes, leaves and stems) between 0.12 and 0.24 mg/g fresh weight, being almost equal in the stems and rhizomes. In addition, *S*-methyl- and *S*-ethylcysteine derivatives have been detected in minute amounts (<3 μg/g fresh wt) in all parts of the plant. 2,4,5,7-Tetrathiaoctane-4-oxide, the primary breakdown product of the amino acid, was also detected and isolated.

Scientific studies have shown that Society Garlic possesses several biological activities which include antioxidant, antimicrobial, anticancer, antiulcerogenic, antithrombotic and antihypertensive properties.

Antioxidant Activity

The antioxidant capacity (oxygen radical absorbance capacity, ORAC value) and total phenolic content for Society Garlic, *Tulbaghia violacea*, was determined as 1.03 μmol of Trolox equivalents (TE)/g of fresh weight, 7.50 mg of gallic acid equivalents (GAE)/g of fresh weight respectively (Zheng and Wang 2001).

Antihypertensive Activity

Tulbaghia violacea was one of the many active plants with antihypertensive properties as determined by the angiotensin-converting enzyme (ACE) inhibition assay; it contained no tannin (Duncan et al. 1999). *T. violacea* leaves had inhibition levels which were above 50 % (aqueous extract gave 72 % inhibition, ethanol extract exhibited 61 % inhibition), while *T. violacea* roots gave 49 and 27 % inhibition for aqueous and ethanol extracts, respectively, with 25 μg plant extract. This was also confirmed in a recent study. A plant was considered to have potential antihypertensive properties if it inhibited the angiotensin-converting enzyme (ACE) and thus the conversion of angiotensin I to angiotensin II by greater than 50 %, and *T. violacea* was one of eight of 16 plants screened that demonstrated ACE inhibitory activity and satisfied these criteria (Ramesar et al. 2008). *T. violacea* in particular showed promise with regard to ACE inhibition as in-vivo administration of this extract showed only a 2.2 % increase in maximum mean arterial pressure when compared to the 14.5 % increase observed in the control group after coadministration with exogenous angiotensin I. Hypertension is treated with medication, including drugs such as angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB). These drugs not only lower blood pressure but also offer additional protection to the brain and heart. ACEI, in particular, provides beneficial properties to patients with type 1 diabetes.

The methanol leaf extract of *Tulbaghia violacea* significantly and dose-dependently reduced the systolic, diastolic, and mean arterial blood pressure and heart rate in male spontaneously hypertensive Wistar rats (Raji et al. 2012). Angiotensin I human acetate salt hydrate (ang I, 3.1–100 μg/kg), angiotensin II human (ang II, 3.1–50 μg/kg), phenylephrine hydrochloride (phenylephrine, 0.01–0.16 mg/kg) and dobutamine hydrochloride (dobutamine, 0.2–10.0 μg/kg) all increased the blood pressure dose-dependently. The hypertensive effect of ang I and the heart rate-increasing effect of dobutamine were significantly decreased by their co-infusion with *T. violacea* (60 mg/kg). However, the co-infusion of ang II or phenylephrine with *T. violacea* (60 mg/kg) did not produce any significant change in blood pressure or heart rate when compared to the infusion of either agent alone in the same animal. The reduction in blood pressure may be due to actions of the *T. violacea* methanol leaf extract on the angiotensin-I-converting enzyme (ACE) and β(1) adrenoceptors.

Anti-atherosclerotic Activity

Co-treatment of rats with an atherosclerogenic (Ath) diet (4 % cholesterol, 1 % cholic acid and 0.5 % thiouracil) and *Tulbaghia violacea* methanolic rhizome extracts (250 and 500 mg/kg body weight) for 2 weeks significantly protected against elevated serum triglyceride (TG), total cholesterol (TC), LDL-cholesterol, VLDL-cholesterol and decreased HDL-cholesterol in a dose-dependent manner when compared with the atherogenic control (Olorunnisola et al. 2012). The extracts also lowered elevated thiobarbituric reacting substance (TBARS) and reversed endothelial dysfunction parameters (fibrinogen and total NO levels) and tissue antioxidant enzyme activities to near normal. The protective ability of the extract was confirmed by the significant reduction in the activities of serum markers of liver (LDH, AST, ALT, ALP, bilirubin) and kidney damage (creatinine and bilirubin) in extract-treated groups compared with the atherogenic control group. Also, the extracts protected against the development of fatty streak plaques (aorta) and fatty changes in hepatocytes. The observed activities of the extracts compared favourably with standard drug atorvastatin. The results showed that the methanol extract of *Tulbaghia violacea* rhizomes could protect against the early onset of atherosclerosis.

Anticancer Activity

Methanol extracts of *Tulbaghia violacea* leaves and bulbs inhibited growth of MCF-7, WHCO3, HT29 and HeLa cancer cell lines (Bungu et al. 2006). At 250 μg/ml, bulb extracts exhibited higher growth inhibition than leaf extracts in MCF-7 (49.6 %), HT29 (26.0 %) and HeLa cells (54.7 %) relative to untreated controls. In WHCO3, the leaf extract was more active, inhibiting growth by 30.3 %. The growth inhibitory activity of *T. violacea* was due to induction of apoptosis in all four cell lines. This was shown by the staining of cells with Hoechst 33342, indicating fragmented nuclear material and condensed chromatin. HeLa and MCF-7 cells treated with bulb extract had higher apoptotic indices than the other two cell lines (HeLa, 25.8 %; MCF-7, 19.0 %). Treated cells stained with annexin V but not with propidium iodide (PI), indicating that the extract induced apoptosis and not necrosis. Using Western blotting, cleavage of poly[ADP-ribose] polymerase-1 (PARP-1) was shown in HeLa cells upon exposure to *T. violacea* bulb extract. These findings provide evidence for anticancer activities in *T. violacea*. The induction of apoptosis by the extract is promising for anticancer therapy as it is desirable for anticancer agents to induce apoptosis. The occurrence of morphological and biochemical changes, typical of apoptosis, in Chinese hamster ovary (CHO) cells treated with the aqueous extract from *T. violacea* was demonstrated (Lyantagaye 2013). Three proapoptotic fractions from the *T. violacea* extract were purified, and methyl-α-D-glucopyranoside was found to be the major component. Methyl-α-D-glucopyranoside was confirmed to be active in the induction of apoptosis.

Antimicrobial Activity

Gaidamashivili and Van Staden (2001) reported *T. violacea* to have antibacterial activities against two Gram-positive bacterial pathogens *Staphylococcus aureus* and *Bacillus subtilis*. *B. subtilis* was aggregated by *Tulbaghia violacea* agglutinins at relatively high concentrations. *Tulbaghia violacea* bulb extract was found to be inhibitory to *Candida albicans*, pathogen of oral candidiasis, which is prevalent in HIV patients, exhibiting an MIC value of 3.25 mg/ml (Motsei et al. 2003). The freshwater extract of *Tulbaghia violacea* maintained activity at 4 °C, but not at higher temperatures.

Methanol extracts (5 mg/100 ml) of *Tulbaghia violacea* showed little free radical scavenging activity against DPPH (29 %) and ABTS (20 %) and exhibited a low reducing power (Ntobaki et al. 2008). However, the extract significantly inhibited the activities of lipoxygenase, xanthine oxidase and other lipid-peroxidative reactions.

Plant extracts exhibited antimicrobial activities against *Staphylococcus aureus*, *Proteus mirabilis* (MIC value <1.0 mg/ml), *Streptococcus faecalis*, *Enterobacter cloacae*, *Escherichia coli*, *Proteus vulgaris* and *Helicobacter pylori* (MIC value = 2.0 mg/ml). The extract was able to protect the stomach lining against indomethacin-induced ulceration. They concluded that *Tulbaghia violacea* root extract had little hydrogen atom donor potential and may not break free radical chain reactions but could act as an antacid. Its potential in the inhibition of free radical generation, along with its antimicrobial activity, justified its use by traditional Zulu healers for the treatment of peptic ulcers and other stomach ailments.

Tulbaghia violacea and *Tulbaghia alliacea* were found to be rich in marasmin, the precursor of the thiosulfinate marasmicin (Kusterer et al. 2011). Marasmicin has attracted considerable attention because of its antifungal and tuberculostatic activities. Somai and Belewa (2011) found that the aqueous extracts of *Tulbaghia violacea* were antifungal and at 10 mg/ml resulted in sustained growth inhibition of greater than 50 % for both *Aspergillus flavus* and *Aspergillus parasiticus*. *T. violacea* extract inhibited conidial germination in a dose-dependent manner.

The petroleum ether (PE) extracts of micropropagated *T. violacea* plants and dichloromethane (DCM) extracts of outdoor-grown plants showed good antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* (Ncube et al. 2011). PE extracts of micropropagated plants showed the best antibacterial activity with a minimum inhibitory concentration (MIC) of 0.39 mg/ml against *Bacillus subtilis.* Good MIC (<1 mg/ml) and minimum fungicidal concentration (MFC) values of 0.78 mg/ml were only obtained in DCM extracts of outdoor-grown plants against *Candida albicans*. MIC and MFC values for water and ethanol extracts of both micropropagated and outdoor-grown plants were similar and in the range 3.125–12.5 mg/ml. Total phenolics, gallotannins, flavonoids and saponins were significantly higher in micropropagated plants than in outdoor-grown ones. In all cases, the contents of phytochemical compounds in micropropagated plants were more than twice that of outdoor-grown plants except for condensed tannins.

Antithrombotic Activity

The bulb and leaf extracts of *T. violacea* exhibited antithrombotic activities which were higher than those found in garlic (Bungu et al. 2008). The IC_{200} values for the leaf and the bulb extract were 0.4 and 0.3 mg/ml, respectively, for the thrombin-induced clotting time (TT) assay. The IC_{50} value was 1.73 mg/ml for the bulb extract of the *T. violacea*. No IC_{50} was obtained for the leaf extract of *T. violacea*. It was also that *T. violacea* exhibited biological activities which were comparable to garlic. These results indicated that *T. violacea* could be used as an alternative to garlic and that it may contribute to pharmaceutical applications and informal health services.

Androgenic Activity

Treatment of male Balb/C mice testicular cells with *Tulbaghia violacea* (312.5–5,000 μg/ml) significantly increased luteinizing hormone (LH)-induced testosterone production as compared to vehicle-treated control (DMSO), whereas testicular cells without LH treatment showed no significant change in testosterone concentrations (Ebrahim and Pool 2010). The data indicated that *T. violacea* had androgenic properties.

Antidiabetic Activity

In an antidiabetic screening of five South African medicinal plants, the ethanol extracts of *Ruta graveolens* (136.9 %) and *Tulbaghia violacea* (140.5 %) produced the highest increase in glucose utilization in C2C12 muscle cells (van Huyssteen et al. 2011).

Traditional Medicinal Uses

Society Garlic is widely used as a herbal remedy for various ailments in traditional medicine, with leaves and bulbs the most commonly used. Its medicinal uses include: treatment for fever and colds, asthma, tuberculosis, high blood pressure, oesophagus cancer, stomach problems such as gastroenteritis, abdominal pain and acute inflammation and sloughing of the intestinal mucosa; and contraction and subdued reaction of the pupils to stimuli (Duncan et al. 1999; van Wyk and Gericke 2000; Gericke et al. 2002; Lyantagaye 2013; Ntobaki et al. 2008). The fresh bulbs are boiled in water, and the decoctions are taken orally to clear up coughs and colds. The bulb has been used as a remedy for pulmonary tuberculosis and to destroy intestinal worms. The leaves of the plant are used to treat oesophageal cancer. Leaves when crushed on the skin will repel fleas, ticks and mosquitoes. Zulus use the bulb to make an aphrodisiac medicine. The crushed leaves may be used to help cure sinus headaches and to discourage moles from the garden (by their strong smell). The smell repels fleas, ticks and mosquitoes when crushed on the skin.

Other Uses

Society Garlic is a popular container plant and is also cultivated in a sunny border, as a bedding plant and in rock garden. It is reported that Society Garlic, planted in a row or border, will deter moles. Wild garlic is a very good snake repellent, and for this reason the Zulus plant it around their homes.

T. violacea has antimicrobial activity against plant pathogens. Crude methanol extracts *of T. violacea* aerial and below-ground parts were found to exhibit antibacterial and broad-spectrum antifungal activity against plant pathogens (Nteso and Pretorius 2006). The extracts significantly inhibited in-vitro growth of *Clavibacter michiganensis*, *Ralstonia solanacearum* and *Xanthomonas campestris*. The extracts significantly inhibited the mycelial growth of six of the seven test fungi, *Botrytis cinerea*, *Sclerotium rolfsii*, *Rhizoctonia solani*, *Mycosphaerella pinodes*, *Botryosphaeria dothidea* and *P. Pythium ultimum*, whereas only the below-soil extract inhibited the mycelial growth of *Fusarium oxysporum* significantly.

Comments

Society Garlic is most readily propagated via the division of large clumps of plants.

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Plumeria obtusa

Scientific Name

***Plumeria obtusa* L.**

Synonyms

Plumeria obtusa var. *typica* Woodson nom. inval.

Family

Apocynaceae

Common/English Names

Frangipani, Pagoda Tree, Red Jasmine, Red Jasmine of Jamaica, Red Paucipan, Singapore Frangipani, Singapore Graveyard Flower, Singapore White Plumeria, Temple Tree, White Kalachuche

Vernacular Names

Brazil: Jasmim-De-Caiena, Jasmim-Do-Pará, Jasmin-Manga (Portuguese)
Chinese: Hong Ji Dan Hua
Cuba: Lirio Colorado
French: Frangipanier
German: Rote Frangipani
India: Kathgolop (Bengali), Champa (Hindi), Chaempae (Konkani), Khageleihao Angouba (Manipuri), Arali (Tamil)
Malaysia: Frangipani, Kemboja
Mexico: Caxtaxanat, Flor De Mayo, Tenech Coahuitl
Panama: Caracucho Colorado
Philippines: Kalasuting-Puti
Peru: Caracucho, Suche
Portuguese: Flor-De-Santo-Antônio
Spanish: Alhelí, Alhelí Cimarrón, Suche
Sri Lanka: Araliya
Swedish: Frangipani
Thai: Dtôn Lân Tom KăAo, Dtôn Lân Tom Lôok Pà-Sŏn, Dtôn-Lee-Laa-Wá-Dee
Vietnamese: Đại Lá Tù; Đại Lá Tà; SứLá Tù

Origin/Distribution

Plumeria obtusa is indigenous to the Greater Antilles, northern Central America and southern–eastern Mexico to Belize, Florida Keys and the Caribbean.

Agroecology

Though tropical by nature, when protected from frost, they are well suited to subtropical climates in the United States in states bordered by the Gulf of Mexico, and in southern California. They are prolific in Hawaii. Plumeria are valued as landscape plants and ornamentals and for their flowers. Singapore plumeria has larger flowers compared to *Plumeria rubra*, and the longish petals are almost not overlapping. Leaves do not have

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pointed ends like plumeria rubra and are rather blunt.

Edible Plant Parts and Uses

Edible flowers consumed as vegetable and used as ingredients in cooking salad and frying (Facciola 1990; Wetwitayaklung et al. 2008; Wongwattanasathien et al. 2010; Kaisoon et al. 2001).

Botany

Large shrub or small tree growing to 5 m high. Stem, branches and leaves with milky sap; branches pale-green, thick and fleshy. Leaves alternate, mostly clustered at branch tips, petiolate, obovate to oblong-obovate, to 25 cm long, dark green and shiny adaxially, tertiary venation strongly prominent abaxially, apex rounded (Plates 1, 2, 3 and 4). Inflorescence of axillary or terminal dichotomous cymes (Plates 2 and 3). Flowers large, fragrant, waxy and showy with large deciduous bracts. Calyx 5-lobed, lobes equal or subequal. Corolla salverform or funnel shaped, white, 4 cm across, throat yellow, lobes 5, spreading, slightly recurved. Stamens inserted at or near base of corolla tube (Plates 2, 3 and 4). Ovaries 2, distinct; ovules numerous, multiseriate on each placenta. Style short with obtusely bifid apex. Follicles 2. Seeds many, flat proximally, with a membranous wing.

Plate 1 Leaves clustered at branch tips

Nutritive/Medicinal Properties

Flower Phytochemicals

Forty-seven components were identified in the essential oil of fresh *Plumeria obtusa* flowers, representing 97 % of the oil, with benzyl salicylate

Plate 2 Terminal cymose inflorescence

Plate 3 Large leaves with prominent venation on the lower surface

Plate 4 Close view of flowers and leaves

(39 %), benzyl benzoate (11 %), (2*E*, 6*E*)-farnesol (8 %) and (*E*)-nerolidol (5 %) as major constituents (Kamariah et al. 1999). The remaining identified constituents of the oil (34 %) were found as minor constituents (≤3 %). Some of the minor components included geraniol, nonadecane, (*E*)-nerolidol, heneicosane, (2*Z*,6*Z*)-farnesol, (2*E*,6*Z*)-farnesol, (2*E*,6*E*)-farnesol, geranyl linalool, neryl benzoate, geranyl benzoate, benzyl benzoate, myristic acid, benzyl salicylate and hexadecanoic acid. The essential oil of *P. obtusa* flower was found to be rich in benzyl salicylate (45.4 %) and benzyl benzoate (17.2 %) (Norsita et al. 2006). Other components were (*E*,*E*)-farnesol 4.8 %, methyl stearate 3.7 %, neryl phenylacetate 2.6 %, (*E*)-nerolidol 2.5 %, geraniol 2.3 %, ethyl palmitate 2.2 %, 1-octadecene 2.0 % and linalool 1.9 % with minute content of alkanoic acids.

An iridoid beta-glucoside, namely, plumieride coumarate glucoside, and a β-glucosidase were isolated from *P. obtusa* flower (Boonclarm et al. 2006). The β-glucosidase purified to homogeneity exhibited high specificity for its natural substrate, plumieride coumarate glucoside, hydrolyzing it to its corresponding 13-*O*-coumarylplumieride. The enzyme showed poor hydrolysis of 4-methylumbelliferyl-β-glucoside and esculin and did not hydrolyze alkyl-β-glucosides, glucobioses, cyanogenic-β-glucosides, steroid β-glucosides, nor other iridoid β-glucosides.

The soluble phenolic acids (per g dry weight) identified in *P. obtusa* flower extract were gallic acid 25.5 μg, protocatechuic acid 3.5 μg, *p*-hydroxybenzoic acid 21.7 μg, vanillic acid 20.4 μg, chlorogenic acid 22.8 μg, caffeic acid 12.8 μg, syringic acid 7.4 μg, *p*-coumaric acid 8.3 μg, ferulic acid 9.8 μg, sinapic acid 149.3 μg and total phenolic acid 281.5 μg (Kaisoon et al. 2001). The flowers contained 329.9 μg total bound phenolic acid made up of gallic acid 2.7 μg, *p*-coumaric acid 17.8 μg, ferulic acid 144.9 μg, and sinapic acid 164.5 μg. The flowers contained 702.5 μg total soluble flavonoid made up of rutin 500.3 μg, myricetin 5.06 μg, quercetin 193.6 μg and kaempferol 3.58 μg, and bound flavonoid 46.8 μg made up of 41.7 quercetin μg and apigenin 5.1 μg. The DPPH radical scavenging activity (% inhibition) of soluble and bound phenolic fraction of the flower was 69.65 and 60.52 %, respectively. The reducing potential of the soluble and bound phenolic fractions of the flower as evaluated by FRAP (ferric reducing antioxidant power) assay (mmol $FeSO_4$/100 g dry weight) were 26.03 and 60.1 mmol, respectively.

The percentage yield of *P. obtusa* flower extracts by water distillation, steam distillation, water–steam distillation, hexane extraction, petroleum ether extraction, and cold and hot enfleurage were 0.0167, 0.0045, 0.0342, 0.4170, 0.3510, 0.3969 and 12.2400 %, respectively (Pitpiangchan et al. 2009). Different extraction methods yielded different chemical compounds and yield. The major chemical components in the essential oils from all distillation methods and both solvents was benzyl salicylate, but the extracts from cold and hot enfleurage were linalool and n-undecanoic acid, respectively. Nineteen compounds were identified in the flower essential oil from water distillation: benzyl salicylate 31.32 %, benzyl benzoate 18.90 %, (*E*)-farnesol 6.70 %, (*Z*)-β-farnesene 4.85 %, linalool 4.72 %, (*E*)-farnesal 4.37 %, (*Z*)-geraniol 4.36 %, (*E*)-geraniol 3.79 %, (*E*)-citral 3.66 %, heneicosane 2.89 %, (*Z*)-farnesol 2.61 %, 1-octadecanol 2.71 %, (*Z*)-citral 2.02 %, α-farnesene 1.97 %, eicosane 1.65 %, (*E*)-farnesyl acetate 1.33 %, 1-hexadecene 1.22 %, (*E*)-farnesyl acetate 0.61 % and 2-methylpentadecane 0.33 %. Thirteen compounds were identified from steam distillation: benzyl salicylate 27.58 %, (*Z*)-geraniol 13.70 %, (*E*)-geraniol 12.15 %, linalool 11.18 %, benzyl benzoate 9.89 %, (*E*)-farnesol 6.95 %; (*Z*)-β-farnesene 4.68 %, (*E*)-citral 4.60 %, (*Z*)-citral 2.54 %, (*E*)-farnesol 2.36 %, α-farnesene 2.27 %, (*Z*)-farnesol 1.41 % and 1-octadecanol 0.69 %. Twenty-one compounds were found in the essential oil from water–steam distillation: benzyl salicylate 31.90 %, benzyl benzoate 13.28 %, (*E*)-farnesol 9.29 %, linalool 6.49 %, (*Z*)-β-farnesene 5.03 %, (*Z*)-geraniol 4.33 %, (*E*)-farnesal 3.42 %, heneicosane 3.20 %, (*E*)-geraniol 3.12 %, (*E*)-citral 3.09 %,1-octadecanol 3.04 %, α-farnesene 2.62 %, (*Z*)-farnesol 2.14 %, eicosane 1.95 %, unknown2 1.69 %, (*Z*)-citral 1.66 %,1-hexadecene 1.40 %, (*E*)-farnesyl acetate 1.05 %, unknown1 0.46 %,2-methylpentadecane 0.45 % and (*E*)-β-farnesene 0.39 %. Hexane extraction afforded

17 compounds: benzyl salicylate 44.69 %, benzyl benzoate 11.67 %, (*E*)-farnesol 7.22 %, (*Z*)-nerolidol 5.53 %, (*Z*)-geraniol 3.93 %, isoeicosane 3.69 %, linalool 3.66 %, (*E*)-geraniol 3.10 %, (*E*)-farnesal 2.84 %,1-octadecanol 2.80 %, (*E*)-geranylacetone 2.72 %, α-farnesene 2.56 %, (*Z*)-farnesol 1.74 %, unknown2 1.43 %, 1-hexadecene 0.88 %, unknown1 0.84 % and 2,4-di-t-butylphenol 0.69 %. Petroleum ether extraction gave 13 compounds: benzyl salicylate 42.63 %, benzyl benzoate 10.64 %, (*E*)-farnesol 9.49 %, (*Z*)-nerolidol 6.53 %, linalool 6.04 %, (*E*)-geraniol 4.44 %, isoeicosane 4.12 %, (*E*)-geranylacetone 3.96 %, α-farnesene 3.39 %, 1-octadecanol 3.33 %, (*E*)-farnesal 2.72 %, (*Z*)-farnesol 1.54 % and 1-hexadecene 1.16 %. Thirteen compound were obtained by cold enfleurage: linalool 23.13 %, benzyl salicylate 15.62 %, benzyl benzoate 14.73 %, (*E*)-farnesal 9.04 %, (*Z*)-β-farnesene 8.16 %, (*Z*)-geraniol 8.31 %, (*E*)-geraniol 4.69 %, (*Z*)-farnesol 4.67 %, (*E*)-citral 4.14 %, (*E*)-farnesol 3.40 %, (*Z*)-citral 1.87 %, (*E*)-nerolidol 1.42 % and (*E*)-β-farnesene 0.81 %. Twelve compound were obtained by hot enfleurage: n-undecanoic acid 31.75 %, benzyl benzoate 9.72 %, benzyl salicylate 9.70 %, (*E,E*)-2,4-dodecadienal 8.49 %, (*E*,*E*)-2,4-decadienal 6.69 %, ethyl pentadecanoate 5.94 %, farnesol 7.91 %, geranyl valerate 4.84 %, unknown1 4.01 %, octanoic acid 3.94 %, linalool 3.80 % and 193 unknown 3.22 %. The major volatile constituents of *Plumeria obtusa* white flowers, Klao Puang (L4), were *L*-linalool, geranial 17.97 %, neral 12.5 % and benzaldehyde 5.46 % (Chitsamphandhvej 2010).

Fourteen chemical constituents were identified in the essential oil of *P. obtusa* flowers: linalool; farnesol; *trans*-farnesol; benzyl benzoate; tetradecan-1-ol; 2,3-dimethyl butane; nonadecane; heneicosane; 1 heptadecene; benzyl salicylate; 9-eicosene-(*E*); nerolidol; tricosane; and eicosane (Sulaiman et al. 2008).

Phytochemicals in Other Plant Parts

Iridoids isoplumericin, plumericin, plumieride, plumieride coumarate and plumieride coumarate glucoside were isolated from *P. obtusa* plant parts (Coppen and Cobb 1983). Pentacyclic triterpenoids isolated from *Plumeria obtusa* leaves included betulinic acid, oleanolic acid and ursolic acid, and obtusalin elucidated as 3β,27-dihydroxylup-12-ene (Siddiqui et al. 1989); 2α,3β-dihydroxy-24-*p*-*E*-coumaroyloxyurs-12-en-28-oic acid; 3β-hydroxy-11-oxours-12-en-28-oic acid; 3β,24-dihydroxyurs-12-en-28-oic acid; 3β-hydroxy-28-*p*-hydroxyphenoxyurs-12-en-27-oic acid; 3β-hydroxy-27-*p*-hydroxyphenoxyurs-12-en-28-oic acid (Siddiqui et al. 1990); kaneroside, oleandrin, α-amyrin, neriucoumaric acid, isoneriucoumaric acid, alphitolic acid, oleanolic acid, methyl *p*-*E*-coumarate, scopoletin and tow new triterpenes obtusin and obtusilic acid characterized as the 24-*E* and 27-*Z*-*p*-coumaric esters of the novel 3β,24-dihydroxyurs-12-en-28-oic acid and 3β,27-dihydroxyurs-12-en-30-oic acid, respectively (Siddiqui et al. 1992); obtusol and zamanic acid elucidated as 3β,27-dihydroxyurs-12-ene and 3β-hydroxyurs-30-*p*-*E*-hydroxycinnamoyl-12-en-28-oic-acid (Siddiqui et al. 1999). Two new iridoids 6″-*O*-acetylplumieride *p*-*E*-coumarate and 6″-*O*-acetylplumieride *p*-*Z*-coumarate and three known iridoids as plumieride, plumieride *p*-*Z*-coumarate and plumieride *p*-*E*-coumarate were isolated from the fresh, whole spring leaves of *Plumeria obtusa* (Siddiqui et al. 1994). Begum et al. (1994) reported the isolation of 32 constituents from *P. obtusa* leaves: 12 new pentacyclic triterpenoids obtusalin, obtusin, obtusinin, obtusilin, obtusidin, obtusinidin, obtusilinic acid, obtusic acid, obtusilinin, courmarobtusanoic acid, courmarobtusane and obtusilic acid; two new iridoids 6′-*O*-acetylplumieride *p*-*E*-coumarate and 6″-*O*- acetylplumieride *p*-*Z*-coumarate besides the known constituents; 11 pentacyclic triterpenoids betulinic acid, oleanolic acid, ursolic acid, α-amyrin, neriucoumaric acid, isoneriucoumaric acid, alphitolic acid, 3β,23-dihydroxyurs-12-en-28-oic acid, 27-*p*-*Z*-coumaroyloxyursolic acid, 27-*p*-*E*- coumaroyloxyursolic acid and oleanolic acid; two cardiac glycosides kaneroside and oleandrin; three iridoids plumieride, plumieride *p*-*Z*-coumarate and plumieride *p*-*E*-coumarate; a cinnamic acid derivative methyl *p*-*E*-coumarate; and a coumarin scopoletin.

Two new iridoid obtusadoids A and B along with eight known compounds plumieridin A; plumieridine; 1α-plumieride; 15-demethylplumieride;

rel-(3R,3′S,4R,4′S)-3,3′,4,4′-tetrahydro-6,6′-dimethoxy[3,3′-bi-2H-benzopyran]-4,4′-diol; glochiflavanoside B; oleanolic acid; and methyl coumarate were isolated from the methanol extract of *Plumeria obtusa* (Saleem et al. 2011).

The following chemical constituents were isolated from the fresh leaves and stem bark of *Plumeria obtusa*: four new triterpenoids dammara-12,20(22)-*Z*-dien-3-one; dammara-12,20(22)*Z*-dien-3β-ol; olean-12-en-3β,27-diol; and 27-hydroxyolean-12-en-3-one and 12 known compounds, which included eight triterpenoids dammara-3β,20(S),25-triol; urs-12-en-3β-hydroxy-27-*Z*-feruloyloxy-28-oic acid; 3β-hydroxyolean-12-en-28-oic acid; 3β,27-dihydroxylupan-29-ene; 3β-hydroxylupan-29-en-28-oic acid; 3β-hydroxyursan-12-en-28-oic acid; 3β-hydroxy-27-*p*-coumaroyloxy-olea-12-en-28-oic acid; and urs-2-en-3-one); an iridoid 1α-plumieride; a cardenolide 3α,14β-dihydroxy-17β-card-20(22)-enolide; a fatty acid ester methyl *n*-octadecanoate; and a steroid 3β-hydroxy-Δ^5-stigmastane (Siddiqui et al. 2004).

Antiproliferative Activity

Leaf extracts of *Plumeria obtusa* displayed antiproliferative activity using the sulforhodamine B assay (Wong et al. 2011). The dichloromethane, methanol and water extract of *Plumeria obtusa* flowers were found not to be mutagenic for *Salmonella typhimurium* strains TA 98 and TA 100 without metabolic activation (Wongwattanasathien et al. 2010). However, after being treated with sodium nitrite in acid solution, the dichloromethane extract of *Plumeria obtusa* was mutagenic on both tester strains, suggesting that consumers who consume these flowers should avoid any nitrite-containing food items.

Antimicrobial Activity

The essential oil of *P. obtusa* flowers exhibited broad spectrum of inhibition of *Staphylococcus aureus* and *Bacillus cereus* (Gram-positive bacteria), *Candida albicans* and *Candida humicola* (yeast) and *Trichophyton mentagrophytes*, *T. rubrum* and *Microsporum canis* (fungi). The largest inhibition zone was l against *C. humicola* (Sulaiman et al. 2008).

Antimutagenic Activity

The dichloromethane of *P. obtusa* flowers inhibited the mutagenicity of the reaction product of 1-aminopyrene nitrite model in the absence of metabolic activation on both *Salmonella typhimurium* strains TA 98 and TA 100, while the methanol flower extract exerted similar effect on TA 98 (Wongwattanasathien et al. 2010). The water–flower extract exhibited highest antimutagenic activity on strain TA 98. The results indicated that the flowers were safe to be consumed.

Antiulcerogenic Activity

The methanol stem bark extracts were found to be effective in healing of gastric ulcers induced by pylorus ligation and indomethacin in rats (Singh et al. 2012). The authors attributed this antiulcerogenic effect to reduction in gastric acid secretion and gastric cytoprotection and proton pump inhibition mechanism.

Algicidal Activity

Iridoids isoplumericin, plumericin, plumieride, plumieride coumarate and plumieride coumarate glucoside were isolated from *P. obtusa* plant parts (Coppen and Cobb 1983). All except for plumieride showed algicidal activity. Roots, and in particular the root bark, contained the highest concentrations of iridoids. Isoplumericin and plumericin, the compounds with the strongest algicidal activity, were rarely found in aerial parts. *Plumeria* samples were found to contain two further highly polar, but unidentified, iridoids.

Traditional Medicinal Uses

A total of 24 plant species including *Plumeria obtusa* were used by Bapedi traditional healers to

treat diabetes mellitus in South Africa (Semenya et al. 2012). *Plumeria obtusa* and *Momordica balsamina* were exclusively used to treat diabetes mellitus, and only in the Sekhukhune District.

Other Uses

Plumeria species including *P. obtusa* are suitable for landscape plantings. The flowers of all *Plumeria* species are utilized to make leis in Hawaii. The flowers are also used for making wreaths and garlands.

Comments

Plumeria species may be easily propagated from cuttings of leafless branch tips in spring. Cuttings are allowed to dry at the base before planting in well-drained soil.

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Plumeria rubra

Scientific Name

***Plumeria rubra* L.**

Family

Apocynaceae

Synonyms

Plumeria acuminata W.T.Aiton, *Plumeria acutifolia* Poir., *Plumeria acutifolia* var. *gasparrini* A.DC., *Plumeria angustifolia* A.DC., *Plumeria arborea* Noronha, *Plumeria arborescens* G.Don, *Plumeria aurantia* Endl., *Plumeria aurantia* Lodd. ex G.Don, *Plumeria aurantiaca* Steud., *Plumeria bicolor* Ruiz & Pav., *Plumeria blandfordiana* Lodd. ex G.Don, *Plumeria carinata* Ruiz & Pav., *Plumeria conspicua* G.Don, *Plumeria gouanii* D.Don ex G.Don., *Plumeria incarnata* Mill., *Plumeria incarnata* var. *milleri* (G.Don) A.DC., *Plumeria jamesonii* Hook., *Plumeria kerrii* G.Don, *Plumeria kunthiana* Kostel., *Plumeria lambertiana* Lindl., *Plumeria loranthifolia* Müll.Arg., *Plumeria lutea* Ruiz & Pav., *Plumeria macrophylla* Lodd. ex G.Don, *Plumeria megaphylla* A.DC., *Plumeria mexicana* Lodd., *Plumeria milleri* G.Don, *Plumeria mollis* Kunth, *Plumeria northiana* Lodd. ex G.Don, *Plumeria purpurea* Ruiz & Pav., *Plumeria rubra* f. *acuminata* (W.T.Aiton) Woodson, *Plumeria rubra* f. *acutifolia* (Poir.) Woodson, *Plumeria rubra* f. *lutea* (Ruiz & Pav.) Woodson, *Plumeria rubra* f. *tricolor* (Ruiz & Pav.) Woodson, *Plumeria rubra* f. *typica* Woodson, nom. inval., *Plumeria rubra* var. *acuminata* (W.T.Aiton) R.S.Rao & Balamani, *Plumeria tenuifolia* Lodd. ex G.Don, *Plumeria tricolor* Ruiz & Pav.

Common/English Names

Common Frangipani, Frangipani, Graveyard Tree, Hawaiian Lei Flower, Nose Gay, Pagoda Tree, Red Frangipani, Red Jasmine, Red Jasmine Of Jamaica, Red Paucipan, Temple Flower, Temple Tree, Tree of Life, West Indian Jasmine

Vernacular Names

Aztec: Cacalloxochitl
Brazil: Jasmim-De-Caiena, Jasmim-Do-Pará, Jasmin-Do-Pará, Jasmin-Manga
Burmese: Mawk-Sam-Ka, Mawk-Sam-Pailong, Sonpabataing, Tayok-Saga, Tayoksaga-Ani
Canary Islands: Flor De Cebo
Chinese: Hong Ji Dan Hua, Ji Dan Hua, Kang Nai Xin
Chuukese: Seewurun, Seur
Cuba: Lirio Colorado
Czech: Plumérie Červená, Plumérie Ostrolistá
Danish: Mexican Frangipani, Pagodetræ
El Salvador: Flor De Mayo
French: Frangipanier
German: Frangipani, Roter Frangipani
Guatemala: Flor De La Cruz
Hawaii: Pumeli, Melia

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India: Deva Ganneru (Andhra Pradesh), Frangipani, Goburchampa, Kath Champa, Kath Golap (Bengali), Dolochampo, Rhada Champo (Gujarati), Chameli, Gulachin, Gulechin, Lal Gulachin (Hindi), Chaempae (Konkani), Vellachampakam (Malayalam), Khageleihao Angouba, Khera Chapha, Pandhra Chapha, Sonchampa (Marathi), Kishirachampa (Sanskrit), Arali, Kallimandarai, Perungalli, Sampangi (Tamil), Vadaganneru (Telugu), Achin (Urdu)
Indonesia: Kamboja, Sambija, Semboja (Java), Kamoja, Samoja (Sundanese)
Italian: Fragipane, Pomelia
Khmer: Champei
Kosraen: For
Laos: Champa, Dok Champa
Malaysia: Kemboja, Bunga Kemboja, Chempaka, Cempaka muliya, Chempa Raya, Chempaka Biru, Pokok Kubur, Bunga Kubur
Mexico: Caxtaxanat, Flor De Mayo, Tenech Coahuitl
Nicaragua: Flor De Leche, Sacuanjoche
Pakistan: Champa
Palauan: Chelilai
Panama: Caracucho Colorado
Persian: Gulacin
Peru: Caracucho, Suche
Philippines: Kalachuche (Bikol), Kachuchi (Cebu Bisaya), Kalanuche, Kalonoche (Iloko), Kalachuche, Kalasusi, Kalatsutsi, Karachucha Karatuche (Tagalog)
Pohnpeian: Pwohmaria
Portuguese: Flor-De-Santo-Antônio
Puerto Rico: Alhelí
Sicily: Pomelia
Spanish: Alhelí Cimarrón, Suche
Sri Lanka: Araliya, Pansal Mal
Tahiti: Tipanier
Thailand: Champa Lao, Champa Khawm, Rantom, Lantom, Leelawadee
Venezuela: Amapola
Vietnam: Sú Cúi, Đai
Yapese: Suwur

Origin/Distribution

Plumeria rubra is native to Mexico, Central America and Venezuela. From its native range, it has been distributed to all tropical areas of the world, especially Hawaii, where it flourishes abundantly.

Agroecology

It thrives in tropical to subtropical areas with warm temperature of 20–32 °C and evenly distributed annual rainfall of 1,000–2,000 mm. It is rather drought hardy but will lose its leaves under prolonged drought. In subtropical areas, it needs to be frequently watered in summer but sparingly so in winter. Frangipani does best in well-drained, fertile soils in full sun or partial shade.

Edible Plant Parts and Uses

The fruits and flowers are edible (Burkill 1966; Kunkel 1984; Facciola 1990; Hu 2005). The fruits are reported eaten in the West Indies. The flowers are eaten in sweetmeats and together with betel nut for ague. The flowers are dried and used for herbal teas. It is one of five floral components in the popular Chinese cooling herbal beverage 'Five Flower Tea.'

Botany

Small, deciduous tree to 8 m high with pale greenish-brown, smooth, thin bark becoming rough with age. Branches swollen and leafy at the tips. Latex copious and milky white. Leaves alternate, glossy dark green on long stout petioles. Lamina simple, elliptic to narrowly elliptic, large, 15–30 cm by 6–8 cm, base acute, apex acute to acuminate, margin entire, glabrous, unicostate with 30–40 pairs of lateral veins (Plates 1, 2, 3 and 4). Inflorescences terminal, 2–3-branched cymes, 2–4-flowered with deciduous bracts. Flowers large and showy, sweetly fragrant, bracteolate, pedicellate, bisexual, actinomorphic, pentamerous, perigynous, 5–7 cm diameter. Calyx synsepalous, five obtuse lobes. Corolla sympetalous, salverform, tube cylindrical, five obovate lobes, contorted, overlapping to the left; lobes pink, red, yellow, or white, with a yellow base (Plates 1, 2, 3, 4 and 5). Stamens 5,

Plate 1 Red-flowered cultivar

Plate 2 Acute tip leaves and red-yellow flowers of a bicoloured cultivar

Plate 3 Close view of the red-yellow flowers

epipetalous alternate the lobes, inserted in corolla tube; the anthers dithecous and linear-oblong. Ovaries 2, distinct, half inferior, each ovary 1-carpelled, 1-loculed with parietal placentation, the ovules numerous in each, the style

Plate 4 Acute-tipped leaves and flowers of white-yellow flowered cultivar

Plate 5 Close view of white-yellow flowers

1, the stigma single and massive. Fruit follicles linear-oblong, 11–25 × 2–3 cm. Seeds oblong, plano-convex, winged, with thin fleshy endosperm.

Nutritive/Medicinal Properties

Flowers, leaves and bark of *Plumeria rubra* contain many bioactive compound with anti-cancerous, antiinflammatory and antimicrobial activities.

Phytochemicals from Flowers

P. rubra flowers were found to contain tannins, flavonoids, terpenoids, reducing sugars and alkaloids (Egwaikhide et al. 2009). Two iridoid

diastereoisomers were isolated from the flowers of *Plumeria rubra* cv. *acutifolia* (Ye et al. 2008). A new iridoid alkaloid containing a spironolactone unit, plumericidine, was isolated from the flowers of *Plumeria rubra* L. cv. *acutifolia* (Ye et al. 2009). Two anthocyanins cyanidin 3-*O*-β-(2″-glucopyranosyl-*O*-β-galactopyranoside) (75 %) and cyanidin-3-*O*-β-galactopyranoside (20 %) were isolated from ornamental reddish flowers of *Plumeria rubra* (Byamukama et al. 2011).

Norsita et al. (2006a) reported *P. rubra* pink flowers to have the following main volatile constituents: lauric acid (30.8 %), myristic acid (17.4 %), palmitic acid (9.8 %), nonadecane (8.2 %), methyl stearate (5.6 %), linalool (4.8 %), docosane (2.8 %) and tricosane (2.8 %); *P. rubra* orange flowers to have linalool (3.3 %), α-fenchyl alcohol (2.1 %), geraniol (4.1 %), (*E*)-nerolidol (14.4 %), caryophyllene oxide (3.1 %), (*E*,*E*)-farnesol (4.4 %), benzyl benzoate (8.6 %), myristic acid (2.9 %). 2-phenyl benzoate (3.9 %), benzyl salicylate (20.9 %), 2,6,10,14-teyramethy lheptadecane (2.8 %), neryl phenylacetate (4.1 %), palmitic acid (4.4 %) and ethyl palmitate (3.1 %); reddish-orange flowers to have *n*-nonadecane (3.6 %), *n*-heneicosane (4.1 %), tricosane (3.6 %), docosane (2.7 %), pentyl benzoate (4 %), benzyl benzoate (4 %), phenylethyl benzoate (12.3 %), benzyl salicylate (4.1 %), methyl stearate (3.4 %), phenylethyl cinnamate (2 %), lauric acid (11.8 %), myristic acid (3.9 %), palmitic acid (9.3 %) and linalool (5.3 %); *P. rubra* red flowers to have *n*-nonadecane (2 %), methyl stearate (3.3 %), lauric acid (10.6 %), myristic acid (18.9 %), palmitic acid (27.2 %), linoleic acid (20.7 %), linalool (2.1 %) and terpinene-4-ol (3.7 %). Norsita et al (2006b) also reported *P. acuminata* yellowish-white flowers to have the following main volatile components: benzyl salicylate (39 %), benzyl benzoate (17.2 %), (*E*)-nerolidol (10.6 %), neryl phenylacetate (10.5 %), linalool (8.9 %), cinnamyl cinnamate (2.9 %), geranial (2.6 %) and camphor (1.9 %) and *P. acuminata* yellow flowers to have palmitic acid (36.2 %), linoleic acid (16.8 %), lauric acid (10.4 %), myristic acid (10.3 %), pentacosane (8.1 %), tricosane (%.1 %) methyl stearate (4.4 %). Earlier Pino et al. (1994) reported the following main volatiles from *P. rubra* var. *acutifolia* flowers: *n*-butyl oleate (13.8 %), *n*-butyl palmitate (11.5 %), methyl palmitate (9.7 %), methyl oleate (9.3 %), linalool (8.2 %), α-terpineol (7.63 %), cinnamyl alcohol (6.3 %), *n*-butyl stearate (5.3 %), benzoic acid (4.3 %), *trans, trans*-farnesol (3.2 %) and methyl stearate (2.8 %).

The major volatile constituents of *Plumeria rubra* white-yellow flowers (L2) were L-linalool, benzaldehyde 22.07 %, methyl salicylate 8.1 %, nerolidol 4.65 %, *trans*-β-ocimene 3.28 % and geranial 3.08 % (Chitsamphandhvej 2010). The major volatile constituents of *Plumeria* sp. pink flowers (L1) were L-linalool 37.61 %, benzene ethanol 20.71 %, *trans*-geraniol 12.66 %, methyl benzoate 8.86 %, benzene acetonitrile 3.73 %, linalool oxide 3.37 % and nerolidol 0.95 %. The major volatile constituents of *Plumeria rubra*, Leung Angthong (L3) flowers, were *trans-β-ocimene* 48.73 %, benzene methanol 12.1 %, benzene ethanol 8.98 %, methyl salicylate 7.18 %, methyl benzoate 6.21 %, L-linalool 4.68 %, *trans*-geraniol 3.06 %, benzene acetonitrile 2.9 %, benzaldehyde 1.46 % and linalool oxide 1.03 %. The major volatile constituents of *Plumeria rubra* red flowers (L5) were isoamyl alcohol 17.96 %, *trans*-geraniol 11.86 %, benzene ethanol 8.51 %, 2-methyl-1-butanol 6.01 %, 2-methyl-2-butenal 4.47 %, benzene acetonitrile 2.34 %, methyl benzoate 1.16 % and L-linalool 1.15 %.

A total of 74 compounds were identified in the essential oil of *Plumeria rubra* forma *acutifolia* (Poir.) Woodson cv. 'Common Yellow' flowers (Omata et al. 1991). Linalool (14.1 %), phenylacetaldehyde (16.1 %), *trans, trans*-farnesol (11 %), β-phenylethyl alcohol (8.8 %), geraniol (5.4 %), α-terpineol (2.8 %), neral and geranial were found to make a major contribution to the floral scent of the flower, the last two comprised 0.9 %. A total of 67 compounds were identified in the essential oil of *Plumeria rubra* 'Irma Bryan' flowers (Omata et al. 1992). β-phenylethyl alcohol (31.6 %), phenylacetaldehyde (12.1 %) and methyl cinnamate (1 %) were found to make a major contribution to the floral spicy scent of the flower, while 2-methylbutan-1-ol (10.5 %) did

not contribute to its scent. Forty-three components were identified from the flower essential oil of *Plumeria rubra* var. *acutifolia* (Li et al 2006). The main components were fatty acid such as hexadecanoic acid, dodecanoic acid and linoleic acid; other components included terpenoids such as *trans*-nerolidol, β-linalool and *trans*-geraniol. Sixteen compounds were identified from the flower essential oil of *Plumeria rubra* cv. *acutifolia* (Han 2007). The major components in essential oil were nerolidol (20.25 %) and geranyl linalool isomer (10.1 %). Other main content components were heptacosane (7.65 %), tetradecanoic acid (6.73 %), hexadecanoic acid, 2,3-dihydroxypropyl ester (2.98 %) and 1,2-benzenedicarboxylic acid, bis(2-methylpropyl) ester (2.68 %). The main components of the essential oil of *Plumeria rubra* var. *acutifolia* extracted by supercritical carbon dioxide fluid extraction comprised 1, 6, 10-dodecatrien-3-ol; 3,7,11-trimethyl; benzoic acid; 2-hydroxy-, phenylmethyl ester; 1,2-benzenedicarboxylic acid; and bis(2-methylpropyl) ester (Xiao et al. 2011). The last components comprised 66.11 % of the total.

Seven compounds, namely, 2-methylbutan-1-ol, β-phenylethyl alcohol, nonadecane, heneicosane, benzyl salicylate, tetradecanoic acid and phenylacetaldehyde were found in the essential oil of *P. rubra* red flower variety; 19 compounds, namely, a-terpineol, geraniol, β-phenylethyl alcohol, nonadecane, heneicosane, *trans*-farnesol, benzyl benzoate, geranial, dodecanoic acid, benzyl salicylate, phenylethyl benzoate, tetradecanoic acid, tetracosane, octadecanoic acid, tricosane, docosane, eicosane and phenylacetaldehyde in the yellow flower variety; and 14 compounds in *P. obtusa* (Sulaiman et al. 2008). The major components found in all three species were 2-hydroxybenzoic acid phenylmethyl ester. All three also shared two alkane hydrocarbons, nonadecane and heneicosane.

Phytochemicals from Plant

Albers-Schönberg and Schmid (1961) isolated isoplumericin, β-dihydroplumericin and β-dihydroplumericin along with plumericin from *Plumeria rubra* var. *alba*. They also isolated β-dihydroplumericinic acid from the same source and also fulvoplumierine (Albers-Schönberg et al. 1962). Stearic acid was isolated from leaf and stem of *P. rubra*, and flavonoids quercetin, quercitrin found in the leaf, flower and stem of *Plumeria rubra* and *Plumeria rubra* var. *alba* (Mahran et al. 1974b).

Taraxasteryl acetate, lupeol, stigmasterol, oleanolic acid, cycloart-22-ene-3 α,25-diol and rubrinol, a new triterpene of the ursane series, were isolated from whole plants of *P. rubra* (Akhtar et al. 1994). The structure of rubrinol was elucidated as 3 β,30-dihydroxy-12-ursene. Two new oleanene-type triterpenes 6α-hydroxy-3-epi-oleanolic acid and 3α,27-dihydroxy-olean-12-ene were isolated from *Plumeria rubra* (Akhtar and Malik 1993).

Acidic proteins with molecular masses between 12.5 and 74.5 kDa predominated in laticifers of *P. rubra* (de Freitas et al. 2010). Strong antioxidative activity of superoxide dismutase was detected in *P. rubra* latices, and to a lesser extent ascorbate peroxidase and isoforms of peroxidase were observed. In laticifer cells of *P. rubra*, four proteinases were detected, including cysteine and serine types. A protease with molecular weight of approximately 81.85 kDa was purified from the latex of *Plumeria rubra* plant and given the trivial name, plumerin-R (Chanda et al. 2011). It remained active over a broad range of temperature but had optimum activity at 55 °C and pH 7.0 when casein was used as substrate. Activation of the protease by a thiol-activating agent indicated the presence of sulfhydryl as an essential group for its activity.

Phytochemicals from Leaves

L-(+)-bornesitol was isolated from the leaves of *Plumeria acutifolia* (Nishibe et al. 1971). A new monoterpene alkaloid, (R)-4′-((S)-1-hydroxyethyl)-5,6-dihydro-5′ H-spiroyclopenta[C]pyridine-7,2’-furan)-5′-one, designated as plumerianine; the iridoid 15-demethylplumeride; and three known triterpenes, namely lupeol, uvaol and ursolic acid, were isolated from the methanol extract of *Plumeria acutifolia* leaves (Hassan et al. 2008). *P. rubra* leaves were found to contain tannins, phlobatannins,

saponins, flavonoids, steroids, terpenoids, reducing sugars, carbonyl and alkaloids (Egwaikhide et al. 2009).

Phytochemicals from Stem/Roots

The stem bark was found to contain highest content of plumierid, and *Plumeria rubra* plant contains a higher percentage of plumierid than those of *Plumeria rubra* var. *alba* (Mahran et al. 1974a). Plumerinine, a novel bicyclic lupin alkaloid, was isolated from *Plumeria rubra* stem (Kazmi et al. 1989). The following compounds were isolated from *P. rubra* bark: iridoids, fulvoplumierin, allamcin, allamandin, plumieride, α-allamcidin, 15-demethylplumieride, β-allamcidin and 13-*O*-*trans*-*p*-coumaroylplumieride; the lignan, liriodendrin, and 2,5-dimethoxy-*p*-benzoquinone (Kardono et al. 1990b). A novel flavan-3-olglycoside, plumerubroside, was isolated from a water-soluble extract of the stem bark of *Plumeria rubra*, and its structure was elucidated as (2*R*,3*S*)-3,4′-dihydroxy-7,3′,5′-trimethoxyflavan-5-*O*-β-D-glucopyranoside (Kardono et al. 1990a). Two new ferulic acid derivatives, 34-hydroxy tetratriacontanyl ferulate and 34-*O*-acetyl tetratriacontanyl ferulate, were isolated, along with plumericin and isoplumericin, from *Plumeria bicolor* stem bark (Dobhal et al. 1999). A new iridoid, 15-demethylisoplumieride acid, was isolated from the bark of *Plumeria rubra* var. *acutifolia* (Barreto et al. 2007).

Four new iridoids, namely, plumeridoids A, B and C and epiplumeridoid C, were isolated from the stem bark of *Plumeria rubra* together with 24 known compounds, namely, 1-(*p*-hydroxyphenyl) propan-1-one; isoplumericin; plumericin; dihydroplumericin; allamcin; fulvoplumierin; allamandin; plumieride; *p*-*E*-coumaric acid; 2,6-dimethoxy-*p*-benzoquinone; scopoletin; cycloart-25-en-3β,24-diol; 2,4,6-trimethoxyaniline; arjunolic acid; ursolic acid; oleanolic acid; β-amyrin acetate; betulinic acid; lupeol and its acetate; 2,3-dihydroxypropyl octacosanoate, glucoside of β-sitosterol, and a mixture of common sterols (stigmasterol and β-sitosterol) (Kuigoua et al. 2010).

Hamburger et al. (1991) isolated six compounds from the heartwood: plumericin, isoplumericin, protoplumericine A, plumieride, 13-*O*-*trans*-*p*-coumaroylplumieride and 4-hydroxyacetophenone 3 and several additional iridoids: 15-demethylplumieride, α-allamcidin and β-allamcidin.

Antioxidant Activity

Methanol leaf extract of *Plumeria acuminata* was found to possess antioxidant and free radical scavenging activity (Gupta et al. 2007a). The extract inhibited peroxidation of linoleic acid emulsion in a dose-dependent manner. Likewise the effect of the extract on reducing power increased in a dose-dependent manner. In DPPH radical and nitric oxide radical scavenging assays, the extract exhibited maximum activity of 60.42 and 56.38 % inhibition at the concentration of 125 μg/ml. Further, the extract was found to scavenge the superoxide generated by PMS/NADH-NBT system. The extract also inhibited the hydroxyl radical generated by Fenton's reaction, where the IC_{50} value of the extract was found to be 74.39 μg/ml and for catechin the IC_{50} value was found to be 5.27 μg/ml.

Anticancer Activity

Six cytotoxic constituents characterized from the bark of *Plumeria rubra*, namely, three iridoids fulvoplumierin, allamcin and allamandin and 2,5-dimethoxy-*p*-benzoquinone from petroleum-ether- and CHCl3-soluble extracts and iridoid plumericin, and the lignan liriodendrin from the water-soluble extract demonstrated general cytotoxic activity when evaluated against a panel of cell lines composed of murine lymphocytic leukemia (P-388) and a number of human cancer cell-types (breast, colon, fibrosarcoma, lung, melanoma, KB) (Kardono et al. 1990a, b). Five additional iridoids: 15-demethylplumieride, plumieride, α-allamcidin, β-allamcidin and 13-*O*-*trans*-*p*-coumaroylplumieride, were obtained as inactive constituents. Of the six compounds isolated from the heartwood, plumericin and isoplumericin exhibited cytotoxic and antibacterial activities, whereas 4-hydroxyacetophenone 3 was weakly cytotoxic (Hamburger et al. 1991). Ethanol leaf extract of *Plumeria rubra* administered orally at

the dose of 200 mg/kg body and 400 mg/kg body weight was found to increase the life span of Ehrlich ascites carcinoma-treated mice and restored the hematological parameters as compared with the untreated Ehrlich ascites carcinoma-bearing mice (Rekha and Jayakar 2011).

Plumericin from *Plumeria rubra* was listed as one of the ten most cytotoxic compounds isolated from 148 medicinal plants listed in Cameroon National Cancer Institute (NCI) database (Kuete and Efferth 2011). The IC_{50} value for plumericin of 60 NCI cell lines were associated with the microarray-based transcriptome-wide mRNA expression. Gene products identified for plumericin activity were mainly involved in enzymatic activity and transcriptional processes or were structural constituents of ribosomes.

Antimutagenic Activity

The ethanol extract of *Plumeria rubra* leaves contains several bioactive compounds that exhibited antimutagenic activities (Guevara et al. 1996). At a dosage of 2 mg isolate/25 g mouse, unidentified compound A1 reduced the number of micronucleated polychromatic erythrocytes induced by the mutagen, mitomycin C, by 75 %; stigmast-7-enol by 80 %; lupeol carboxylic acid by 57 %; and ursolic acid by 76 %.

Antiinflammatory Activity

The methanol leaf extract also possessed potent antiinflammatory activity (Gupta et al. 2006). It exhibited significant antiinflammatory activity in both acute and chronic experimental animal models. The extract (500 mg/kg/bw) exhibited maximum antiinflammatory effect, that is, 30.51, 47.06, 34.48 and 32.50 % at the end of 3 hours using carrageenan, dextran, histamine and serotonin assays, respectively. Administration of the extract (500 mg/kg/bw) and indomethacin (10 mg/kg/bw) significantly reduced the formation of granuloma tissue induced by cotton pellet method at a rate of 45.06 and 51.57 %, respectively. The effect produced by the extract was comparable to that of indomethacin, a prototype of a nonsteroidal antiinflammatory agent. The crude methanol extract of *Plumeria rubra* leaves was found to possess antiinflammatory (Rastogi et al. 2009). The antiinflammatory activity was dose dependent and found to be statistically significant at the concentration 100 and 200 mg/kg.

In the passive cutaneous anaphylaxis model, plumerianine isolated from the root bark of *Plumeria acutifolia* elicited a significant dose-dependent decrease in the leakage of Evans blue dye leaked at the site when compared with control (Vijayalakshmi et al. 2011). In the passive paw anaphylaxis model, plumerianine produced as significant dose-dependent decrease in paw volume induced by antiserum. Plumerianine also exhibited significant inhibition of rat paw oedema and granuloma tissue formation, including significant protection of red blood cells against the haemolytic effect of hypotonic solution, an indication of membrane-stabilizing activity. The authors postulated that anti-anaphylactic activity of plumerianine may be possibly due to inhibition of the release of various inflammatory mediators. Antiinflammatory activity of plumerianine may be related to the inhibition of the early phase and late phase of inflammatory events.

Antimicrobial Activity

Rubrinol isolated from the whole plant was found to be active against *Bacillus anthracis*, *Pseudomonas aeruginosa*, *Pseudomonas pseudomallei* and *Corynebacterium pseudodiphtheriticum* (Akhtar et al. 1994). Ethanol extract of the stem bark exhibited in vitro antimicrobial activity against Gram-positive bacteria (*Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*), Gram-negative bacteria (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*) and fungi (*Aspergillus niger* and *Candida albicans*) (Rasool et al. 2008). The ethanol extract showed the strong in-vitro antimicrobial activity against *E. faecalis*, *B. subtilis, S. aureus*, *P. aeruginosa*, *S. typhimurium*, *A. niger* and *C. albicans*.

The crude methanol leaf extract of *P. acuminata* inhibited the growth of both Gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus* and *Micrococcus luteus*) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*) (Gupta et al. 2008). Gram-positive bacteria tested appeared to be more susceptible to the extract than the Gram-negative bacteria. The extracts also showed significant antifungal activity against *Aspergillus niger* and *Candida albicans*. All tested microorganisms showed dose-dependent susceptibility towards the methanol extracts. Ethanol and chloroform leaf extracts of *P. rubra* exhibited partial antibacterial activity in vitro against *Staphylococcus epidermidis* at 750 and 1,000 µg/ml but at 1,500 µg/ml was completely inhibitory to *S. epidermidis* and *Escherichia coli* (Baghel et al. 2010). The ethyl acetate and aqueous leaf extract was partially inhibitory to *S. epidermidis at* 1,000 µg/ml but at 1,500 µg/ml was completely inhibitory to *S. epidermidis* and *Escherichia coli*. The standard drug ciprofloxacin is showing complete antibacterial activity against *S. epidermidis* and *Escherichia coli* at 500 and 750 µg/ml, respectively.

The methanol extract of *P. rubra* flowers inhibited significantly in-vitro growth of *Corynebacterium pyogenes*, *Staphylococcus aureus*, *Streptococcus faecalis*, *Bacillus stearothermophilus*, *Staphylococcus epidermidis*, *Bacillus cereus*, *Bacillus polymyxa*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus anthracis*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas fluorescens* and *Clostridium sporogenes* (Egwaikhide et al. 2009). The methanol leaf extract was also inhibitory but comparatively less to all the bacteria tested and was not inhibitory to *Corynebacterium pyogenes* and *Klebsiella pneumoniae*.

The essential oil of *P. rubra* red flower variety inhibited growth of *Bacillus cereus*, *Candida albicans*, *Candida humicola* and *Trichophyton rubrum*, while the essential oil from the yellow flower variety inhibited growth of *Bacillus cereus* and *Candida humicola* (Sulaiman et al. 2008). *Plumeria rubra* was one of four Latin American plant extracts that exhibited inhibitory activity against the subcutaneous fungus *Fonsecaea pedrosoi* with MIC of 12.5 µg/ml (Gaitán et al. 2011)

Antiviral Activity

Plumeria rubra yielded the iridoid, fulvoplumierin—an active, inhibitory compound with an IC_{50} 45 µg/ml against the human immunodeficiency virus type 1 reverse transcriptase (HIV-1 RT) (Tan et al. 1991).

Larvicidal Activity

Silver nanoparticles (AgNPs) synthesized using *Plumeria rubra* plant latex were found to be toxic to second and fourth larval instars of *Aedes aegypti* and *Anopheles stephensi* (Patil et al. 2012). AgNPs were more toxic to the larval stages than the crude latex extract. Toxicity studies carried out against nontarget fish species *Poecilia reticulata*; the most common organism in the habitats of *A. aegypti* and *A. stephensi* showed no toxicity at LC_{50} and LC_{90} doses of the AgNPs.

Hypoglycemic Activity

P. rubra was reported as one of several Mexican medicinal plants used in folkloric medicine to control diabetes mellitus (Hernandez-Galicia et al. 2002). Treatment of alloxan-induced hyperglycaemic rats with the flavone glycoside from *P. rubra* significantly reduced the level of serum triglycerides but did not alter blood glucose and serum total cholesterol (Merina et al. 2010). Administration of the glycoside significantly reduced the elevated levels of blood urea and creatinine and the activities of aspartate aminotransferase (SGOT) and alanine aminotransferase (SGPT) when compared with the hyperglycaemic control animals. Antioxidant activity of the flavone glycoside was also confirmed through in-vitro studies wherein the rate of malondialdehyde formation was markedly inhibited. The authors concluded that the beneficial effect of the flavone glycoside treatment on triglycerides observed assumes greater significance as a useful drug to decrease hyperlipidemic risks in diabetes.

Antipyretic and Antinociceptive Activity

Gupta et al. (2007b) showed that a single oral administration of different doses (100, 250 and 500 mg/kg) of the methanol leaf extract of *P. acuminata* significantly reduced brewer's yeast-induced hyperthermia in rats. The extract also elicited pronounced inhibitory effect on acetic acid-induced writhing, hot plate, tail-flick and tail immersion responses in mice in the antinociceptive tests.

Intraperitoneal administration of boiled milk at a dose 0.5 ml/kg body weight in albino rabbit led to pyrexia; this pyrexia was reverted by intraperitoneal administration of ethanol leaf extract of *P. rubra* at a dose 200 mg/kg body weight (Misra et al. 2012). The extract significantly reduces the elevated body temperature of rabbit which was compared with aspirin (standard drug) and solvent used.

Anxiolytic Activity

Subchronic oral administration of *Plumeria rubra* flower ethanol extract at 100 mg/kg p.o. to male Swiss mice increased the time spent in the open arms of the elevated plus-maze test (Chatterjee et al. 2013). The extract was further fractionated into hexane, chloroform, butane soluble and *n*-butane-insoluble fractions, out of which the butanol-insoluble fraction (BIF) showed significant anxiolytic activity comparable to standard anxiolytic drug, diazepam. Both the flower ethanol extract and BIF did not show any significant alterations in the horizontal activity, total distance and stereotypy count in the activity monitor. No motor incoordination side effects were observed after the extract and BIF pretreatment in the rotarod test in mice.

Antifertility Activity

Studies in female Sprague–Dawley rats showed that the aqueous (2 g/kg), ethanol (0.75 g, 1.3 and 1.5 kg/kg), methanol and dichloromethane (1.3 g and 1.5 g/kg) extracts of stem bark of *Plumeria rubra* exhibited antifertility activity (Gunawardana et al. 1998). The extracts were embryotoxic causing foetal death and subsequent resorption. Toxic symptoms observed in these experiments included reduced food intake, loss of body weight, and diarrhoea. Two deaths were recorded in the dichloromethane-treated group. The weight loss observed with some extracts, which showed significant antifertility activity, varied from slight to moderate to large.

The aqueous, alcohol, ethyl acetate and chloroform extract of *P. rubra* pods exhibited abortifacient activity (8–10 %) when administered to pregnant rats from day 11 to 15 of pregnancy (Dabhadkar and Zade 2012). The extracts significantly reduced the number of live foetuses, and the resorption index and post-implantation losses increased significantly. The percent of abortion was found to be highest (100 %) with 200 mg/kg dose of alcohol extract of *P. rubra* pods. In another paper, they reported that the ethanol extracts of *P. rubra* pods exhibited abortifacient activity (13.46–100 %) (Dabhadkar et al. 2012). The extract significantly reduced the number of live foetuses, whereas the resorption index and post-implantation losses increased significantly. The rate of abortion was found to be highest (100 %) at 200 mg/kg dose of alcoholic extract of *P. rubra* pods. In ovariectomized immature young rats, the extract showed significant estrogenic effect (vaginal opening, vaginal cornification and increased uterine weight) at the dose 200 mg/kg body weight. The phytochemical screening revealed the presence of alkaloids, flavonoids, simple phenolics, steroids, tannins and saponins in the extract.

Anthelmintic Activity

The crude methanol extract of *Plumeria rubra* leaves was found to possess anthelmintic activity (Rastogi et al. 2009). The anthelmintic effect of at 25 mg/ml concentration was comparable to the reference standard piperazine citrate.

Molluscicidal Activity

Of the six compounds isolated from the heartwood, plumericin and isoplumericin exhibited molluscicidal activity (Hamburger et al. 1991).

Toxic Immunoreactive Activity

Radford et al. (1986) found significant amounts of immunoreactive cardiac glycoside in *Plumeria rubra*. Awareness of the existence of such compound in *Plumeria* and their dangers allows them to be avoided and poisoning prevented.

Traditional Medicinal Uses

In traditional medicinal system, different parts of the plant have been mentioned to be useful in a variety of diseases. In India, the plant material is widely used as a purgative, remedy for diarrhoea and cure for itch. The milky juice is employed for the treatment of inflammation and rheumatism. The bark has been reported to be useful in hard tumours, diarrhoea, fever and gonorrhoea. The flowers are eaten with betel nut to cure ague.

In Mexico, the natives used it for skin complaints, for intermittent fevers and for dispersing dropsies by purging when applied to the stomach. In the West Indies, the bark is diuretic and the latex is used for purging. In the Philippines, the bark is used as a purgative, emmenagogue and febrifuge; the latex has the same effects. In Java and Madura, the bark is given for gonorrhoea, dropsy and dysuria due to venereal disease. The milky latex is used as a counterirritant for toothache and for sores. A decoction of the leaves is applied as lotion for cracks and eruptions on the sole of the feet and the paste of the leaves for poulticing swellings. In Thailand, a flower infusion is used as cosmetic applied after bathing but is slightly rubefacient. In Myanmar, the shoot, bark and flowers are employed for leprosy, for pruritis and for healing boils, carbuncles, and ascites. They are analgesic and employed as febrifuge for persistent fever. The bark and leaves are used for rheumatism, abdominal tumours and inflammation. The flower and shoots are used also for Malaria. In Mexico, decoction of flowers is used in diabetes.

Flowers of *Plumeria rubra*, *Chrysanthemum morifolium*, *Lonicera japonica*, *Bombax morifolium*, and *Sophora japonica* are the five primary constituents of the popular cooling herbal beverage 'Five Flower Tea' (Hu 2005; Kong et al. 2006). This Five Flower Tea is one of the top five remedies for 'Hot Qi' (Kong et al. 2006). 'Hot Qi' is often used by Chinese parents to describe listless symptoms in their children in Hong Kong. Eye discharge (37.2 %), sore throat (33.9 %), halitosis (32.8 %), constipation (31.0 %), and irritability (21.2 %) were the top five symptoms of 'Hot Qi' in children In Hong Kong.

P. rubra is one of several plants reported to be used for permanent sterilization for birth control in different parts of Assam, India (Tiwari et al. 1982). The Irula tribe of the Chittoor district of Andhra Pradesh use the flowers to treat itch (Vedavathy et al. 1997).

Other Uses

P. rubra has become a popular ornamental landscape tree in many tropical and subtropical countries. Flowers are popularly used in garlands or leis in Hawaii and also for wreaths elsewhere. In 2005 over 14 million blooms were sold for lei in Hawaii (Criley 2009). Collectors have descended upon Hawaii to find different colour forms, fragrances and flower shapes, and the fever to own a new plant has brought prices as high as $75 per cutting for rare and unusual forms. The blooms are often used for decorating bath in aroma therapy. *P. rubra* is Laos national flower.

Comments

It can be differentiated from *Plumeria obtusa* using salient leaf characteristics; in *Plumeria rubra*, the leaf blade is acute or acuminate at apex, matte adaxially and glaucous. In *Plumeria obtusa*, the leaf blade is rounded at apex, shiny adaxially and dark green.

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Telosma cordata

Scientific Name

***Telosma cordata* (Burm.f.) Merrill**

Synonyms

Asclepias cordata Burm.f., *Asclepias pallida* Roxb., *Cynanchum odoratissimum* Loureiro, *Oxystelma ovatum* P.T. Li & S.Z. Huang, *Pergularia minor* Andrews, *Pergularia odoratissima* (Loureiro) Roxb. ex Smith, *Telosma minor* (Andrews) W.G. Craib, *Telosma odoratissima* (Loureiro) Coville

Family

Asclepiadaceae

Common/English Names

Chinese Violet, Cowslip, East Coast Creeper, Fragrant Telosma, Night Fragrant Flower, Pakalana Vine, Primrose Creeper, Tonkin Creeper, Tonkin Jasmine, Tonkin Telosma

Vernacular Names

Chinese:Ye-Lai-Xiang,Yeh-Lai-Hsiang,Ye-Xiang-Hua, Yeh-Hsiang-Hua
French: Parfum Nocturne, Pergulaire
Hawaiian: Miulana Ke'oke'o, Pakalana
India: Surkilla (Hindi), Cambangikkodi (Tamil), Alapaala, Errumalle-tige, Konda Male-tige, Seethamanoharamu (Telugu), Kusiyari (Uttar Pradesh), Kanjalate, Seetamanoharam
Malaysia: Bunga Siam, Bunga Tonkin, Melati Tonkin
Spanish: Fragancia Nocturna
Thai: Salit
Vietnamese: Thiên Lý, Hoa Thiên Lý

Origin/Distribution

The plant is a native of India, Burma, Indochina and South China. It is widely cultivated in Southeast Asia especially in Thailand, Vietnam and Malaysia. It was introduced and cultivated in Java from the seventeenth century.

Agroecology

In its native range, the plant is found in secondary forest, bushland and open woods in low elevation in the subtropics and tropics. It is also cultivated in home gardens. It thrives in full sun in well-drained, fertile sandy-loam soil with optimum pH 6.1–7.5. It is tolerant to drought and poor soil but sensitive to flooding and cold.

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Edible Plant Parts and Uses

Opened and unopened flowers in umbels and young leaves are eaten as vegetables in China, Thailand, Vietnam, Kampuchea and Laos, cooked in soups or stir-fries with eggs and with meat (Burkill 1966; Uphof 1968; Facciola 1990; Hu 2005; Tanaka and Nguyen 2007; Yang et al. 2008). Tuberous roots are also eaten as sweetmeat by the Chinese in Java. Flowers yield an oil which is used in cooking.

Botany

Small, perennial, climber growing to 10 m long with much-branched, yellowish green stem, pubescent when young becoming pale grey and glabrescent (Plate 1). Leaves borne on 1.5–5 cm long petioles. Leaf lamina ovate, 6–11 cm long, base deeply cordate with narrow sinus, apex acuminate; basal veins 3, lateral veins to six pairs, glabrous or puberulous on the nerves (Plates 1, 2 and 3). Flowers in 15–30-flowered, umbellate cymes, puberulent, fragrant especially at night (Plates 4 and 5). Bract linear, caducous. Sepals oblong-lanceolate, puberulent on the outside. Corolla greenish-yellow to pale yellow, salver-shaped, tube 6–10 × 4–6 mm, puberulent outside, with ciliate, oblong-linear lobes, twisted in bud (Plates 1 and 3). Corona in one series with slightly fleshy lobes, basal part ovate, apex acuminate, often notched to deeply lobed, internal appendage often longer than lobe proper. Pistil with two carpels with numerous ovules on submarginal placenta. Filaments united, anthers with two locules each with one oblong or reniform pollinia. Stigma large, capitate. Follicles lanceolate 6–12 × 2–3.5 cm, glabrous, somewhat

Plate 1 Fragrant Telosma vine

Plate 2 Close view of leaves

Plate 3 Mature, opened flowers

Plate 4 Unopened flower buds

Plate 5 Harvested flowers and buds on sale in a local market

obtusely 4-angled. Seeds broadly ovate, 1 × 1 cm, flat, apex truncate, margin membranous bearing 3–4 cm long silky coma.

Nutritive/Medicinal Properties

The flower bud was reported to have the following nutrient compositions: 11 g dry matter, 1.18 g fiber, 2.62 g sugar, 3.13 g protein, 0.74 mg vitamin C, 52 mg β-carotene, 19 mg Ca and 0.92 mg Fe (Kuo 2002). Flavonoid content (mg/100 g FW) of the flower bud amounted to 12.8 % dry matter made up of the following flavonoids (mg/100 g FW): quercetin 0.2 mg, kaempferol 8.7 mg and total flavonoids 8.9 mg (Yang et al. 2008). A total of 43 compounds were identified from the essential oil of *Telosma cordata* flowers (Arai et al. 1993). Geraniol, β-ionone, dihydro-β-ionone, dihydro-β-ionol and *cis*-theaspirane and *trans*-theaspirane were found to contribute largely to the characteristic scent of the flower.

Comparison of mean vitamin C concentrations resulting from different cooking methods in leaves and tender tips and flower vegetables showed conventional stir-fried pagwanpa, pagwanban and cowslip creeper (*Telosma cordata*) to be excellent sources of vitamin C (64.4–70.8 mg/100 g) (Somsub et al. 2008)

The methanol extract from the leaves of *Telosma cordata* showed in-vitro cytotoxic activity against Hep-G2 (hepatonema carcinoma), Fl (fibril sarcoma of uterus) and RD (rhabdosarcoma) with the ED_{50} values of 39.0, 12.6, and 5.6 %, respectively (Le et al. 2005). Fractionation of the extracts gave compounds belonging to different classes. Four compounds lutein, I-dotriacontanol, 24*E*-stigmasta-5,22-dien-3β-ol and daucosterol were isolated from the n-hexane extracts.

Traditional Medicinal Uses

Fragrant Telosma oil is used medicinally in traditional medicine to treat conjunctivitis. The plant is used as antipyretic, an antidote to poison, tranquilizer and fatigue reducer. It is also used to relive backbone aches and to decrease hematuria (Tanaka and Nguyen 2007).

The Kol tribes of Vindhyan region of Uttar Pradesh apply latex of the fruit and fruit paste of *Telosma pallida* externally on the localized white patches during the initial stage of leucoderma disease (Singh and Narain 2010).

Other Uses

It is also planted as an ornamental creeper. The flowers are very fragrant and yield a perfumed oil. The plant is readily propagated from stem cuttings or seeds.

Comments

Some botanists are of the view that *Telosma cordata* is possibly a cultigen of *T. pallida* selected for fragrant flowers.

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Agave sisalana

Scientific Name

***Agave sisalana* Perrine ex Engelmann**

Synonyms

Agave amaniensis Trel. & Nowell, *Agave sisalana* var. *armata* Trel., *Agave sisalana* f. *armata* (Trel.) Trel., *Agave rigida* var. *sisalana* (Perrine) Engelm., *Agave rigida* var. *sisalana* Perrault ex Engelmann, *Agave rigida* var. *sisalana* Baker, *Agave segurae* D. Guillot & P. Van der Meer

Family

Asparagaceae

Common/English Names

Agave, Century Plant, Hemp Plant, Mescal, Sisal, Sisal Agave, Sisal Hemp

Vernacular Names

Afrikaans: Garingboom
Angola: Ngwengwe (Umbundu)
Arabic: Sabrâ
Brazil: Sisal (Portuguese)
Chinese: Jian Ma
Danish: Sisalagave
Democratic Republic of Congo: Cinusi (Mashi), Umugwegwe (Kinyarwanda)
Czech: Agáve Sisal, Agáve Sisalová
Estonian: Sisaliagaav
Ethiopia: Alge (Oromo), Qacha (Amharic)
Fiji: Dali, Mescal, Natali, Ndali
Finnish: Sisalagaave
French: Agave, Sisal, Langue De Bœuf, Pite Sisal
German: Agavendicksaft; Sisal-Agave
Hawaiian: Malina
Hungarian: Szizál, Szízal Agave
India: Khetki (Hindi)
Kenya: Ikonge (Kamba, Taita), Makonket (Sabaot), Tuoro (Kit Mikayi Region), Mûkongo (Kikuyu), Kamakonge, Kumukonge, Likonge, Sisal (western Kenya)
Kiribati: Te Rob', Te Robu
Latvian: Sisals
Madagascar: Tareta
Mayan: Tsootquij
Mexico: Ixtle Manso, Maguey Africano, Maguey Delgado, Mescal Casero, Mescal Del Monte, Pita-ci, Zapupe Fuerta
Polish: Agawa Sizalowa
Portuguese: Agave, Linho Sisal, Sisal
Spanish: Maguey De Sisal
Swahili: Mkatani, Mkatani Mkonge
Swedish: Sisalagave
Vietnamese: Agao Sợi, Dứa Sợi Cu Ba, Dứa Sợi Không Gai, Thùa Sợi
Zambia: Ubukonge (Bemba)

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Origin/Distribution

The origin of *Agave sisalana* is in Central America, probably in southern Mexico based on the strength of traditional local usage (Gentry 1982). In the nineteenth century, sisal cultivation spread to Florida, the Caribbean islands, Brazil, parts of Africa notably Tanzania, Kenya and Madagascar, Asia, the Pacific Islands and Australia where it has become naturalized. Agave has become an invasive weed species in some countries like Australia where it develops dense infestations which can prevent the regeneration of trees and exclude understorey species in native bushland.

Agroecology

Sisal is a robust, hardy tropical species found growing from near sea level to a 1,800 m altitude as in tropical Africa. In its native and naturalized range, it can be found in bushland, roadsides, savanna and along drainage lines. It thrives in full sun, in areas with a maximum temperature of 27–32 °C and minimum temperatures of 16 °C or higher and daily fluctuations not exceeding 7–10 °C. It grows best in regions with an average annual rainfall of 1,000–1,250 mm but is often grown with less rain as in semiarid areas. Excessive rainfall is detrimental to the plant. Under dry conditions or at low average temperatures, it forms fewer leaves per year and has a longer life cycle. Sisal prefers sandy-loam soils but can be grown on a range of soils, provided they are rich in bases, especially calcium, and well drained. Sisal is intolerant of waterlogging. Optimum pH is between 5.5 and 7.5, though sisal has been grown on soils with pH 4–5.

Edible Plant Parts and Uses

Five major parts of the Agave are edible: the flowers, the leaves, the stalks or basal rosettes, the sap (called aguamiel—honey water) (Davidson 2006; Deane 2012), and the roots (Deane 2012). Each Agave plant will produce several pounds of edible flowers during the summer. The flower stalks before flower opening can be harvested, roasted and eaten; they are sweet, like molasses. During inflorescence development, the base of the young flower stalk is rich in sap and yields a syrup (also called Agave nectar) when tapped, which is used as an alternative to sugar in cooking, and is promoted as a healthy alternative or fermented into alcoholic beverage, pulque or mescal. The leaves may be collected in winter and spring—when the plants are rich in sap—boiled and eaten. In Java, the heart of new shoot is eaten (Tanaka 1976). The root is caustic, but once cooked for a couple of days it is sweet and can be eaten.

Botany

A robust, monocarpic herbaceous perennial with a short thick stem 120 cm by 20 cm, with a basal rosette of numerous (50–>150) leaves, 1.5–2 m high (Plates 1 and 2). Leaves glaucous when young, margin minutely spiny, later dark blue-green, ensiform, linear-lanceolate, straight 100–150 cm long by 10–15 cm wide, succulent, adaxially concave, abaxially convex, margin not spiny, apex straight and tipped with a red-brown spine 2–3 cm. Inflorescence a panicle on a long peduncle, 2–8 m tall, branching at the upper half, branches widely spreading, 30–100 cm by 2 cm, apically 5–6 times branched trichotomously, bearing about 40 flowers per branch and bearing numerous bulbils on the inflorescence branches after anthesis (Plate 2). Flowers strongly odorous,

Plate 1 Immature sisal plant

Plate 2 Mature, flowering sisal plants

erect, protandrous; pedicel short; perianth tubular, 6-lobed, 5–6 cm long, pale yellowish green, tube 1–2 cm long, lobes obovate-oblanceolate, on inner side of the top with a tuft of hairs; stamens 6, attached above the middle of the perianth tube, 6–8 cm long; ovary inferior, 3-loculed, style 6–7 cm long, stigma 3-lobed. Fruit (rarely produced) an ellipsoid capsule, green becoming black when matured containing about 150 seeds. Seeds rounded-deltoid, thin, flat and black.

Nutritive/Medicinal Properties

Agave sisalana juice was found to be acidic (pH = 5.42) and to contain abundant water 93.73 %, 11.56 % crude protein, 1.11 % total soluble sugar, 1.48 % ash and 8.7 % inulin content (stored juice), while fresh juice had 20.87 % inulin (Sharma and Varshney 2012). Wilson (1971) reported that sisal fibre contained 78 % cellulose, 8 % lignin, 10 % hemicelluloses, 2 % waxes and about 1 % ash by weight. Rowell (1992) reported sisal to contain 43–56 % cellulose, 7–9 % lignin, 21–24 % pentosan and 0.6–1.1 % ash. Joseph et al. (1996) reported sisal to contain 85–88 % cellulose. *Agave sisalana* was found to contain 77.3–84.4 % cellulose and 6.9–10.3 % hemicelluloses, lignin 7.4–11.4 (Martin et al. 2009). Sisal leaf was reported to contain about 4 % by weight of extractable hard fibre, with the remains from the leaf still possessing up to 20 % by weight of extractable pulp and short fibres, the remainder being water and soluble sugars and the stem (bole) and the pole contained abundant solid pulp and liquid juice with a high concentration of soluble sugars (Bisanda and Enock 2003). Sisal pulp was found to have a crude protein of 7.3 %, crude fibre of 15.2 % and NFE (nitrogen free extract) 59.6 %(Gebremariam and Machin 2008). Sisal plant was reported to contain three types of fibres: structural (mechanical) occurring in the periphery of the leaf (most useful fibre); ribbon, longest fibres, occurring in association with the conducting tissues in middle of the leaf; and xylem fibres with thin-walled cells in the conducting vascular bundles (Bisanda and Ansell 1992; Li et al. 2000).

Agave sisalana and kenaf (*Hibiscus cannabinus*) were found to contain highly gamma-acylated lignins with acetate groups (del Río et al. 2008). The structures of all these highly acylated lignins were characterized by a very high syringyl/guaiacyl ratio, a large predominance of β-*O*-4′ linkages (up to 94 % of all linkages), and a strikingly low proportion of traditional beta-beta′ linkages. The occurrence of beta-beta′ homocoupling and cross-coupling products of sinapyl acetate in the lignins from sisal and kenaf indicated sinapyl alcohol to be acetylated at the monomer stage and that, therefore, sinapyl acetate should be considered as a real monolignol involved in the lignification reactions. The acetylated heteroxylan *O*-acetyl-(4-*O*-methylglucurono)xylan with a molecular weight (Mw) of 18 kDa was isolated from *Agave sisalana* (Marques et al. 2010). The heteroxylan backbone was composed of (1 → 4)-linked β-D-xylopyranosyl units (Xyl*p*) partially branched with terminal (1 → 2)-linked 4-*O*-methyl-α-D-glucuronosyl

(MeGlc*p*A, 9 mol%) and a small proportion of α-D-glucuronosyl (Glc*p*A, <1 mol%) residues. Roughly 61 mol% of Xyl*p* residues were acetylated.

Agave sisalana was also reported to contain sapogenins and saponins. The distribution of the steroid sapogenin constituents of *Agave sisalana* at various phases of growth was studied by Dawidar and Fayez (1961). It was suggested that in the bulbils, gitogenin (as first generation in sapogenin biogenesis) afforded tigogenin (as second generation) which was transformed during the course of the long life of the plant to hecogenin and neotigogenin (as third generation). At the end of the life cycle, neotigogenin and hecogenin of the old leaves were transformed by a reverse mechanism to tigogenin in the flowering top and then to gitogenin. They found that hecogenin was most abundant (0.235 %) in the leaves of the old plant. The major sapogenins (hecogenin, 9(11)-dehydrohecogenin and tigogenin) occurring in the *Agave* species including *A. sisalana* were analyzed by reversed-phase high-performance liquid chromatography (Higgins 1976). Sarsasapogenin, 9(11)-dehydrotigogenin and diosgenin were also analyzed by this rapid and accurate method. Rockogenin was found to be formed from hecogenin during processing of *A. sisalana* leaves (Blunden et al. 1977); hecogenin 3β-hydroxy-(25R)-5α-spirostan-12-one and tigogenin (25R)-5α-spirostan-3β-ol were isolated from *A. sisalana* leaf and leaf juice, crude saponin concentrates known as 'coffee grounds' (Cripps and Blunden 1978). In East African samples, the tigogenin proportion of the total sapogenin content is usually about 10 %. Leaves of Tanzanian, Kenyan and Angolan *A. sisalana* plants were found to have 0.34, 0.47 and 1.16 % hecogenin and 0.2, 0.2 and 0.1 % tigogenin, respectively (Sitton et al. 1982).

Barbourgenin a steroidal sapogenin, rockogenin and chlorogenin were isolated from coffee grounds produced from the acid hydrolyzed juice of the leaves of *A. sisalana* (Blunden et al. 1986). Three steroidal saponins, dongnosides C–E, were isolated from the methanol extracts of the fermented residues of leaf juices of *Agave sisalana* and their structures elucidated as tigogenin-3-*O*-*β*-D-xylopyranosyl(1 → 2)[β-D-glucopyranosyl(1 → 3)] β-D-glucopyranosyl(1 → 4)β-D-galactopyranoside, tigogenin-3-*O*-β-D-xylopyranosyl(1 → 3)β-D-xylopyranosyl(1 → 2)[β-D-glucopyranosyl (1 → 3)] β-D-glucopyranosyl(1 → 4)β-D-galactopyranoside and tigogenin-3-*O*-α-L-rhamnopyranosyl (1 → 4) β-D-xylopyranosyl(1 → 2)[β-D-glucopyranosyl (1 → 3)]β-D-glucopyranosyl(1 → 4)β-D-galactopyranoside, respectively (Ding et al. 1989).

Two major steroidal saponins, named dongnosides B and A, were isolated from *A. sisalana* leaf juice, and their structures characterized, respectively, as tigogenin 3-*O*-alpha-L-rhamonpyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 2)-[β-D-glucopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside and 3-*O*-α-L-rhamnopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → >4)-β-D-galactopyranoside (Ding et al. 1993). Two furostanol saponins were isolated from *Agave sisalana* leaves, and their structures established as(25S)-26-(β-D-glucopyranosyl)-22xi-hydroxyfurost-12-one-3β-yl-*O*-α-L-rhamnopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 3)-*O*-[*O*-β-D-glucopyranosyl-(1 → 2)]-*O*-β-D-glucopyranosyl-(1 → 4)-β-D-galacto-pyranoside and (25S)-26-(β-D-glucopyranosyl)-22xi-hydroxyfurost-5-en-12-one-3β-yl-*O*-α-l-rhamno-pyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 3)-*O*-[*O*-β-D-glucopyranosyl-(1 → 2)]-*O*-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (Zou et al. 2006). Three flavonoids 5,7-dihydroxyflavanone (1), kaempferol 3-rutinoside-4′-glucoside (9) and kaempferol 3-(2G-rhamnosylrutinoside) (10) and seven homoisoflavonoids 7-*O*-methyleucomol (2) [9], 3′-deoxysappanone (3), (±)-3,9-dihydroeucomin (4), dihydro-bonducellin (5), 7-hydroxy-3-(4-hydroxybenzyl)chromane (6) 5,7-dihydroxy-3-(4′-hydroxybenzyl)-4-chromanone (7), and 5,7-dihydroxy-3-(3′-hydroxy-4′-methoxybenzyl)-4-chromanone (8) were isolated from methanol extraction of *Agave sisalana* leaves (Chen et al. 2009).

A furostanol saponin, sisalasaponin C (1), and a spirostanol saponin, sisalasaponin D (2), were isolated from the fresh leaves of *Agave sisalana*, along with three other known steroidal saponins and two stilbenes (Yu et al. 2011). Their structures were identified as (3β,5α,6α,22α,25*R*)-3,26-bis[(β-D-glucopyrano-syl)oxy]-22-hydroxy furostan-6-yl β-D-glucopyranoside (1); (3β,5α,25*R*)-12-oxospirostan-3-yl 6-deoxy-α-L-manno pyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 3)-[β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (2); (3β,5*α*,6*α*,22*α*,25*R*)-22-methoxy-furostane-3,6,26-triyl tris-β-D-glucopyranoside; cantalasaponin-1; polianthoside D; (*E*)-2,3,4′,5-tetrahydroxystilbene 2-*O*-β-D-glucopyranoside; and (*Z*)-2,3,4′,5-tetrahydroxystilbene 2-*O*-β-D-glucopyranoside.

The most predominant compounds identified in the lipophilic extract of *A. sisalana* fibres were fatty acids (30 % of total lipids) including α- and ω-hydroxy fatty acids, fatty alcohols (20 %), free sterols (11 %), alkanes (11 %) and a series of ferulic acid esters of long-chain alcohols and ω-hydroxy fatty acids (10 %) (Gutiérrez et al. 2008). Additionally, steroid hydrocarbons and ketones, monoglycerides, aldehydes, waxes and sterol glycosides were also found together with minor amounts of diglycerides and sterol esters. D-mannitol was isolated from an ethanol extract from the liquid residue of *Agave sisalana* (Branco et al. 2010). D-mannitol was isolated from an ethanol extract from the liquid residue of *Agave sisalana* leaf waste (Branco et al. 2010). *Agave sisalana* juice waste aqueous extract was found to contain saponins, glycosides, phlobatannins, terpenoids, tannins, flavonoids and cardiac glycosides (Ade-Ajayi et al. 2011).

Anticancer Activity

Steroidal sapogenins and saponins—tigogenin (1), neotigogenin (2), hecogenin (3), neohecogenin (4), rockogenin (5), cantalasaponin-1 (6), hecogenin 3-*O*-β-D-glucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (7), hecogenin 3-*O*-α-L-rhamno pyranosyl-(1 → 3)-β-D-xylopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (8), a furostanol saponin, polianthosides E (9) and neotigogenin 3-*O*-α-L-rhamnopyranosyl-(1 → 4)-β-D-lucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (10)—were isolated from *A. sisalana* (Chen et al. 2011). Compounds 7–10 showed significant cytotoxicity against MCF-7, NCl-H460 and SF-268 cancer cells compared to the positive control actinomycin D. Compound 10 was the most cytotoxic with IC_{50} values of 1.2, 3.8 and 1.5 μM against MCF-7, NCl-H460 and SF-268 cancer cells, respectively.

Immunomodulatory Activity

The following flavonoids from *A. sisalana* leaves, (+/−)-3,9-dihydroeucomin (4), dihydrobonducellin (5), and 5,7-dihydroxy-3-(4′-hydroxybenzyl)-4-chromanone (7), showed inhibitory effects on human peripheral blood mononuclear cell (PBMC) proliferation activated by PHA with IC_{50} values 19.4, 73.8, and 58.8 μM, respectively (Chen et al. 2009). All three compounds significantly inhibited the production of interleukin IL-2 and interferon IFN-gamma in activated PBMC in a concentration-dependent manner.

Gastroprotective Activity

Studies showed that pretreatment of mice with hecogenin, a steroid saponin isolated from *Agave sisalana*, before ethanol or indomethacin challenge, exhibited significant gastroprotective effect (Santos Cerqueira et al. 2012). The hecogenin pretreatment normalized GSH levels and significantly reduced lipid peroxidation and nitrite levels in the stomach, as evaluated by the ethanol-induced gastric lesion model. It was further found that the gastroprotective effect appeared to be mediated by K^+(ATP) channels opening and the COX-2/PG pathway.

Anthelmintic Activity

In-vitro tests showed sisal juice caused more than 95 % reduction in larval counts of the genus *Haemonchus* spp. at concentrations between 86.5 and 146.3 mg/ml (Domingues et al. 2010). In-vivo sisal juice also reduced larvae of the fourth (L4) and fifth (L5) stages of *Haemonchus, Oesophagostomum* and *Trichostrongylus* in goats. *A. sisalana* shredded leaf extract showed in-vitro dose-dependent activity against sheep and goat gastrointestinal nematodes (Silveira et al. 2012). The LC_{50} and LC_{95} in the egg hatch test were 6.90 and 24.79 mg/ml, in the larval development test were 0.041 and 0.067 mg/ml and in the larval feeding inhibition test were 0.053 and 0.24 mg/ml. The development and feeding inhibition on L(1) larva were both 100 % at a dose of 0.12 mg/ml. In the adult motility test, there was 100 % inhibition at 75 mg/ml after 24 hours of exposure. The extract of *A. sisalana* therefore demonstrated significant action on L(1) at 0.12 mg/ml. Treatment of goats naturally infested by gastrointestinal nematodes with aqueous extract from sisal waste and levamisole phosphate caused a significant reduction in the number of eggs and infective larvae (L(3)) (Botura et al. 2011). The maximum reductions of the faecal egg counts were 50.3 and 93.6 % for both treatments, respectively, whereas the percent reductions of the total number of L(3) larvae were 80 % (the extract) and 85.6 % (levamisole phosphate). There was no difference between extract-treated and untreated goats with respect to worm burden, and the percent reductions were 28.8 and 63.4 % for *Oesophagostomum columbianum* and *Trichostrongylus colubriformis*, respectively. No reduction was detected for the *Haemonchus contortus*.

Studies showed that *A. sisalana* extracts exhibited activity in vitro against gastrointestinal nematodes (eggs and larva) of goats (Botura et al. 2013). The EC_{50} values for egg hatching inhibition 4.7, 0.1 and 0.05 mg/ml for EE (ethyl acetate extract), EA (aqueous extract) and FF (flavonoid fraction), respectively. The SF (saponin fraction) showed no ovicidal activity. The percent efficacies that were observed for the larval migration inhibition were 50.3, 33.2 and 64.1 % for the AE, EE and SF, respectively. The FF fraction did not show activity against the larvae.

Antimicrobial Activity

Crude methanol extracts of only *Agave sisalana* toothbrush sticks showed antibacterial activity against *Staphylococcus aureus* and *Bacillus cereus* (Kassu et al. 1999). The extract at concentrations up to 500 µg/ml showed weak toxicity to brine shrimp.

Sisal extract was found to have antibacterial activity against *Escherichia coli* and *Bacillus stearothermophilus* and is used as an ingredient in petroleum jelly (Zwane et al. 2010). Crude methanol and aqueous *A. sisalana* extract showed antibacterial activity against the tested bacteria (Hammuel et al. 2011; Ade-Ajayi et al. 2011). The methanol extract of sisal juice exerted more effect on *Shigella dysenteriae*, *Pseudomonas aeruginosa*, *Enterococcus faecalis* and *Candida albicans* and least on *Bacillus atrophaeus* than the aqueous extract. The minimum inhibitory concentration (MIC) of both the methanol and aqueous extract was between 10 and 20 mg/ml, and the minimum bactericidal concentration (MBC) was between 20 and 40 mg/ml for both extracts. Different results were obtained in another study wherein the hydroalcoholic extract obtained from sisal leaves and sisal waste showed significant inhibition of *Candida albicans* but was inactive against three strains of *Staphylococcus aureus*, two strains of *Escherichia coli*, and a strain of *Micrococcus luteus*, *Bacillus cereus*, *Pseudomonas aeruginosa* and *Salmonella choleraesuis* (Santos et al. 2011). The methanol extract of leaves showed weaker reduction in the inhibitory action of *C. albicans* when compared with the above extracts and was also inert against the other microorganisms tested.

Ecbolic Activity

Studies by Sharaf and Zahran (1967) found that *A. sisalana* juice stimulated intestinal and uterine

musculature in dogs, mouse and rat; lowered blood pressure in dogs; and produced abortion in pregnant mice and rats. The results suggested Agave juice to be a uterine stimulant, emmenagogue, laxative and hypotensive drug.

Larvicidal Activity

Waste residue of sisal leaves was found to have larvicidal activity (Pizarro et al. 1999). Various components of the extract were effective in eliminating mosquito larvae; the LC_{50} values for *Aedes aegypti* was 322 and 183 ppm for *Culex quinquefasciatus*. Under field conditions, the formulation used at 100 ppm caused 100 % mortality of *C. quinquefasciatus* larvae after 3–4 days.

Allergy Problem

Sisal processing was found to be associated with increased risk of immunoglobulin E (IgE) sensitization (Kayumba et al. 2008). Significantly higher prevalence of positive skin prick tested (SPTs) to sisal was found among 74 % of sisal workers compared to 17 % among controls. All exposed workers had elevated IgE levels, and 27 % of tested sera had elevated sisal specific IgE. A high prevalence of respiratory symptoms was found in both sensitized and non-sensitized sisal workers. In further studies, Kayumba et al. (2011) conducted a cross-sectional study on chronic respiratory symptoms and lung function among male Tanzanian sisal processing workers from six sisal estates in 2006. They found that chronic cough and chest tightness were experienced by 38 and 68 % of workers in brushing departments, 20 and 6 % of workers in decortication, and 7 and 0 % of security workers, respectively. A reduced FEV(1) [forced expiratory volume in 1 s]/FVC (forced ventilatory capacity) ratio related to years of work was found among workers in brushing departments when adjusting for age, smoking, previous respiratory illnesses and body mass index, using regression analyses. The overall results indicated a relationship between work in sisal brushing departments and the development of obstructive lung disorders.

Traditional Medicinal Uses

In northern Morocco, leaf juice is used as a wash for skin diseases (El-Hilaly et al. 2003). It is also used for syphilis, pulmonary tuberculosis, and jaundice and as a laxative. In Angola, lightly heated pounded roots are used for intercostal pain; also pounded plant is used for nephralgia (Bossard 1996). In Kenya, sap from young leaves is used as disinfectant, for stomachache, and for constipation (Kokwaro 1976; Phanuel et al. 2010); fibres are used as bandage (Njoroge and Bussmann 2007); and roasted leaves are used for burns (Okello et al. 2010). In Bahamas, salted decoction of central bud is used for jaundice (Debnath et al. 2010). The plant sap has been used in Central America as a binding agent for powders used as poultices for wounds (Chevallier 1996). The plant is used internally for the treatment of indigestion, flatulence, constipation, jaundice and dysentery (Bown 1995). The water used for soaking Agave fibres is used as scalp disinfectant and tonic for thinning hair (Lust 1974).

Other Uses

Sisal is a valuable forage for honey bees because of its long flowering period and is also commonly planted as an ornamental plant for landscaping purposes in parks, gardens and homes. In India, sisal plant is extensively planted as hedges along railroads. Sisal is also planted as fencing, to mark field boundaries, and to stabilize soil. The long and straight inflorescence stalks are used for house construction, fencing and thatching. A very hard wax is obtained from the leaf cuticle, and pectin can be obtained from sisal leaves. *Agave sisalana* toothbrush sticks are commonly used by people who cannot afford to buy the commercial toothbrush and toothpaste in Ethiopia (Kassu et al. 1999).

D-mannitol isolated from *Agave sisalana* is a compound widely used in the pharmaceutical industry and is also used as a raw material for producing several types of polymers (Branco et al. 2010). The steroidal saponins, tigogenin and hecogenin, extracted from the waste residues

after production of sisal fibres from *A. sisalana* and *A. americana*, are important raw materials in the synthesis of steroid hormones, as starting materials in the production of corticosteroids (cortisone, cortisol, prednisolone, prednisone, dexamethasone, betamethasone, triamcinolone, etc.) (Escamilla-Treviño 2012). Utilization of sisal waste for mushroom growing, animal feed, and production of biogas had already been demonstrated at pilot scale in Tanzania (Bisanda and Enock 2003). Several edible mushrooms, notably *Coprinus cinereus*, grow in large quantities on the waste heaps of sisal factories in Tanzania and provide a year-round source of food (Oyen 2011).

Sisal fibre is one of the four most common widely used natural fibres, and it accounts for half of total production of textile fibres (Mukhjee and Sat 1984). Sisal fibre is used for the manufacture of ropes for use in the marine industry and agriculture, coarse fabrics, geotextiles, sisal wall coverings, carpets, twines, macramé, nets, upholstery padding, carpet padding, baskets, mats, blankets, jewellery, sandals, clothing, mattresses, fish stringers, biodegradable storage bags for agricultural produce, musical instruments, ceremonial objects, paper pulp, construction materials, cat scratching posts and dart boards (Usher 1974; Chand et al. 1984; Murkherjee and Satyanarayana 1984; Li et al. 2000) and as raw material for medium-density fibreboard production (Gillah et al. 1998). New applications for sisal fibre is being focused on the manufacture of flat corrugated roofing panels that are strong and cheap with good fire resistance and natural fibre-reinforced composites (Chand et al. 1984; Murkherjee and Satyanarayana 1984; Rowell 1992; Joseph et al. 1996; Li et al. 2000; Mu et al. 2009; Barreto et al. 2011). The matrix used in sisal fibre-reinforced composites include thermoplastics (polyethylene, polypropylene, polystyrene, PVC, etc.), thermosets (epoxy, polyester, etc.), rubber (natural rubber, styrene-butadiene rubber, etc.), gypsum and cement (Li et al 2000). Sisal fibre is an effective reinforcement of polymer, rubber, gypsum and cement matrices. This has created a range of technological applications beyond its traditional usage as ropes, carpets, mats, etc. Research showed that biopolymers and natural fibres like sisal (*A. sisalana*) can be used to develop biocomposite plate materials that can be externally coated with calcium phosphate and hydroxyapatite (hybrid) composite and used for inside fixation and also external fixation of fractured bones (Chandramohan and Marimuthu 2011). Sisal fibre is also used for making specialty papers, such as cigarette paper, newsprint, bag paper, carbon paper, safety and banknote paper, filter paper, tea bags and biodegradable storage bags for agricultural produce. Whole leaves and sisal waste material may also be used as a source of pulp for papermaking.

Waste material after fibre extraction and boles remaining at the end of the life cycle of a crop may serve as animal feed, either directly or after ensilage. Studies showed dried sisal pulp to be a good feed for sheep, and that their performance improved increasingly when this was used to replace barley straw in the diet (Gebremariam and Machin 2008). Sisal pulp had a crude protein of 7.3 %, crude fibre of 15.2 % and NFE (nitrogen-free extract) of 59.6 %. The dry matter digestibility was 68.5 %, and organic matter digestibility was 73.3 %.

Some *Agave* species including *A. sisalana* have a real potential to compete economically with other bioenergy crops for biofuel production (Davis et al. 2011; Escamilla-Treviño 2012). Being CAM (crassulacean acid metabolism) plants, they have high water-use efficiency and can be grown in semiarid areas too dry to grow food crops, possessing potential for producing biomass feedstocks in large amounts while minimizing competition with the food supply. They contain cellulose and hemicelluloses as the main components in the cell wall that can be hydrolyzed to simple sugars for further fermentation to produce ethanol or other liquid biofuel. Theoretically, a crop area alone could provide 6.1 billion l of ethanol if *Agav*e were re-established as a bioenergy feedstock without causing indirect land use change (Davis et al. 2011).

Agave sisalana is also used in veterinary for animal diseases. In western Kenya, leaf preparations are used to treat gastrointestinal diseases, (diarrhoea, unthriftyness, drooping wings) in poultry (Okitoi et al. 2007). Juice of fleshy leaves or leaves and stems fermented in urine is applied on the animal's body surface against ticks (Wanzala et al.

2012). Aqueous extract made from chopped leaves and stem is applied on the animal's body surface while still fresh, or leaves are dried and ground to flour and applied on the animal's body surface as dust. Dried leaves are also used as fumigation against ticks. In Kivu, Democratic Republic of Congo, Agave leaves mixed with leaves of other plants are burn, and the ashes mixed in palm oil is applied to wounds on animals (Balagizi et al. 2005). In Zambia, leaves and stalks are pounded and added to drinking water to control Newcastle disease in poultry (Alders 2001). In Ethiopia, the roots are used to control blackleg in animals (Giday et al. 2003).

Comments

According to FAO Stat (2012), the leading producers (tonnes production) of sisal in 2011 are Brazil 283,797; Kenya 27,560; Tanzania 24,828; Mexico 20,113; Madagascar 18,937; and China 14,683.

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Muscari neglectum

Scientific Name

***Muscari neglectum* Guss ex Ten.**

Synonyms

Botryanthus atlanticus (Boiss. & Reut.) Nyman, *Botryanthus breviscapus* Tod., *Botryanthus granatensis* (Freyn) Nyman, *Botryanthus lelievrii* var. *strangwaysii* (Ten.) Nyman, *Botryanthus mandraliscae* Lojac., *Botryanthus mordoanus* (Heldr.) Nyman, *Botryanthus neglectus* (Guss. ex Ten.) Kunth, *Botryanthus neglectus* var. *speciosa* (Marches.) Nyman, *Botryanthus odorus* Kunth [Illeg.], *Botryanthus racemosus* (L.) Fourr., *Botryanthus saulii* Jaub. & Spach, *Botryanthus speciosus* (Marches.) Nyman, *Botryanthus strangwaysii* (Ten.) Kunth, *Botryanthus vulgaris* var. *strangwaysii* (Ten.) Nyman, *Etheiranthus jacquinii* Kostel *Eubotrys odorata* Raf. [Illeg.], *Hyacinthus juncifolius* Lam. [Illeg.], *Hyacinthus neglectus* (Guss. ex Ten.) E.H.L. Krause, *Hyacinthus racemosus* L., *Leopoldia neumayeri* Heldr., *Muscari atlanticum* Boiss. & Reut., *Muscari atlanticum* subsp. *alpinum* (Fiori) Garbari, *Muscari atlanticum* var. *valentinum* Pau, *Muscari bootanense* Griff., *Muscari bootanensis* Griff., *Muscari botryoides* var. *bucharicum* Regel, *Muscari breviscapum* (Tod.) N.E.Br., *Muscari bucharicum* Regel, *Muscari compactum* Baker, *Muscari dolioliforme* Sobko, *Muscari elwesii* Baker, *Muscari flaccidum* O. Schwarz, *Muscari fontqueri* Sennen, *Muscari granatense* Freyn, *Muscari grandifolium* Baker, *Muscari grandifolium* var. *populeum* (Braun-Blanq. & Maire) Maire, *Muscari grandifolium* var. *rifanum* Maire, *Muscari grossheimii* Schchian, *Muscari letourneuxii* Boiss., *Muscari leucostomum* Woronow, *Muscari macranthum* Freyn, *Muscari mordoanum* Heldr., *Muscari neglectum* subsp. *atlanticum* (Boiss. & Reut.) O. Bolòs & Vigo, *Muscari neglectum* var. *atlanticum* (Boiss. & Reut.) Maire, *Muscari neglectum* f. *bertramii* Maire, *Muscari neglectum* var. *fontqueri* (Sennen) O. Bolòs & Vigo, *Muscari neglectum* subsp. *odorum* O. Bolòs & Vigo, *Muscari neglectum* subsp. *speciosum* (Marches.) Garbari, *Muscari neglectum* var. *valentinum* (Pau) O. Bolòs & Vigo, *Muscari neumayeri* (Heldr.) Boiss., *Muscari nivale* Stapf, *Muscari odoratum* Montandon, *Muscari populeum* Braun-Blanq. & Maire, *Muscari racemosum* (L.) Medik. [Illeg.] *Muscari racemosum* Lam. & DC., *Muscari racemosum* var. *alpinum* Fiori, *Muscari racemosum* var. *neglectum* (Guss. ex Ten.) St.-Lag., *Muscari skorpili* Velen., *Muscari speciosum* Marches., *Muscari strangwaysii* Ten., *Muscari szovitsianum* Rupr. ex Boiss. [Illeg.], *Muscari vandasii* Velen., *Scilla suaveolens* Salisb. [Illeg.]

Family

Asparagaceae, was also placed in Hyacinthaceae, Liliaceae

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Common/English Names

Blue Bottle, Cipollini, Common Grape Hyacinth, Edible Muscari, Grape Hyacinth, Hairy Muscari, Muscari, Musk Hyacinth, Nutmeg Hyacinth, Southern Grape Hyacinth, Starch Hyacinth, Tufted Grape Hyacinth

Vernacular Names

Finnish: Terttuhelmililja
French: Muscari À Grappe, Muscari En Grappe, Muscari Négligé, Muscari Oublié, Ail Des Chiens
German: Weinbergs-Traubenhyazinthe
Hungarian: Fürtös Gyöngyike
Italian: Lampascione, Muscari Ignorato
Portuguese: Enfuste
Spanish: Agüelicos, Ajo De Perro, Azulete, Cebolla De Lagarto, Cebollica De Milano, Cebollita De Milano, Chapín De Reina, Clavos De Dios, Espartillo, Frailes, Gatos, Guitarrillos, Hierba Del Querer, Hierbas De Los Amores, Jacinto, Jacinto Racimosa, Jacinto Racimoso, Jacinto Silvestre, Jacintos, Lloricas, Macandil, Moras, Moro, Nazareno, Nazarenos, Nazarones, Pajarillos, Penitents
Turkish: Dağ Sümbülü
Welsh: Clychau Dulas

Origin/Distribution

The species is native to southwestern Asia and the Mediterranean region.

Agroecology

The species occurs naturally in dry grassland, foothills, grassy mountain slopes and forests in its native range. The plant is commonly cultivated in lawns, borders, rock gardens and containers. It prefers well-drained, moderately moist sandy soil that is acid to neutral and not too rich. It can be grown in full sun to partial shade and requires little feeding or watering in the summer; it flowers in spring. It is frost tolerant, withstanding temperatures down to −23 °C.

Edible Plant Parts and Uses

The blue flower buds and bulbs of these plants are featured heavily in Mediterranean cuisine, particularly in dishes originating from southern Italy. Muscari flowers have a sweet, nutlike flavour and are used as flavoring, while the bulb tastes like a slightly bitter onion and garlic hybrid (Wright 2001; Facciola 1990). The flowers and flower buds can be pickled in vinegar. The different parts of this plant including the leaves are edible raw, boiled, grilled or pickled.

Botany

The herbaceous plant grows to 25 cm with ovoid bulbs 2–3 by 2–2.5 cm covered with dark brown tunic. Leaves 3–6, linear to lanceolate, 5–35 cm long and 0.25–0.75 cm wide. Scape to 25 cm long. Inflorescence racemose with 20–40 blue to purplish-blue flowers (Plates 1, 2). Flowers on 1–5 mm nodding pedicels, sterile flowers smaller and paler than fertile ones. Perianth tube 3–7 mm, ovoid to oblong-urceolate or cylindric, teeth white, stamens biseriate at middle of tube. Capsule 5–9 × 8–10 mm, broadly ovate to orbicular, tip rounded or shortly emarginated.

Plate 1 Grape hyacinth plant

Plate 2 Grape-like flowers in a racemose inflorescence

Nutritive/Medicinal Properties

From the bulbs of *Muscari neglectum*, a scillascillinoid homoisoflavanone was isolated and elucidated as 2′,5-dihydroxy-4′,7-dimethoxyspirol [2*H*-1-benzopyran-3(4*H*),7′-bicyclo[4.2.0] octa[1,3,5]-trien]-4-one (Barone et al. 1988). Also isolated were scillascillin and four known 3-benzyl-4-chromanones including 4′-demethyl-3,9-dihydropunctatin; 5,7-dimethoxy-3(4-methoxybenzyl)chroman-4-one. From the bulbs, two 3-benzylidene-4-chromanones were isolated, namely, 5,7-dihydroxy-6-methoxy-3-(3,4-duhydroxybenzylidene)chromane-4-one and 7-hydroxy-5-methoxy-3-(3,4-dihydroxybenzylidene) chromane-4-one together with known homoisoflavanone (Maśterová et al. 1991). Uracil and succinic acid were isolated from the aerial parts.

Homoisoflavonoid compounds had been reported to exhibit antiinflammatory, estrogenic, antiestrogenic, anticancer and angioprotective bioactivities (Jiang et al. 2007).

The homoisoflavonoids from *Muscari racemosum* were found to have antioxidative property (Juránek et al. 1993). The extract of the bulb rich in 3-benzylidene-4-chromanones (homoisoflavonoids) was found to have antimutagenic and anticlastogenic properties using the Ames assay on four bacterial strains *Salmonella typhimurium* TA97, TA98, TA100, TA102, in the toxicity and mutagenicity/antimutagenicity assay on the yeast strain *Saccharomyces cerevisiae* D7, and in the simultaneous phytotoxicity and clastogenicity/anticlastogenicity assay on *Vicia sativa* (Miadoková et al. 2002). The homoisoflavonoid fraction obtained from the *Muscari racemosum* bulb ether extract (MRBEE) exhibited a dose-dependent estrogenic activity by inducing proliferation of MCF7 cells (Urbancíková et al. 2002). In the presence of estradiol, MRBEE exhibited a dose-dependent antiestrogenic activity.

Other Uses

The plant is planted as ornamental in borders, containers and rock gardens and flowers profusely in spring.

Comments

The plant is propagated from seeds, small or large bulbs or by division of offsets.

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Polianthes tuberosa

Scientific Name

***Polianthes tuberosa* L.**

Synonyms

Agave polianthes (L.) Thiede & Eggli, *Agave tuberosa* (L.) Thiede & Eggli nom. illeg., *Crinum angustifolium* Houtt., *Polianthes gracilis* Link, *Polianthes tuberosa* var. *gracilis* (Link) Beurl., *Polianthes tuberosa* f. *plena* Moldenke, *Tuberosa amica* Medik.

Family

Asparagaceae, also placed in Agavaceae, Amaryllidaceae

Common/English Name

Tuberose

Vernacular Names

Chinese: Wan Xiangyu, Ye Lai Xiang, Yue Xia Xiang
Cuba: Azucena, Guacamaya
Czech: Tuberóza
Danish: Tuberose
Esperanto: Tuberozo
Estonian: Mugul-Säraõis
French: Jacinthe Des Indes, Tubéreuse
German: Nachthyazinthe, Tuberose
Hungarian: Tubarózsa
India: Nelasampenga (Andhra Pradesh), Rajanigandha, Rajoni-Gandha (Bengali), Galshabbo, Gulchari, Rajnigandha (Hindi), Sugandharaja, Sukandaraji (Kannada), Kundalei Angouba (Manipuri), Gulcheri, Nishigandha (Marathi), Nilasambangi, Nila Sampangi, Sambangi (Tamil), Nelasampengi, Sukandaraji (Telugu), Gul Shabbo (Urdu)
Indonesia: Sundel Malem (Javanese), Sundel Malem, Sedep Malem (Sundanese)
Iran: Gole Maryam
Italian: Tuberosa
Malaysia: Harum Sundal Malam, Kerak Nasi, Sandaramlam, Sedap Malam, Siku Dangan, Siku Dengan, Sundal Malam
Mexico: Omixochitl (Aztecs), Amiga De Noche, Amole, Azucena, Nardo, Tuberosa (Spanish)
Philippines: Nador (Cebu Bisaya), Azucena, Baston De San Jose (Tagalog)
Polish: Tuberoza Wonna
Slovaščina: Tuberoza
Spanish: Nardo, Nardo Com, Tuberose, Vara De Nardo
Swedish: Tuberos
Thai: Dtôn Dòk Lee-Laa, Dtôn Dòk Ruang Kâao, Dtôn Sôn Chóo, Dtôn Sôn Glìn, Dtôn Sôn Glìn Tai

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Origin/Distribution

It is indigenous to Central and southern Mexico. The plant was distributed all over the world as an ornamental and is grown in tropical, subtropical and subtemperate areas. Kenya and Egypt are the leading producers of tuberose for the export market.

Agroecology

Tuberose grows best in mild climate without extremes of high or low temperatures. It thrives in warm humid areas with mean temperatures of 20–32 °C. It is sensitive to low temperatures and frost. High temperatures close to 40 °C reduces flower spike length and quality. Tuberose prefers a sunny position. Although it can grow in a wide range of soils including saline and alkaline soils, it prefers well-drained and aerated sandy loams rich in organic matter with pH of 6–7.5. It requires copious watering during the growth stage. The plant can also be grown in pots and in greenhouses in temperate areas.

Edible Plant Parts and Uses

The flowers are eaten as vegetables (Burkill 1966; Uphof 1968; Tanaka 1976; Kunkel 1984; Facciola 1990; Roberts 2000). In Java, the Chinese cook the flowers in a kind of soup. The cooked flowers are also added to the substrate of 'kecap', an Indonesian soy sauce. Fragrant flowers are added along with other ingredients to the favourite beverage prepared from chocolate and served either hot or cold as desired. The flowers are the source of tuberosa-flower water.

Botany

Tuberose is a hardy perennial, erect herb, 45–70 cm high with tuberose rootstock and shallow adventitious roots and a short stem. It has elongated linear, bright green leaves clustered at the base of the plant (Plate 1) and smaller clasping leaves along the stem. The flowers in a long (up to 45 cm), simple, unbranched terminal racemous spike with 4–6, waxy, fragrant white flowers borne in pairs (Plate 2). The perianth is tubular or funnel-shaped with short subequal, curved oblong-lanceolate tepals, 10–15 mm long. Stamens 6 with filaments adnate to the upper part

Plate 1 Clumps of tuberose plants

Plate 2 Unbranched terminal spike with white flowers

of the perianth tube, anthers dorsifixed. Ovary 3-loculed with numerous ovules, stigmas 3 ovate. Fruit a capsule.

Besides the normal 'single-tepal' flower, 'double-tepal' tuberose flowers have been developed in white and various colours such as reddish purple, pale purple, pale red, reddish pink, yellow and orange (Huang et al. 2001a, b) and also tuberose with variegated yellow-striped leaves.

Nutritive/Medicinal Properties

Polianthes tuberosa tuber was found to contain lycorine, an alkaloid that causes vomiting (Gorter 1919). A glucofructosan (Srinivasan and Bhatia 1954), transfructosidase (Bhatia and Srinivasan 1954) and sucrose (Wali and Hasan 1965) were found in the plant. Chandravadana et al. (1995) found indole in the absolute from various varieties and hybrids, varying in contents ranging from 0.36 to 2.15 %. Several steroid sapogenins, such as hecogenin, 9-dehydroxyhecogenin and tigogenin (Zhou et al. 1965), as well as glycosides, 29-hydroxystigmast-5-en-3β-yl β-D-glucoside (Rashid et al. 1999), (22*S*)-2β,3β,22-trihydroxycholest-5-en-16β-yl β-D-glucoside (Firdous et al. 1999b) and diribofuranosylethyleneglycol (Firdous et al. 1999a) and spirostanol pentaglycosides (Mimaki et al. 2002) were identified from the underground parts of *P. tuberosa*. Four new spirostanol saponins with five monosaccharides (1–4) were isolated from *P. tuberosa* underground parts (Mimaki et al. 2002). Three glycosides and a long-chain alcohol were isolated from the bulbs of *Polianthes tuberosa*; these were identified as 3,29-dihydroxystigmast-5-ene-3-*O*-β-D-galactopyranoside (1), ethyl β-D-galactopyranoside (2), ethyl-α-D-galactopyranoside (3) and 1-tricosanol (4) (Khan et al. 2002). None of the compounds showed any significant cytotoxicity, antibacterial and antifungal activities.

A bisdesmosidic cholestane glycoside (1) and three new spirostanol saponins (2–4), along with a known cholestane glycoside, were isolated from the aerial parts of *Polianthes tuberosa* (Mimaki et al. 2000).

A new cholestane glycoside, (22*S*)-cholest-5-en-1β,3β,16β,22,25-pentaol 1-*O*-β-D-GLUCOPYRANOSYL-16-*O*-β-D-apiofuranoside which was named tuberoside A, together with two known cholestane glycosides were isolated from the tubers of *Polianthes tuberosa* (Jin et al. 2003a). The two known cholestane glycoside 1 and 2 were identified as (22*S*)-cholest-5-en-1B, 3B, 16 B, 22-tetraol 1-*O*-B-D-glucopyranosyl-16-*O*-B-D-apiofuranoside (Mimaki et al. 2000) and (22*S*)-cholest-5-en-1B, 3B, 16 B, 22-tetraol 3, 16-di-*O*-B-D-glucopyronoside (Mimaki et al. 1995), respectively.

Six new steroid glycosides comprising two spirostanols, polianthosides B and C (1, 2) and four furostanols, polianthosides D–G (3–6) together with eight known saponins (7–14), were isolated from the fresh tubers of *P. tuberosa* (Jin et al. 2004). Polianthoside B (1) was characterised as tigogenin 3-*O*-β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-glucopyranosy-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside and polianthoside C (2) as tigogenin 3-*O*-β-D-glucopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-glucopyranosyl-(1 → 3)]-β-d-glucopyranosyl-(1 → 4)-β-D-galacto pyranoside. Polianthoside D (3) was elucidated as 26-*O*-β-D-glucopyranosyl-(25*R*)-5*R*-furost-3β,22*R*,-26-triol-12-one 3-*O*-β-D-glucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside. Polianthoside E (4) was elucidated as 26-*O*-β-D-glucopyranosyl-(25*R*)-5*R*-furost-3β,22*R*,-26-triol-12-one3-*O*-β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside. Polianthoside F (5) was deduced to be as 26-*O*-β-D-glucopyranosyl-(25*R*)-5*R*-furost-3β,22*R*,-26-triol3-*O*-β-D-xylopyranosyl-(1 → 3)-β-d-glucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside and polianthoside G (6) deduced to be 26-*O*-β-D-glucopyranosyl-(25*R*)-5*R*-furost-3β,22*R*,-26-triol 3-*O*-β-D-xylopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-glucopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside. The eight known steroid saponins were identified as hecogenin 3-*O*-β-D-

glucopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (7) (Xu et al. 2000),hecogenin3-*O*-β-D-glucopyranosyl-(1 → 2)-[β-D-xyloyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (8) (Mimaki et al. 1995), hecogenin 3-*O*-β-D-xyloyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-xylo yranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (9) (Mimaki et al. 2000), agamenoside F (10) (Jin et al. 2003b), tigogenin 3-*O*-β-D-glucopyranosyl-(1 → 2)-[β-D-xyloyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (11) (Wang et al. 1996), tigogenin 3-*O*-β-D-xyloyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-xyloyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (12) (Mimaki et al. 2000), chlorogenin 3-*O*-β-D-xyloyranosyl-(1 → 3)-β-D-glucopyranosyl-(1 → 2)-[β-D-xyloyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (13) (Mimaki et al. 2000) and 26-*O*-β-D-glucopyranosyl-(25*R*)-5*R*-furost-3β,22*R*,-26-triol3-*O*-β-D-glucopyranosyl-(1 → 2)-[β-D-xylopyranosyl-(1 → 3)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (uttroside B) (14) (Sharma et al. 1983), respectively.

Six unsaturated γ-lactones, (*Z*)-5-octen-4-olide (1), (*Z*)-5-decen-4-olide (2), (*Z*)-6-nonen-4-olide (3), (*Z*)-6-dodecen-4-olide (4), (*Z*, *Z*)-6,9-dodecadien-4-olide (5) and tuberolide (6), were identified in tuberose absolute (from *Polianthes tuberosa*) (Maurer and Hauser 1982).

Seventeen volatile components were identified from *P. tuberosa*; the major components were benzyl benzoate (16.76 %), *trans*-methyl isoeugenol (15.3 %) and ethyl myristate (14.0 %) (Wahba et al. 1998). The presence of the N-containing compound methyl anthranilate, constituting 7.1 %, was confirmed. Volatiles of *Polianthes tuberosa* showed no significant increase in blood glucose, blood urea nitrogen, serum glutamic-oxalacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) when applied to the skin of rabbits indicating that it had no subacute dermal toxicity.

Percentage yields of tuberose oil from cold enfleurage, hot enfleurage, hexane and petroleum ether extractions of double-flower variety of tuberose (*Polianthes tuberosa*) were 0.3137, 6.5808, 0.0279, and 0.0182 %, respectively (Rakthaworn et al. 2009). The main chemical component detected in both enfleurage absolutes was methyl benzoate, while benzyl benzoate and pentacosane were found to be the main chemical components in hexane and petroleum ether absolutes, respectively. Ten compounds were detected in cold enfleurage absolute with the major components being methyl benzoate (30.17 %), benzyl benzoate (23.64 %), 7-decen-5-olide (13.33 %) and methyl salicylate (12.11 %). Other compounds included (*E*)-methyl isoeugenol (8.83 %), methyl anthranilate (4.45 %), (*Z*)-β-farnesene (2.43 %), methyl eugenol (1.80 %), indole (1.78 %) and (*E*)-citral (1.47 %). Ten chemical constituents were also detected in the hot enfleurage absolute, with methyl benzoate being the main component again, but with a higher percentage yield (44.85 %) followed by (*Z*)-3-hexenyl 2-oxopropanoate (27.38 %) as major components. Other components included methyl salicylate (7.18 %), 1-tetradecene (4.15 %), benzyl benzoate (3.75 %), (*Z*)-nerolidol (3.35 %), 1-hexadecene (3.39 %), 2,4-decadien-1-al (2.91 %), (*E*)-methyl isoeugenol (1.78 %) and 2-heptadecanone (1.26 %). Fourteen chemicals were detected in the tuberose hexane absolute with benzyl benzoate (24.25 %), pentacosane (19.23 %) and 7-decen-5-olide (14.96 %) as the major components. Others included 1-hexadecene (8.85 %), 2,4,-di-tert-butylphenol (8.36 %), eicosanol (4.96 %), heptacosane (4.60 %), (*Z*)-3-hexenyl 2-oxopropanoate (3.70 %), tricosane (2.47 %), methyl isoeugenol (2.32 %), α-farnesol (1.94 %), (*E*)-methyl isoeugenol (1.89 %), benzyl salicylate (1.39 %) and methyl eugenol (1.07 %). There were 14 chemicals identified in the petroleum ether absolute. The main components were pentacosane (29.44 %), 7-decen-5-olide (18.13 %) and heptacosane (12.53 %). Others included benzyl benzoate (10.28 %), (*E*)-methyl isoeugenol (6.05 %), methyl isoeugenol (4.85 %), methyl anthranilate (4.15 %), alpha-farnesol (4.06 %), tricosane (3.65 %), methyl eugenol (1.89 %), 1-hexadecene (1.69 %), benzyl salicylate

(1.34 %), 1-tetradecene (0.98 %) and (*Z*)-methyl isoeugenol (0.96 %). Petroleum ether extracted more wax, for example, pentacosane and heptacosane, from plant cells than hexane.

Coloured varieties of *P. tuberosa* and its hybrids with *P. howardii* were found to contain anthocyanins and carotenoids in their petals (Huang et al. 2001a, b). White-flowered varieties contained no anthocyanin. The main anthocyanidin in the petals of coloured flowers was cyanidin, and some hybrids also contained delphinidin. Reddish purple or pale purple flower hybrids contained delphinidin glycoside with cyanidin glycoside, whereas only cyanidin glycosides were contained in the flowers of orange, pale red and reddish pink.

Soaking or spraying tuberose bulbs in solutions of bioregulators such as spermidine and ATP increases the contents of indoles, phenols, carotenoids, carbohydrate, essential oil and phytohormones (endogenous gibberellin (GA3), total cytokinins and abscisic acid (ABA)) of the tuberose plants (Lobna and Rawia 2011). Bioregulator treatment (100 ppm) augmented plants bulblets and flowering characteristics (number of bulblets, fresh and dry weights of bulblets, number of days to flowering, number of florets/spike, spike length, length of rachis and fresh and dry weights of spike).

A lactone-designated tuberolactone was isolated from tuberose leaves (Kaiser and Lamparsky 1976). Three flavonoid compounds isolated from the leaves of *P. tuberosa* were kaempferol, kaempferol-3-*O*-xyloside and kaempferol-3-4′-*O*-dixyloside (El-Moghazy et al. 1980). Rammamurthy et al. (2010) isolated 9,11dehydrohecogenin 3-*O*-glucose xylose galactoside, kaempferol-3-*O*-xyloside, α-D-glucoside and polianthosides B and C from *P. tuberosa* leaves.

Antimicrobial Activity

Both Gram-positive and Gram-negative bacteria were found susceptible to *P. tuberosa* flower essential oil (Lodhia et al. 2009).

Anticancer Activity

Four new spirostanol saponins isolated from tubers exhibited cytotoxic activities against HL-60 human promyelocytic leukaemia cells and HSC-2 human oral squamous cell carcinoma cells (Mimaki et al. 2002). Six new steroid glycosides comprising two spirostanols, polianthosides B and C (1, 2) and four furostanols, polianthosides D–G (3–6) together with eight known saponins (7–14), were isolated from the fresh tubers of *P. tuberosa* (Jin et al. 2004). Cytotoxicity activity of the isolated compounds against HeLa cells in terms of IC_{50} values were polianthoside B >20 μg/ml, polianthoside C >20 μg/ml, furostanol polianthoside D 7.86 μg/ml, furostanol polianthoside E 5.21 μg/ml, furostanol polianthoside F 20 μg/ml, furostanol polianthoside G 5.36 μg/ml, furostanol polianthoside H 8.61 μg/ml, saponin 9 8.17 μg/ml, saponin 10 4.02 μg/ml, saponin 11 3.54 μg/ml, saponin 12 7.20 μg/ml, saponin 13 7.50 μg/ml, saponin 14 18.83 μg/ml and cisplatin 0.75 μg/ml. It was observed that most of the saponins (3, 4 and 7–10) with a carbonyl group at C-12 of the aglycone showed stronger cytotoxicities (IC_{50} 4.02–8.61 μg/ml) against HeLa cells than saponins 1, 2, 5 and 14, with no carbonyl group attached at the aglycone (IC_{50} > 18.83 μg/ml).

Molluscidal Activity

Powder of *Polianthes tuberosa* bulb and its sapogenins tigogenin and hecogenin caused a significant reduction in fecundity, hatchability and survival of young snails of *Lymnaea acuminata* (Singh et al. 1999). Exposure to sublethal concentration caused a small but significant reduction in protein, amino acids, nucleic acids and phosphatase activities in gonadal tissue of treated snails. Withdrawal after 7 days indicated that the effect of powder of *P. tuberosa* bulb, tigogenin and hecogenin on the reproduction and different biochemical parameters was reversible.

Immunosuppressive Activity

An acidic polysaccharide (ANK-102) produced by *P. tuberosa* cells in liquid culture was found to deteriorate resistance of mice to lethal infection of *Listeria monocytogenes* (Majima et al. 1995). Pretreatment with ANK-102 resulted in the accumulation of Mac 1 and Mac 2 positive cells in the peritoneal cavity of the infected animals and the reduction of Thy1.2 expression on the surface of the thymocytes.

Larvicidal and Deterrence Activity

Both crude and chloroform–methanol (1:1, v/v) extract of fresh mature *P. tuberosa* buds showed larvicidal activity against *Culex quinquefasciatus* (Rawani et al. 2012). The chloroform–methanol extract also showed biting deterrence activity against *Anopheles stephensi* and *Culex quinquefasciatus*.

Traditional Medicinal Uses

Tuberose has been reported to be used in traditional folk medicine (Burkill 1966; Perry 1980; Chopra et al. 1986; CSIR 1969; Jin et al. 2004; Kuppast et al. 2006; Stuart 2012).

In Chinese folk medicine, the tubers are used for the treatment of acute infectious diseases and pyrogenic inflammations, burns and swellings. The tubers are also considered emetic antispasmodic and diuretic. The tubers are dried, powdered and used as a remedy for gonorrhoea and used with turmeric for curing rashes in infants and wound healing in India and also used to treat malaria. Poultice of the tubers are used as maturative in the formation of pus in boils or abscesses. In aromatherapy, the warm and seductive scent of the tuberose oil is useful as a hypnotic for women suffering from insomnia and depressed with low sexual drive.

Other Uses

Tuberose is gaining in popularity and importance as an ornamental in Asia. Besides the normal 'single-tepal' flower, tuberose is available as 'double-tepal' tuberose flowers and in various colours such as reddish purple, pale purple, pale red, reddish pink, yellow and orange (Huang et al. 2001a, b) and tuberose with variegated yellow-striped leaves.

Tuberose flowers are the source of the high-grade tuberose oil which remains today as one of the most expensive of the perfumer's raw material. Flowers are used for artistic garlands, leis, floral ornaments, bouquets and buttonholes. The long fragrant flower spikes are excellent as cut flowers for table decoration with a long vase-life. In Malaysia, Chinese ladies make chaplets of the flowers for binding the hair. Tuberose flowers were considered a funeral flower in Victorian times. The Chinese used the cut flowers on the altars for religious and ancestral worships.

Tuberose absolute (100 % tuberose oil) showed only mild fungicidal activity at a concentration of 500 mg/l against *Colletotrichum gloeosporioides* (Nidiry and Babu 2005). However, three constituents present in the absolute, namely, geraniol, indole and methyl anthranilate, exhibited significant activity showing total inhibition of the mycelial growth at this concentration.

Comments

The quality and vase-life of tuberose flowers were improved greatly by harvesting at tight bud stage and pulsing cut flower stems in silver nitrate ($AgNO_3$), silver thiosulfate (STS) chemicals or a solution containing sucrose (Bakhsh et al. 1999).

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Yucca filamentosa

Scientific Name

***Yucca filamentosa* L.**

Synonyms

Yucca filamentosa var. *bracteata* Engelm., *Yucca filamentosa* var. *elmensis* Sprenger, *Yucca filamentosa* var. *laevigata* Engelm., *Yucca filamentosa* var. *maxima* Baker, *Yucca filamentosa* var. *media* Carrière, *Yucca filamentosa* var. *mexicana* S.Schauer, *Yucca filamentosa* var. *nobilis* Sprenger, *Yucca filamentosa* var. *patens* Carrière, *Yucca filamentosa* var. *recurvifolia* Alph.Wood, *Yucca filamentosa* var. *variegata* Carrière

Family

Asparagaceae

Common/English Names

Adam's Needle, Adam's Needle Yucca, Beargrass, Common Yucca, Filament Yucca, Silkgrass, Spoonleaf Yucca, Desert Candle, Needle Palm

Vernacular Names

Czech: Juka Vláknitá
Danish: Palmelilje, Trævlet Palmelilje
Eastonian: Kiuline Tääkliilia
French: Yucca
German: Fädige Palmlilie, Yucca
Hungarian: Kerti Jukka, Pálmaliliom
Norwegian: Plamelilje, Yucca
Polish: Juka Karolińska; Jukka Karolińska; Jukka Nitkowata; Jukka Ogrodowa
Spanish: Yuca
Swedish: Fiberpalmlilja

Origin/Distribution

The plant is a native of southeastern N. America to Mexico. It has been introduced and become naturalized in Europe.

Agroecology

In its native range, it occurs in sand dunes, waste ground and pine forests along the coastal plain. The plant thrives in sandy to sandy loam soils in full sun and is very drought tolerant and do well in outdoor container even without supplementary irrigation.

Edible Plant Parts and Uses

Flowers are eaten fresh and raw, cooked or dried, crushed and used as flavouring (Kunkel 1984; Bird 1990; McPherson 2007). Flowers can be added to salad (Facciola 1990). Some common recipes include yucca flower soup, stuffed yucca flowers

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and apple crumble pie (Roberts 2000). Another recipe is braised yucca flowers with peas (Belsinger 1990). Flowering stem is cooked and used like asparagus (Bird 1990). The fruits are eaten raw or cooked (Uphof 1968; Usher 1974; Facciola 1990). The fruit is often dried for winter use.

Botany

An acaulescent herbaceous perennial 1–4 m high (Plate 1). Leaves basal, strap-like, 2–4 cm wide and 0.6–1 m long, all originating from a point in the form of a rosette. Leaf lamina occasionally erect, proximal leaves often becoming reflexed near middle, lanceolate, flattened, abruptly narrowed and furrowed to apex, thin, widest near middle, usually soft and limp, scabrous, margins entire, long and curling, filiferous (producing threads) (Plate 2). The inflorescence paniculate, showy and borne on an erect scape 1–3 m high (Plates 1 and 3). Flowers up to two dozen, pendent, perianth globose; tepals distinct, creamy-white to nearly white, ovate, 5–7 × 2–3 cm, glabrous with short-acuminate apex; filaments shorter than pistil; pistil 1.5–3.8 cm with lobed stigmas (Plates 3, 4 and 5). Fruits erect, capsular, dehiscent, oblong, 3.8–5 by 2 cm. Seeds dull black, thin, 6 mm across.

Plate 2 Strap-like leaves with threads (filiferous)

Plate 1 Yucca plant with 1–3 m long flowering scape

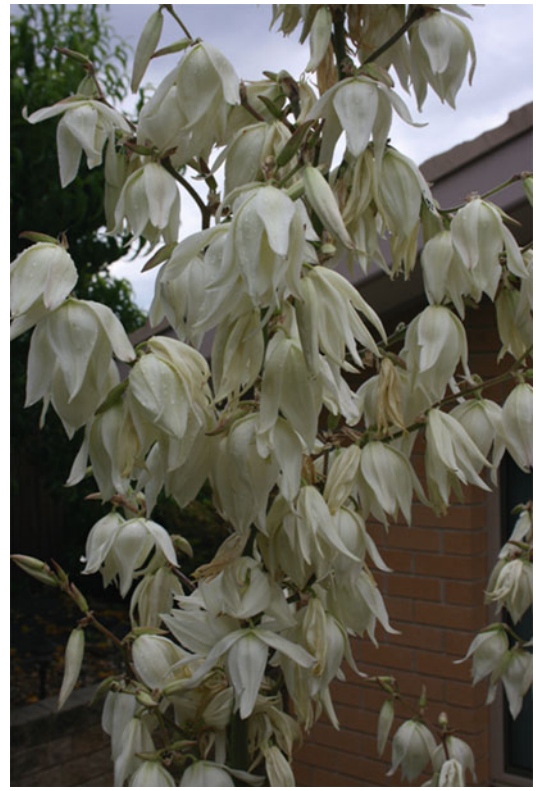

Plate 3 Flowering spike with paniculate branching

Plate 4 Pendant flowers with creamy-white tepals

Plate 5 Close view of flowers

Nutritive/Medicinal Properties

The roots of *Yucca filamentosa* were found to contain steroid saponins, steroid glycosides (Chernoff et al. 1917; Wells 1935; Kintya et al. 1972; Lazur'evskiĭ et al. 1975; Dragalin and Kintya 1975) and inulin (Wells 1935). Chernoff et al. (1917) isolated a saponin $C_{24}H_{40}O_{14}$ from the rootstock of *Y. filamentosa* which on hydrolysis yielded a sapogenin. From the roots and leaves of *Yucca filamentosa*, steroidal saponins sarsapogenin, hecogenin, tigogenin and chlorogenin and glycosides were isolated (Kintya et al. 1972). Glycoside A was identified as trillin, and glycoside B designated as yuccoside B. Two new saponins, yuccoside C and protoyuccoside C, were isolated from the methanolic extract of *Yucca filamentosa* root (Dragalin and Kintya 1975). The structure of yuccoside C was elucidated as 3-*O*-[α-D-galactopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl]-(25*S*)-5β-spirostan-3β-ol, whereas protoyuccoside C was 3-*O*-[α-D-galactopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl]-26-*O*-[β-D-glucopyranosy]-(25*S*)-5β-furostan-3β, 22α,26-triol. A new sarsasapogenin glycoside, yuccoside E was isolated from the roots and elucidated as 3-*O*-{[*O*-α-D-galactopyranosyl(1 → 2)]-[−*O*-β-D-galactopyranosyl (1 → 6)]-*O*-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl}-(25*S*),5β-spirostan-3β-ol (Dragalin et al. 1975).

A new gitogenin-based steroidal saponin with a strong leishmanicidal activity was isolated by bioactivity-guided fractionation of the ethanolic extract of *Yucca filamentosa* leaves (Plock et al. 2001). The saponin was characterized as 3-*O*-((β-D-glucopyranosyl-(1 → 3)-β-D-glucopyranosy-(1 → 2))(α-L-rhamnopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 3))-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranosyl)-25R,5α-spirostan-2α,3β-diol.

Twenty-one volatile scent compounds were identified in the floral headspace of *Yucca filamentosa* (Svensson et al. 2005). Most of the compounds could be categorized into two major classes: (1) homoterpenes derived from the sesquiterpene alcohol nerolidol and (2) long-chain aliphatic *n*-alkenes and alkanes with 15–19 carbons. The homoterpene *E*-4,8-dimethylnona-1,3,7-triene was produced in highest relative amounts in all populations (14.2–82.5 %), followed by a C_{11} alcohol (2.5–31.6 %) and 1-heptadecene (3.4–27.1 %). The remaining compounds typically comprised <10 % of the total sample. Two compounds were identified as di-oxygenated compounds with unknown structures.

Traditional Medicinal Uses

The genus *Yucca* (including *Y. filamentosa*) plant extracts were used to soothe joint pain, bleeding, urethral and prostate inflammations (Patel 2012). The leaves were brewed for common ailments as psoriasis, dandruff, hair loss and skin sores. Navajo Indians used it on sunburns and scratches. In northern New Mexico, traditional healers used a tea from the leaves and roots to treat asthma and headache. The Catawba, Cherokee, Nanticoke and other Native American tribes used *Yucca filamentosa* as medicines and soap. The roots were crushed to make poultice for wound healing and were used to cure gonorrhoea and rheumatism.

Other Uses

Y. filamentosa is excellent ornamental in rock gardens and as an accent among other perennials in natural areas and in mixed borders. It combines well with Agaves, grasses, cactus and palms to create low-maintenance xeriscapes of interesting textures and forms.

The leaves are used as paint brushes (Balls 1962). A fibre obtained from the leaves is used for making ropes, cloth, baskets and mats (Uphof 1968; Usher 1974) The fibre can also be used for making cream paper (Bell 1988). The roots are rich in saponins and can be used as a soap substitute for washing the hair, body and clothing (Uphof 1968; Usher 1974).

Comments

The plant is propagated by seeds, root cuttings and offshoots. Botanists report that *Yucca filamentosa* and *Y. flaccida* are very closely related and perhaps are not distinct species.

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Achillea millefolium

Scientific Name

***Achillea millefolium* L.**

Synonyms

Achillea albida Willd., *Achillea alpicola* (Rydb.) Rydb. (illeg.), *Achillea ambigua* Boiss., *Achillea ambigua* Pollini, *Achillea anethifolia* Fisch. ex Herder, *Achillea angustissima* Rydb., *Achillea arenicola* A.Heller, *Achillea bicolor* Wender., *Achillea borealis* var. *arenicola* J.T.Howell, *Achillea borealis* subsp. *arenicola* (A.Heller) D.D.Keck, *Achillea borealis* subsp. *californica* (Pollard) D.D.Keck, *Achillea borealis* var. *californica* (Pollard) J.T. Howell, *Achillea borealis* f. *fusca* (Rydb.) Hultén, *Achillea californica* Pollard, *Achillea ceretanica* Sennen, *Achillea compacta* Lam., *Achillea coronopifolia* Willd., *Achillea crassifolia* Colla, *Achillea cristata* Hort. ex DC., *Achillea cuspidata* Wall.(inval.), *Achillea dentifera* Rchb., *Achillea eradiata* Piper, *Achillea fusca* Rydb., *Achillea gigantea* Pollard, *Achillea gracilis* Raf., *Achillea haenkeana* Tausch, *Achillea intermedia* Schleich., *Achillea lanata* Lam., *Achillea lanulosa* Nutt., *Achillea lanulosa* subsp. *alpicola* (Rydb.) D.D.Keck, *Achillea lanulosa* var. *alpicola* (Rydb.) Rydb., *Achillea lanulosa* var. *arachnoidea* Lunell, *Achillea lanulosa* var. *eradiata* (Piper) M.Peck, *Achillea lanulosa* subsp. *megacephala* (Raup) Argus, *Achillea lanulosa* f. *peroutkyi* F.Seym., *Achillea lanulosa* f. *rubicunda* Farw., *Achillea laxiflora* A.Nelson, *Achillea laxiflora* Pollard & Cockerell, *Achillea magna* All. (illeg.), *Achillea magna* L. *Achillea magna* Haenke (illeg.), *Achillea marginata* Turcz. ex Ledeb., *Achillea megacephala* Raup, *Achillea millefolilium* E.Mey., *Achillea millefolium* f. *albiflora* Dabrowska, *Achillea millefolium* var. *alpicola* (Rydb.) Garrett, *Achillea millefolium* var. *arenicola* (A.Heller) Nobs, *Achillea millefolium* var. *arenicola* (A.Heller) Ferris, *Achillea millefolium* var. *asplenifolia* (Vent.) Farw., *Achillea millefolium* subsp. *atrotegula* B.Boivin, *Achillea millefolium* subsp. *balearica* Sennen, *Achillea millefolium* var. *borealis* (Bong.) Farw., *Achillea millefolium* var. *californica* (Pollard) Jeps., *Achillea millefolium* f. *californica* (Pollard) H.M.Hall, *Achillea millefolium* var. *colliniformis* Dabrowska, *Achillea millefolium* subsp. *compacta* (Lam.) Bonnier & Layens, *Achillea millefolium* var. *dipetala* Dabrowska, *Achillea millefolium* f. *discolor* B.Boivin, *Achillea millefolium* var. *dissecta* Dabrowska, *Achillea millefolium* var. *fulva*, *Achillea millefolium* var. *fusca* (Rydb.) G.N.Jones, *Achillea millefolium* var. *gigantea* (Pollard) Ferris, *Achillea millefolium* var. *gigantea* (Pollard) Nobs, *Achillea millefolium* f. *iserana* (Podp.) Hayek, *Achillea millefolium* var. *iserana* Podp., *Achillea millefolium* var. *lanata* W.D.J.Koch, *Achillea millefolium* var. *lanulosa* (Nutt.) Piper, *Achillea millefolium* subsp. *lanulosa* (Nutt.) Piper, *Achillea millefolium* var. *litoralis* Ehrenb. ex Nobs, *Achillea millefolium* var. *lobata* Dabrowska, *Achillea millefolium* var. *maritima* Jeps., *Achillea millefolium* var. *megacephala* (Raup) B.Boivin, *Achillea millefolium*

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var. *nigrescens* E.Mey., *Achillea millefolium* var. *occidentalis* DC., *Achillea millefolium* var. *pacifica* (Rydb.) G.N.Jones, *Achillea millefolium* subsp. *pallidotegula*, *Achillea millefolium* subsp. *pannonica* (Scheele) Hayek, *Achillea millefolium* subsp. *pannonica* (Scheele) Oborny, *Achillea millefolium* var. *parviligula*, *Achillea millefolium* var. *parvula*, *Achillea millefolium* var. *puberula* (Rydb.) Nobs, *Achillea millefolium* var. *puberula* (Rydb.) Ferris, *Achillea millefolium* f. *rhodantha* Lepage, *Achillea millefolium* f. *rosea* (Desf.) E.L.Rand & Redfield, *Achillea millefolium* var. *rosea* (Desf.) Torr. & A.Gray, *Achillea millefolium* f. *roseiflora* B.Boivin, *Achillea millefolium* f. *roseoides* Breitung, *Achillea millefolium* f. *rubicunda* (Farw.) Farw., *Achillea millefolium* var. *russeolata*, *Achillea millefolium* var. *sordida* W.D.J.Koch, *Achillea millefolium* var. *spathulata* Dabrowska, *Achillea nabelekii* Heimerl, *Achillea nigrescens* (E.Mey.) Rydb., *Achillea occidentalis* (DC.) Raf., ex Rydb., *Achillea ochroleuca* Eichw., *Achillea ossica* K.Koch, *Achillea pacifica* Rydb., *Achillea palmeri* Rydb., *Achillea pannonica* Scheele, *Achillea pannonica* f. *laxa* Dabrowska, *Achillea pecten-veneris* Pollard, *Achillea pratensis* Saukel & R.Länger, *Achillea pseudotanitifolia* Wierzb. ex Rchb., *Achillea puberula* Rydb., *Achillea pumila* Schur, *Achillea rosea* Desf., *Achillea seidlii* J.Presl & C.Presl, *Achillea setacea* Schwein., *Achillea sordida* (W.D.J.Koch) Dalla Torre & Sarnth., *Achillea subalpina* Greene, *Achillea subhirsuta* Gilib. (inval.), *Achillea submillefolium* Klokov & Krytzka, *Achillea sylvatica* Becker, *Achillea tanacetifolia* Mill., *Achillea tenuifolia* Salisb. (illeg.), *Achillea tenuifolia* var. *albicaulis* (C.A.Mey.) Trautv., *Achillea tenuis* Schur, *Achillea tomentosa* Pursh (illeg.), *Achillea virgata* Hort. ex DC., *Achillios millefoliatus* St.-Lag., *Alitubus millefolium* (L.) Dulac, *Alitubus tomentosus* Dulac, *Chamaemelum millefolium* (L.) E.H.L.Krause, *Chamaemelum tanacetifolium* (All.) E.H.L.Krause, *Chamaemelum tomentosum* (L.) E.H.L.Krause (illeg.)

Family

Asteraceae

Common/English Names

Bad Man's Plaything, Bloodwort, Carpenter's Weed, Common Yarrow, Devil's Nettle, Devil's Plaything, Fernweed, Gordaldo, Knight's Milfoil, Milfoil, Musk Milfoil, Nosebleed, Nosebleed Plant, Old Man's Pepper, Plumajillo, Sanguinary, Sneezewort, Soldier's Friend, Soldier's Woundwort, Staunchweed, Thousand-Seal, Thousand-Seal Bad Man's Plaything, Thousand Weed, Thousand-Leaf, Thousand-Seal, Thousand Weed, Thousand-Leaf, Western Yarrow, Woundwort, Yarrow, Yarrow Bloodwort, Yarrow Milfoil, Yarroway

Vernacular Names

Argentina: Milhojas (Spanish)
Azerbaijan: Adi boymadərən
Brazil: Aquileia, Mil em Folhas, Mil-Folhas
Burmese: hta.ri:hpweing
Catalan: Milfulles
Chinese: Shi, Shi Cao, yang shi cao
Croatian: Armanj, Božja haluga, Božje drvce, Hajdučka trava, Hrb, Jezičec, Jutrocel, Kačak, Kačak, Koromačić, Kostenica, Kostret, Kostretica, kostrešica, koštenica, Malankovica, Mali stozlat, mekušica, Mesečina, Mrmanj, Mrmonj, Paprac, Rebrac, Reza, Rman Vodeni sporiš, Spor, Sporić-stolistak, sporiš, Stolika, Stoliska, Stolist, Stolista, Stolistak, Stolistac, Stolisnik, Tučija trava
Czech: Řebříček obecný, Řebříček obecný pravý
Danish: Almindelig røllike, Finbladet røllike, Røllike, Soldaterurt, Tømrerurt
Dutch: Duizendblad, Gewoon duizendblad
Eastonian: Harilik raudrohi
Egypt: Om alf waraka (Arabic)
Esperanto: Akileo milfolia, Milfolio
Finnnish: Aivastusjuuri, Akantupakki, Hurstinkukka, Pietarinkukka, Pyörtänäpöllö, Pyörtänöpöllö, Siankärsäheinä, Siankärsämö
French: Achillée, achillée mille-feuille, Herbe à Dinde, Herbe aux charpentiers, Herbe aux cochers, Herbe aux Militaires, Herbe de Saint-Jean, Herbe de St-Jean, Mille feuille
Gaelic: Athair thalún

German: Achillenkraut, Augenbraue der Venus, Bauchwehkraut, Blutkraut, Blutstillkraut, Feldscharfgarbe, Frauendank, Frauenkraut, Garbenkraut, Gebenkraut, Gemeine Schaf garbe, Gerwel, gewöhnliche Schafgarbe, Gliedkraut, Gotteshand, Grillengras, Katzen kraut, Katzenschwanz, Lämmerzunge, Marga retenkraut, Schafgarbe, Schafrippen, Schaf zunge, Tausendblatt, Tausendblättchen, Teekraut, Wiesen-Schafgarbe, Wiesen-Schafgarbe

Hungarian: Egérfarkfû, Közönséges cickafark, Mezei cickafark

Icelandic: Vallhumall

India: Biranjasipha, Gandana, Gandrain, Puthkanda, Bhut Kesi (Hindi), Bimjasif (Joshimath), Rajmari (Konkani), Rojmaari (Marathi), Achchilliya (Tamil), Tukhm gandana, Buiranjasif, Brinjasuf (Urdu)

Italian: Achillea, Achillea millefoglie, millefoglio, Millefoglio montano

Japanese: Seiyou no kogirisou, Yaroo

Kashmir: Momadrichopandiga

Korean: seoyangtobpul

Ladakh: Chabu, Chuang

Mexico: Alcanfor, Ciento en rama (Spanish)

Norwegian: Bakkeryllik, Broksjit, Hardhaus, Jordhumle, Kanelblom, Krydderblom, Ølkong, Røllik, Rølløkka, Ryllik, Soldaturt, Teblom, Tobakksblomst, Vanlig Ryllik

Persian: biranjasib, bu-l-maderan

Polish: Krwawnik pospolity

Portuguese: Aquiléia, Espuma-do-mar, Mil-em-rama, Mil-folhas, milefólio

Russian: tysâčelistnik obyknovennyj

Serbian: Ajdučica, Ajdučka trava, Aspra, Beli ravanj, Belo ivansko cveće, Hajdučica, Hajdučka trava, Jalova mesečina, Jalovi mesečnjak, Jalovo mesečje, Krvavac, Kunica, Kunji rep, Kučja trava, Ljutica, Mesečina, Moračika, Paprac, Petrovsko cveće, Ravan, Ravanj, Ravunika, Spor, Sporiš, Sporiševina, Stolistnik, Stolisnik, Tintorova trava

Slovašcina: Arman, Armanc, Erman, Grenki rman, Hrman, Jermanec, Kaček, Kačjek, Korancelj, Korocelj, Mezinec, Mezinic, Navadni rman, Rman navadni, Rmanc, Runica, Skorejca, Zavrelec, Zevrelčec

Slovencina: Rebříček obyčajný

Spanish: Aquilea, Aquillea, Artemisa bastarda, Cientoenrama, Flor de la pluma, Hierba de las heridas, Hierba de los carpinteros, Hierba de San José, Meona, Mil hojas, milenrama, Milfohas, Milfullas, Milhojas, Milorri

Swedish: Backhumle, Jordhumle, Karibacka, Näsegräs, Näsgräs, Rölleka, Röllika

Turkish: Beyaz civanperçemi, civanperçemi, Civanpercemiotu, Kandil Çiçek

Vietnamese: Cỏ thi, Cúc vạn diệp, Dương kỳ thảo, Xương cá

Welsh: Milddail, Gwilffrai, Llys Y Gwaedlif, Llysiau Marwolaeth, Llysiau'r Gwaedlin, Llysiau'r Gwaedlif, Milfyd, Milfydd, Minfel, Wrisgan Llwyd

Origin/Distribution

The plant is indigenous to temperate and alpine areas in Eurasia, including most of Europe and many parts of Asia (i.e., from Turkey eastwards to Siberia and northwestern India). It has been introduced into North America, China, New Zealand and Australia.

Agroecology

Yarrow is a cool climate plant; it is occasionally grown in the cooler highland parts of subtropical regions. In its native range, it grows at low or high altitudes, up to 3,500 m above sea level. It grows in disturbed habitats, neglected gardens, waste areas, grasslands, woodlands, pastures, turfed areas, gullies and along roadsides in relatively moist locations. It grows in full sun to partial shade, on acidic to alkaline soils. It is frost and drought tolerant.

Edible Plant Parts and Uses

The flowers and leaves are edible (Uphof 1968; Grieve 1971; Facciola 1990; Roberts 2000; Schofield 2003). An aromatic tea is made from the dried flowers and leaves. An essential oil

extracted from the flowering heads is used as a flavouring for soft and alcoholic beverages. Yarrow flowers can be fried with butter sprinkled with sugar or orange juice. The bitter leaves are eaten raw or cooked as spinach or in soups and are best used when young and tender. They are also used in mixed salads. Yarrow leaves were part of a herbal mixture known as 'gruit' used in the flavouring and preservation of beer prior to the use of hops. The leaves are also used as a substitute for tobacco, nutmeg, cinnamon and hops.

Botany

An erect, branched herbaceous perennial, 20–100 cm high with rhizomatous or stoloniferous growth form and sparingly branched or unbranched tomentose or glabrous stems. Leaves are petiolate; large near the middle and bottom or sessile, cauline and smaller towards the tip. Leaf blades lanceolate or oblong-lanceolate, 3.5–25 cm × 5–3.5 cm, bipinnate or tripinnate, feathery and arranged spirally on the stem, glabrous to sparsely tomentose or densely lanate (Plates 1 and 2). Inflorescence heads 10 to >100, in terminal, simple or compound, slightly rounded or flat-topped corymbs on the expanded end (receptacle) of the flower stalk (Plate 2). Involucre oblong or subovoid with 20–30 phyllaries (involucral bracts) in 3 overlapping series, ovate to lanceolate and hairy. Each flower head (capitulum) contains ray florets (female) and disk florets (bisexual) which are white and cream to pink to deep purple (Plate 3). There are generally 3–8 ray florets that are ovate to round. Disk florets 10–20, at the centre of the flower head, tubular, and greyish white or cream. Fruit tiny, oblong achenes, 2 mm, with broadly winged margins and no pappus.

Nutritive/Medicinal Properties

Plant Phytochemicals

Sesquiterpenes and sesquiterpene lactones found in the leaf and flowering head included acetylbalchanolide, millefolide, and an unknown lactone

Plate 1 Juvenile plant with fine, feathery pinnately compound leaves

with mp 138 °C (Hochmannová et al. 1961); leucodin and achillin (Romo de Vivar and Olmos 1968); desacetylmatricarin, matricarin and millefin (Kasymov and Sidyakin 1972); austricin (deacetylmatricarin), millefin, 8-hydroxyachillin and an isomer of matricarin (Adekenov et al. 1979; Kasymov and Sidyakin 1972); and artecanin, estafiatin, leucomisin and balchanolide from the plant (Konovalov and Chelombit'ko 1991). Achillicin, the major proazulene (prochamazulene) of *Achillea millefolium*, was isolated and identified as 8-acetoxyartabsin (Cuong et al. 1979a); chamazulene (2, 13–15) and chamazulene carboxylic acid were also isolated (Cuong et al. 1979b). Other sesquiterpenes isolated included proazulenes, 8-acetoxyartabsin, 8-anelooxyartabsin, 2,3-dihydrodeacet oxymatricin, (Verzár-Petri et al. 1979a) and azulene (Verzár-Petri et al. 1979b). Three main azulenogene sesquiterpene lactones were isolated from *A. millefolium* plant and identified as 8-acetoxy-artabsine, 8-angeloxy-artabsine and

Plate 2 White-flowering head

Plate 3 Purple flowering head

2,3-dihydro-desavetoxy-matricin (Verzár-Petri et al. 1980). Ulubelen et al. (1990) isolated a new sesquiterpene lactone, achillifolin, together with known sesquiterpene lactones, dihydroparthenolide and dihydroreynosin, from the aerial parts. Known flavonoids, terpenoids and vanillic acid were also isolated. Ohir et al. (1991) isolated desacetylmatricarin, two sesquiterpene lactones of a new 3-oxa-guaianolide type, 8-acetyl egelolide and 8-angeloyl egelolide from the aerial parts. The structures of 8 α-angeloxy-, 8 α-tigloxy- and 8 α-acetoxy-10-epi-artabsin (achillicin) as well as of the respective 3-oxa-analogues were revised by Schröder et al. 1994). On the basis of 2D-NMR spectral data, it was shown unequivocally that these compounds were artabsin derivatives. *Achillea millefolium* was reported to contain α-peroxyachifolid, dehydromatricaria ester, pontica epoxide (Rücker et al. 1991; Hausen et al. 1991) and isoachifolidiene, a precursor of guaianolide peroxides (Rücker et al. 1992). Three new antitumor sesquiterpenoids, achimillic acids A, B and C, were isolated as methyl esters from *Achillea millefolium* (Tozyo et al. 1994) Three new sesquiterpenes which were trivially named as sesquiterpene lactone esters A and B (1 and 2) and sesquiterpene lactone-diol (3) were isolated from the plant (Farooq et al. 2012).

Several species of the polyploid *A. millefolium* group, however, could be characterized by their distinct sesquiterpene pattern (Montsko et al. 2008). *A. millefolium* was characterized by the presence of 8-desacetylmatricarin, santonin, matricarin, achillicin and artabsins; *A. pratensis* by arglanin, 4-hyperoxy-arglanin, santonin and santamarin; and *A. collina* by 8-desacetylmatricarin, santonin, matricarin, achillicin, 3-oxa-achillin, 8α-angeloxy-artabsin, 8α-angeloxy-3-oxa-art absin, 8α-tigloxy–artabsin and 8α-tigloxy–3-oxa-artabsin.

Five sesquiterpenoid, i.e., seco-pseudo guaianolides (paulitin, isopaulitin, psilostachyin C,

desacetylmatricarin and sintenin) and five flavonoids (apigenin, luteolin, centaureidin, casticin and artemetin) were isolated and identified from the aerial parts of the *Achillea millefolium* aggregate (Csupor-Löffler et al. 2009). Flavonoids found in the plant included rutin, apigenin, luteolin and the 7-glucosides of apigenin and of luteolin, cosmosiin and luteolin 7-*O*-β-D-glucopyranoside (Kaloshina and Neshta 1973). The main flavonoid constituents of leaf and flower heads of *Achillea millefolium* subspecies were found to be apigenin and luteolin, mainly found as 7-*O*-glucosides and 7-malonylglucosides (Guédon et al. 1993). This represented the first report of flavone glycoside malonylesters in *Achillea* genus. White-flowering populations, i.e., the ssp. *millefolium* and *ceretanum*, showed a similar distribution of flavonoid compounds, whereas the presence of rutin in the leaves of the *alpestris* ssp. appeared to be characteristic. The flowering tops of this taxon were distinguished from the other two by their amount of schaftoside and isoschaftoside. The following sesquiterpenoids were isolated from *A. millefolium* group (*A. collina* and *A. pratensis*): achillicin, 8α-tigloxy-artabsin, 8α-angeloxy-artabsin, arglanin and santamarin (Glasl et al. 1999).

The flavonoids found in *A. millefolium* of the section *Millefolium* comprised of flavonoid aglycones and flavonoid glycosides—C-glycosylflavones, flavonol and flavones O-glycosides (Ivancheva et al. 2002). The flavonoid aglycones comprised large amounts of quercetagetin 3,6,7-trimethyl ether (chrysophenol-D), quercetagetin 3,6,7,3′,4′-pentamethyl ether (artemetin); small amounts of scutellarein 6,7, 4′-trimethyl ether (salvigenin), quercetagetin 3,6, 4′-trimenthyl ether (centaureidin); and traces of scutellarein 6-methyl ether (hispidulin), scutellarein 6,7-dimethyl ether (cirsimarin) and 6-hydroxyluteolin 6-methyl ether (nepetin). The flavonoid glycosides comprised small amounts of vitexin (5,7,4′-trihydroxyflavone-8-C-glycosyl), vicenine 2 (5,7,4′-trihydroxyflavone-6,6-di-C-glycosyl) and swertjponin (5,3′,4′-trihydroxy-7-OMeflavone-6-C-glycosyl) and traces of swertisin (5,4′-dihydroxy-7-OMeflavone-6-C-glycosyl). The flavonol and flavones *O*-glycosides were large amount of quercetin-3-*O*-glycoside, small amount of quercetin-3-*O*-*rhamnoglycoside*, and traces of luteolin-7-*O*-glycoside, diosmetin-7-*O*-glycoside and kaempferol-3-*O*-glycoside. The flavonoid casticin was isolated from *Achillea millefolium* (Haïdara et al. 2006). The following flavonoid compounds were found in *Achillea* species belonging to the *A. millefolium* L. group (Gherase et al. 2004): rutin, apigenin-7-*O*-*glucoside* and luteolin-7-*O*-glucoside were found in the methanol extract. The free aglycones, apigenin and luteolin, were also detected. Total phenolic contents reported for *A. millefolium* herb were 9.55 mg GAE/100 g DW (Wojdyło et al. 2007). Major phenolic compounds (mg/100 g DW) found were phenolic acids, 429 mg caffeic acid, 118 mg neochlorogenic acid and 35 mg ferulic acid, and flavonoids, 103 mg luteolin and 84.3 mg apigenin. The following phenolic compound were isolated from the methanol extract of *A. millefolium*: chlorogenic acid (1), rutin (2), luteolin 7-*O*-glucoside (3); 1,3-dicaffeoylquinic acid (4); 1,4-dicaffeoylquinic acid (5); 3,4-dicaffe oylquinic acid (6); apigenin 4′-*O*-glucoside (7); apigenin 7-*O*-glucoside (8); luteolin 4′-*O*-glucoside (9); and 3,5-dicaffeoylquinic acid (10) (Vitalini et al. 2011). Polyphenolic compounds (g/kg dry matter) in the aerial yarrow plant parts were determined as follows: chlorogenic acid 8.12 g, 3,5-DCQA (dicaffeoylquinic acid) 21.59 g, 1,5-DCQA 8.88 g, 4,5, DCQA 3.31 g, total caffeoyl derivatives 41.90 g, total dihydroxycinnamic acid derivatives 52.67 g, total flavonoids 12.92 g, total dihydroxycinnamic acid derivatives + flavonoids 65.59 g and total polypenolic compounds 63.06 g (Fraisse et al. 2011).

Thirty-five compounds were isolated from various fractions of the ethanol extract of the dried plant material of *Achillea millefolium* (Tunón et al. 1994). From the C:1 fraction, adenine, betaine, betonicine, choline, homostachydrine, mandelonitrile glucoside, rutin, staydrine and trigonelline were isolated; from fraction C:2, caffeic acid, chlorogenic acid, ferulic acid, mandelic acid, salicylic acid and vanillic acid; and from fraction F:2, apigenin, capric acid methyl ester, caprylic acid methyl ester, carvacrol, eugenol, gallic acid, hydroquinone, isorhamnetin, linoleic acid ethyl ester, linoleic acid methyl

ester, linolenic acid methyl ester, luteolin, palmitic acid ethyl ester, palmitic acid methyl ester, phloroglucinol, protocatechuic acid, pyrocatechol, quercetin, tannic acid and undecylenic methyl ester were isolated.

Beta-sitosterol was identified as the major sterol and α-amyrin as the major triterpene of *A. millefolium* (Chandler et al. 1982b). The sterols stigmasterol, campesterol and cholesterol; and the triterpenes β-amyrin, taraxasterol and pseudotaraxasterol were also identified.

From above ground parts of *Achillea collina* within the *A millefolium* group, proline, stachydrine, betonicine, betaine and choline were isolated as the major nitrogen containing compounds (Mehlführer et al. 1997). The TLC screening of 11 different species belonging to *A. millefolium* group showed qualitatively identical betaine patterns but quantitative differences were observed.

From the lipophilic extract of subterranean parts of *Achillea millefolium* s.str. 17 different alkamides together with (+)-sesamin were isolated and identified (Greger and Hofer 1989). Besides a rare decadienoic acid tyramide and the corresponding novel *p*-methoxy derivative, the amide pattern was especially characterized by the dominating olefinic piperideides. Greger and Werner (1990) compared the alkamides from the subterranean parts of different members of the *Achillea millefolium* group. They found that the European representatives (*A. millefolium*, *A. pannonica*, *A. collina*, *A. asplenifolia*, *A. setacea*) were predominated by deca-2 *E*,4 *E*,6*Z*-trienoic piperideide with some cytotypes accumulating two isomeric decatetraenoic piperideides and (+)-sesamin. The alkamide patterns of the Asian and North American members (*A. asiatica*, *A. lanulosa*) were characterized by a preponderance of decadienoic acid-derived isobutylamide and piperideide.

Thirteen compounds were identified in the essential oil: borneol, camphene, camphor, 1,8 cineole, α-pinene, *p*-cymene, furfuryl alcohol, isobutyl acetate, isovaleric acid, limonene, menthol, sabinene and terpinene-4-ol (Bejnarowicz and Smolenski 1968). Haggag et al. (1975) reported the following constituents in the essential oil: azulene, caryophyllene, eucalyptol, borneol, bornyl acetate, α-pinene, β-pinene, limonene and α-thujone. The major components of the essential oil hydrodistilled from the stems, leaves and inflorescences were found to be β-thujone (8.3–21.7 %), camphor (8.6–11.7 %), 1, 8-cineole (7.7–15.2 %), β-pinene (3.8–7.8 %) and sabinene (5.7–8.9 %) (Hachey et al. 1990). More than 60 components have been identified, 40 of which were mainly oxygenated compounds. Several monoterpenes and sesquiterpenes were identified in the essential oil of wild *Achillea millefolium* complex in northern Greece, although the main component was ascaridole (47.2 %) (Chatzopoulou et al. 1992). Lesser amounts of 1, 8-cineole (10.5 %), *p*-cymene (7.4 %), α-terpinene (7.0 %) and camphor (8.1 %) were found. Bélanger and Dextraze (1993) reported the following as main components (range) in the essential oils of *A. millefolium* plants: chamazulene (51.3–1.16 %), germacrene D (54.7–5.6 %), β-thujone (35.1–0 %), α-thujone (20.7–0 %), α-phellandrene (17.4–0 %), sabinene (17.2–0.29 %), myrcene (14.7–0.10 %), β-pinene (9.74–0.2 %), β-caryophyllene (7.68–0.54 %), camphor (6.7–0.2 %), 1,8-cineole (6.45–0.26 %) *p*-cymene (1.73–0 %), bornyl acetate (3.88–0 %), camphene (2.68–0.11 %), limonene (3.11–0 %) and γ-terpinene (5.5–0.2 %).

The main volatile constituents found in *Achillea millefolium* growing wild in Greece were 1,8-cineole, camphor, borneol and lavandulol (Kokkalou et al. 1992). A comparison of the main volatile constituents currently found in *A. millefolium* oils revealed that great infraspecific variation occurred. One hundred twenty-three components were identified in the oil of aerial parts of *A. millefolium* from Kazakhstan representing 93.1 % of the oil (Suleimenov et al. 2001). Camphor (16 %), 1,8-cineole (8.7 %), borneol (6.2 %), β-eudesmol (6.1 %), α-terpineol (5.9 %), α-bisabolol (5.5 %) and terpinen-4-ol (3.1 %) were found as the major compounds.

Twenty components were identified in the essential oil of aerial parts of *A. millefolium* grown in Siberia (Smelcerovic et al. 2010). Major constituents were 1,8-cienole (28.8 %), camphor (11 %), borneol (5.9 %), β-pinene (5,4 %), caryophyllene oxide (3.3 %), β-caryophyllene (3.1 %),

α-elemol (3 %) and α-terpineol (2.9 %). Other components included α-pinene (2.5 %), terpinen-4-ol (2.3 %), camphene (0.7 %), sabinene (0.1 %), *p*-cymene (1.9 %), germacrene D (0.7 %), γ-terpinene (0.5 %), humulene (0.4 %), (*Z*)-β-farnesene (0.3 %), α-muurolene (0.2 %), cadina-3,9-diene (0.1 %) and hexahydrofarnesyl acetone (0.1 %). 1,4-dimethyl azulene, chamazulene, chamazulenecarboxylic acid and achillin were also found.

Trans-nerolidol (1–31.9 %), caryophyllene oxide (2.1–23 %), β-pinene (0.5 –20.0 %), 1,8-cineole (0.5–11.9 %) were found to be the first predominant constituents in all 20 leaves and flower oils of white- and pink-flowering *A. millefolium* plants (Judzentiene and Mockute 2010). Other components found in all 20 samples included β-caryophyllene (1.7.7 %), α-pinene (0.1–6.3 %), sabinene (0.1–8.0 %), α-terpinene (tr – 0.6 %), borneol (tr – 8.4 %), terpinen-4-ol (tr – 2.8 %), α-terpineol (tr – 0.9 %), bornyl acetate (0.1–6.0 %), α-humulene (tr – 1.2 %), germacrene D (tr – 3.8 %) and (2Z,6*E*)-farnesyl acetate (tr – 3.5 %). Selin-11-en-4-α-ol (tr – 10.4 %) was also dominant and found in both leaf and flowers of ten pink- and seven white-flowered plants. 10-epi-γ-eudesmol was also dominant in 17 samples comprising 10 samples (tr – 12.2 %) in both flower and leaves of white cultivars and seven samples (0.8–5.8 %) in both flower and leaves of pink cultivars. Spathulenol was also dominant in 19 samples (tr – 10.2 %) in 10 white- and 9 pink-flowering plants. Other compounds found in 17–19 samples (leaf and flowers) included camphene (tr – 3.7 %), myrcene (tr – 1.1 %), *p*-cymene (tr – 2.4 %), γ-terpinene (0.1–1.4 %), terpinolene (tr – 2.3 %), camphor (tr – 6.7 %), *cis*-chrysanthenol (tr – 0.9 %), β-bourbonene (tr – 0.3 %), β-bisabolene (tr – 2.6 %), δ-cadinene (tr – 7.6 %), α/β-caryophylla—4(14), 8(15)-dien-5-ol (tr – 6.7 %) and (2Z,6*E*)-farnesol (tr – 1.7 %). Chamazulene was found in five samples (tr – 1.4 %) of the leaf and flower of the pink-flowered plants and one sample in the flower of white-flowered plant (2.7 %). 1-epi-cubenol was only found in white-flowered plants (nine out of ten samples, tr – 2.7 %). (2*E*, 6*E*)-farnesol was only found in pink-flowered plants (tr – 1.9 %). Chrysanthenone and carvotanacetone were found only in the flower (7.2, 2.1 %) and leaf (7.6, 2.6 %) samples, respectively, of pink-flowered plant in the same one locality. Significant qualitative and quantitative variations were also found in the total content of monoterpenes (1.2–57.2 %) and sesquiterpenes (39.9–98.8 %).

Studies in Norway reported that the essential oil content of *Achillea millefolium* differed greatly between the vegetative stage (0.13 %) and the stage of full bloom (0.34 %) (Rohloff et al. 2000). Changes in the composition of yarrow essential oil were found to be related to maturation of the plant, with increasing amounts of monoterpenes in relation to the sesquiterpene. A clear trend was detected only for the monoterpenic compounds with increasing levels of α-pinene and β-pinene and α-thujone and decreasing levels of sabinene, borneol and bornyl acetate. Previously reported as major compounds, chamazulene and germacrene D could be found only in insignificant amounts. Sesquiterpenic compounds such as β-bisabolene, α-bisabolol and δ-cadinene were detected in substantial amounts by solid-phase microextraction (SPME) in contrast to the steam-distilled samples.

Twenty-one volatile constituents were isolated from the oil of Iranian *A. millefolium* (Afsharypuor and Asgary 1996). The oil possessed a high percentage (55.4 %) of sesquiterpenes. The major components of this fraction were α-bisabolol (22.9 %), spathulenol (12.4 %), *cis*-nerolidol (5.7 %), *cis*-carveol (5 %) and *trans,trans*-farnesol (4.0 %). Other components included phenol (3.9 %), *trans*-carveol (3.7 %), $C_{IO}H_{18}O_2$ (3.5 %), *cis*-sabinol (2.5 %), *cis-β-farnesene* (2.7 %), α-patchoulene (2.2 %), 2-pentyl- 5-propylresorcinol (1.8 %), campherenone (1.7 %), C_{15} H_{26} O (1.7 %), bornyl acetate (1.3 %), β-himachalene (1.2 %), geranyl acetate (0.9 %), caryophyllene (0.9 %), 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin (0.9 %),6,10,14-trimethyl pentadecan-2-one (0.8 %) and neryl acetate (0.7 %). The percentage of sesquiterpenes in the oil obtained from flowers and leaves of the plants grown in Portugal was much lower (up to 8.5 %) and was dominated by germacrene-D. The oil obtained from

Iranian *A. millefolium* ssp. *millefolium* possessed a high percentage of sesquiterpenes (55.4 %) in which α-bisabolol was the main compound, while no proazulene or 1,8-cineole was detected (Saeidnia et al. 2004). The major components of the oil were α-copaene (11.1 %) and (*E*)-nerolidol (8.8 %). The main constituents of *A. millefolium* essential oil from the Balkans (21 compounds) were β-pinene (32.63 %), β-caryophyllene (16.52 %), sabinene (11.48 %) and chamazulene (5.86 %), and these four compounds constituted 66.49 % of the oil (Boskovic et al. 2005). Other constituents included 1,8-cineole (4.57 %), caryophyllene oxide (3.74 %), bicyclogermacrene (2.70 %), α-pinene (2.52 %), bornyl acetate (2.42 %), germacrene D (2.12 %), α-humulene (2.12 %), α-phellandrene (0.76 %), α-terpinene (0.47 %), α-copaene (0.75 %), α-thujene (0.51 %), terpinolene (0.42 %), β-bourbonene (0.41 %), γ-terpinene (0.39 %), 4-terpineol (0.36 %), β-longipinene (0.20 %) and borneol (1.68 %). A total of 102 components were identified from the essential oil of *A. millefolium* plants from various European countries (Orav et al. 2006). The quantitatively most important components of yarrow were sabinene, β-pinene, 1,8-cineole, artemisia ketone, linalool, α-thujone, β-thujone, camphor, borneol, fenchyl acetate, bornyl acetate, (*E*)-β-caryophyllene, germacrene D, caryophyllene oxide, β-bisabolol, δ-cadinol, chamazulene and others.

Another study on the essential oil of *Achillea millefolium* subsp. *millefolium* in Iran identified 20 volatile components (Srabi and Meshkatalsadat 2010). The predominant compounds were geraniol (33.43 %), neryl acetate (17.48 %), farnesol (7.61 %), benzyl benzoate (6.08 %), nerolidol (5.61 %), limonene (5.38 %) and linalool (3.15 %). Other constituents included neral (2.93 %), geranyl butyrate (2.67 %), α-pinene (2.53 %), 1,8-cineole (1.93 %), chrysanthenone (1.77 %), δ-elemene (1.00 %), β-pinene (0.68 %), α -terpineol (0.57 %), nerol oxide (0.54 %), *cis*-jasmone (0.47 %), sabinene (0.34 %), camphor (0.27 %) and geranial (0.11 %). The Italian volatile extracts (SFE (supercritical extraction with CO2) and essential oil) of aerial parts were predominantly composed by α-asarone (25.6–33.3 %), and in the SFE extract and in the HD oil, respectively, β-bisabolene (27.3–16.6 %) and α-pinene (10.0–17.0 %), whereas the main components of the Portuguese extracts were *trans*-thujone (31.4–29.0 %), *trans*-chrysanthenyl acetate (19.8–15.8 %) and β-pinene (1.2–11.1 %) (Falconieri et al. 2011).

The populations *Achillea millefolium* from two different high-altitude Himalayan habitats (1,600 m, 2,850 m) proved to represent two different ecotypes: the 1,8-cineole type and the borneol type with appreciable differences in the contents of oils and mono- and sesquiterpenes (Agnihotri et al. 2005). The major components were characterized as β-pinene (10.6–17.7 %), 1,8-cineole (3.0–15.1 %), borneol (0.2–12.1 %), and β-caryophyllene (8.5–16.2 %). Thirty components were identified in the essential oil of *A. millefolium* cultivated under the tropical conditions of Delhi, India, comprising 93.43 % of the oil content (Nadim et al. 2011). The predominant constituents were sabinene (17.58 %), 1,8-cineole (13.04 %), borneol (12.41 %), bornyl acetate (7.98 %), α-pinene (6.28 %), β-pinene (6.26 %), terpinine-4-ol (6.17 %) and chamazulene (5.28 %). Other minor components included: β-caryophyllene (2.31 %), camphene (2.07 %), germacrene D (1.49 %), limonene (1.27 %), δ-terpinene (1.19 %), *p*-cymene (1.11 %), α-terpineol (1.04 %), methanol (1.03 %), α-thujone (1.00 %), δ-cadinene (0.94 %), α-cadinol (0.90 %), azulen (0.85 %), myrcene (0.81 %), thujanol (0.54 %), pentadecanoic acid (0.49 %), *trans*-carveol (0.44 %), myristic acid (0.23 %), dodecane (0.18 %), α-thujenal (0.16 %), α-copaene (0.13 %), myrtenol (0.13 %) and cyclohexene (0.12 %).

The terpenoid profile of homeopathic tincture prepared from fresh *A. millefolium* plant material comprised 1,8-cineole (18.28 %), α-pinene (11.96 %), germacrene D (11.62 %), phytol (11.20 %) and *trans*-caryophyllene (10.52 %), as dominant components (Lyakina 2002). Other components were sabinene (4.93 %), 1,4-terpineole (3.08 %), camphor (2.57 %), *trans*-sabinene hydrate (2.49 %), β-fenchol (2.49 %), lavandyl acetate (1.85 %), α-humulene (1.26 %) and 4-thujen-2-α-yl-acetate (1.07 %). In contrast, the terpenoid

profile of homeopathic tincture prepared from dried plant material comprised 1-limonene (29.92 %), sabinene (9.44 %), *trans*-caryophyllene (8.78 %) and phytol (7.59 %) as dominant components. The minor components were 1,8-cineole (5.27 %), lavandyl acetate (5.19 %), germacrene D (5.09 %), β-pinene (3.59 %), pseudocumene (3.20 %), episonarene (3.14 %), caryophyllene oxide (2.54 %), α-pinene (2.42 %), α-humulene (1.27 %), γ-selinene (0.94 %), α-longipinene (0.60 %) and camphene (0.24 %).

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Leaf Phytochemicals

Rutin was isolated from the leaves (Neshta et al. 1972). 6-Hydroxyflavones, 6-hydroxyflavonols, and their methyl ethers predominated in the leaf exudates in various combinations in 78 collections of species forming the *Achillea millefolium* group (Valant-Vetschera and Wollenweber 1988). Leaves of field-grown plants accumulated higher concentrations (%w/w dw) than those of hydroponic grown plants in apigenin glycosides (0.25 versus 0.07 %) and total flavonoids (apigenin, luteolin and apigenin glycosides) (0.26 versus 0.08 %) but lower amount of aglycone flavonoids of luteolin and apigenin (0.009 versus 0.012 %), respectively (Pedneault et al. 2002).

During the flowering period of *Achillea millefolium*, the leaf oil consisted mainly of monoterpenes (about 80 %);1,8-cineole was the dominant component (18 %) followed by *trans*-sabinene hydrate (10 %) (Figueiredo et al. 1992a). The sesquiterpene fraction was dominated by germacrene-D (7 %). In the essential oil isolated from leaves collected during the vegetative phase, the monoterpene fraction was small (<3 %), whereas sesquiterpenes amounted to 92 %, germacrene-D being the major component (65 %) of the oil. Forty-two compounds were identified in the leaf oil of Cuban *A. millefolium*; caryophyllene oxide (20 %) was the major volatile constituent (Pino et al. 1998).

The major volatile aroma components of the leaf (area units divided by 100,000 per g dry matter) was α-pinene (96) and the rest were detected in very small to trace amounts: propanal, 2-methyl; butanal, 2-methyl; butanal, 3-methyl; pentanal; α-thujene; hexanal; β-pinene; sabinene; 1,8-cineole; and *p*-cymene (Dokhani et al. 2005). Total phenolics in the leaves were 32.7 mg/g dm and total tartaric esters were 11.7 mg/g dm.

Flower Phytochemicals

Three flavones, 5-hydroxy-3,6,7,4′-tetramethoxyflavone, artemetin and casticin, were isolated from the petroleum ether extract of the flowering heads of *Achillea millefolium* (Falk et al. 1975). From the ether extract of *Achillea millefolium* flowers, two guaianolides with a peroxide bridged cyclopentane ring and an α-methylene-γ-butyrolactone structure were isolated and the compounds were designated α-peroxyachifolid and β-peroxyisoachifolid. Three flavonoid aglycones, one triterpene, one germacranolide and five guaianolides were isolated and characterized from the dichloromethane extract of flower heads of a Hungarian taxon of the *Achillea millefolium* group (Glasl et al. 2002, 2003). Besides apigenin, luteolin and centaureidin, β-sitosterol, 3β-hydroxy-

11α,13-dihydrocostunolide, desacetylmatricarin (= austricin, austrisin), leucodin (= desacetoxymatricarin, leucomisin), achillin, 8α-angeloxyleucodin and 8α-angeloxy-achillin were isolated. Eight phenolic compounds—chlorogenic acid and flavonoids—namely, vicenin-2, luteolin-3′,7-di-*O*-glucoside, luteolin-7-*O*-glucoside, rutin, apigenin-7-*O*-glucoside, luteolin and apigenin, were identified in the extracts from yarrow (*Achillea millefolium*) flowers (Benetis et al. 2008). The total amount of the identified phenolics in yarrow flowers from different populations varied from 13.290 to 27.947 mg/g.

Achillinin A (2β,3β-epoxy-1α,4β,10α-trihydroxyguai-11(13)-en-12,6α-olide), a new guaianolide, was isolated from the flower (Li et al. 2011). Ten 1,10-secoguaianolides were isolated from the flowers of *Achillea millefolium* (Li et al. 2012a). Three of them (millifolides A–C) including two dimeric sesquiterpenoids exhibit new skeletons. Seco-tanapartholide A was found to be cytotoxic. Sesquiterpene dimers, Achillin B and C, were isolated from the flowers (Li et al. 2012b)

Inflorescences of *A. millefolium* grown in the Sibiu district, Romania was found to contain between 0.18 and 0.59 % (mean 0.34 %) volatile oil (Popescu and Pop-Hakkel 1980). The azulenes from the oil varied between 1.5 and 19.6 % (mean 7.04 %). The following components were identified in the volatile oil: caryophyelene, chamazulene, linalyl, acetate, bornyl acetate, limonen, 1,8-cineole, linaleol, borneol, terpineol and geraniol. Two of the samples showed a different chemical composition, one of them lacking 1,8-cineole, the other bornyl acetate. During the flowering period of *Achillea millefolium*, the flower oil consisted mainly of monoterpenes (about 80 %);1,8-cineole was the dominant component followed secondly by sabinene (15 %) (Figueiredo et al. 1992a). The sesquiterpene fraction was dominated by germacrene-D (0.7 %). The monoterpene fraction was dominant in the oils (ca 80 %) from two populations of *Achillea millefolium* L. ssp. *millefolium*, growing in the Botanical Garden of Lisbon (BGL) and in the Caneco Garden of Almada (CGA) (Figueiredo et al. 1992b). The main components differed: sabinene and 1,8-cineole were dominant in the BGL oils, while camphor, 1,8-cineole and β-pinene were the main constituents of CGA oils. Germacrene-D was the major component of the sesquiterpene fraction of all the oils analyzed. Chamazulene was only detected in the oils from the flower heads collected in CGA; its amount decreases through flower-head development.

The major volatile aroma flower components of *A. millefolium* grown in Iran (expressed as area units divided by 100,000 per g dry matter) were α-pinene (1,350), 1,8-cineole (950), β-pinene (674), sabinene (400), β-pinene (381), γ-terpinene (325), *trans*-caryophyllene (328), α-terpinene (205) and DL-limonene (200) (Dokhani et al. 2005). Other minor components included propanal, 2-methyl; butanal, 2-methyl; butanal, 3-methyl; pentanal; α-thujene; α-fenchene; camphene; hexanal; α-phellandrene; β-phellandrene; 3,7-dimethyl-1,3,6-octatriene; *p*-cymene; α-terpinoline; allocimene, camphor; *trans*-caryophyllene; α-humulene, cadinene isomer; (*E*)-farnesene; δ-cadinene; γ-cadinene; and an unknown terpinene. Total phenolics in the flowers was 35.7 mg/g dm and total tartaric esters were 12.9 mg/g dm.

Achillea millefolium L. sensu lato, is a cytogenetically, morphologically and chemically polymorphic aggregate (Benedek et al. 2007a). Besides possessing sesquiterpenes that have chemotaxonomic relevance and mediate the antiphlogistic activity, the plant contains phenolic compounds such as dicaffeoylquinic acids and flavonoids causing choleretic and spasmolytic effects. The investigated species displayed differences in the quantitative and qualitative composition of phenolic acids and flavonoids. The following flavonoids were found in the flower heads of *Achillea* species belonging to the *A. millefolium* group (Trendafilova et al. 2007): *A. collina*, artemetin (1.6 mg), casticin (1.3 mg), centaureidin (7.4 mg), quercetagetin 6,7,3′,4′-tetramethyl ether (1.0 mg), 6-hydroxykaempferol 3,6,7,4′-tetramethyl ether (1.0 mg), santin (4.0 mg), pectolinarigenin (1.5 mg) and diosmetin (1.5 mg); *A. asplenifolia*, artemetin (6.0 mg),

casticin (1.7 mg), centaureidin (1.4 mg), quercetagetin 6,7,3′,4′-tetramethyl ether (1.1 mg), 6-hydroxykaempferol 3,6,7,4′-tetramethyl ether (1.0 mg) and apigenin (3.0 mg); and *A. distans*, centaureidin (2.0 mg), santin (1.5 mg), pectolinarigenin (1.5 mg), ermanin (1.0 mg), acacetin (1.3 mg), mixture of diosmetin and chrysoeriol (1.5 mg) and luteolin (1.5 mg).

Root Phytochemicals

Roots of hydroponic grown plants accumulated higher concentrations (%w/w dw) than those of field-grown plants in apigenin glycosides (1.91 versus 0.49 %) and total flavonoids (apigenin, luteolin and apigenin glycosides) (1.92 versus 0.51 %) but lower amount of aglycone flavonoids of luteolin and apigenin (0.007 versus 0.014 %), respectively (Pedneault et al. 2002).

The various pharmacological activities of *Achillea millefolium* species may be due to the presence of a broad range of secondary active metabolites in the essential oils and extracts of various plant parts such as flavonoids, phenolic acids and dicaffeoylquinic acids, coumarins, proazulenes, monoterpenes, sesquiterpenes, sesquiterpene lactones, diterpenes, triterpenes and sterols (Chandler et al. 1982b; Nemeth and Bernath 2008; Saeidnia et al. 2011). The largest number of data accumulated for antioxidant and antiinflammatory effects, and there are positive results on the analgesic, antiulcer, choleretic, hepatoprotective and wound-healing activities (Nemeth and Bernath 2008). Interesting findings have highlighted antihypertensive, antidiabetic, antitumor and antispermatogenic activities. Recent findings have confirmed several traditional uses. However, human clinical studies are still warranted.

Antioxidant Activity

Achillea millefolium essential oil strongly reduced the diphenylpicrylhydrazyl radical (IC_{50} = 1.56 µg/ml) and exhibited hydroxyl radical scavenging effect in the Fe^{3+}-EDTA-H_2O_2 deoxyribose system (IC_{50} = 2.7 µg/ml) (Candan et al. 2003). It also inhibited the nonenzymatic lipid peroxidation of rat liver homogenate (IC_{50} = 13.5 µg/ml). Eucalyptol, camphor, α-terpineol, β-pinene and borneol were the principal components comprising 60.7 % of the oil. The polar phase of the methanol extract also showed antioxidant activity. Antioxidant activity in terms of TEAC (µM trolox/100 g DW) of *A. millefolium* herb reported was 11.2 µM for ABTS, 200 µM for DPPH and 191 µM for FRAP (ferric reducing antioxidant power) assays (Wojdyło et al. 2007). Total phenolic content was 9.55 mg GAE/100 g DW.

Studies showed that all plant infusions of 15 *Achillea* species were effective on antioxidant enzyme systems of erythrocytes and leucocytes when compared with the hydrogen peroxide-induced group (Konyalioglu and Karamenderes 2005). Among the plant infusions, *Achillea millefolium* subsp. *pannonic*a showed highest activity on superoxide dismutase. The methanol and aqueous extracts of *Achillea millefolium* exhibited DPPH radical scavenging activity with 75 and 50.8 % inhibition, respectively (Eghdami and Sadeghi 2010). The extracts contained 123.9 and 48.4 mg GAL/g total phenolic content and 41.2 and 13.15 mg QE/g flavonoids, respectively. The methanol extract of *A. millefolium* and its flavonol glycosides and chlorogenic acids exhibited significant antioxidant properties as measured by free-radical scavenging activity against 2,2-diphenyl-pycrilhydrazyl, total antioxidant capacity (based on the reduction of Cu^{2+} to Cu^{+}), and ability to inhibit lipid peroxidation as measured by TBARS assay (Vitalini et al. 2011). The results from the TBARS assay showed that among the compounds isolated, only luteolin 7-*O*-glucoside and apigenin 7-*O*-glucoside displayed an activity somewhat comparable to that of chlorogenic acid, even at the lowest concentration tested (1 µM); all the other phenolic compounds were able to inhibit the TBARS formation only at the highest concentration tested (10 µM). Total antioxidant capacity (%) (DPPH

scavenging activity) of yarrow aerial plant parts was 8.29 % and contribution from the main caffeoyl derivatives was as follows: chlorogenic acid 10.01 %, 3,5-DCQA (dicaffeoylquinic acid) 33.17 %, 1,5-DCQA 13.63 %, 4,5-DCQA 4.99 %, total caffeoyl derivatives 61.80 % (Fraisse et al. 2011).

An on-line HPLC-DPPH assay showed that *Achillea millefolium* possessed significant antiradical activity attributable to the presence of active phenolic compounds (Trumbeckaite et al. 2011). Its phenolic compounds had no effect on mitochondrial State 3 respiration rate. The extract at concentrations that had no effect on the State 3 respiration rate significantly decreased H_2O_2 production in mitochondria.

Vahid et al. (2012) conducted a randomized controlled trial involving 31 chronic kidney disease patients; 16 were administered 1.5 g of powdered *A. millefolium* flower 3 days a week for 2 months and 15 received placebo for the same period. They found that countercurrent to the placebo group, plasma nitric oxide metabolites, were marginally decreased after *A. millefolium* administration in chronic kidney disease patients. Nitric oxide-scavenging properties had been reported with some *Achillea* species.

Anticancer Activity

Three sesquiterpenoids, achimillic acids A, B and C, were found to be active against mouse P-388 leukemia cells in vivo (Tozyo et al. 1994). The flavonoid casticin, derived from *Achillea millefolium*, was found to have antitumor activity (Haïdara et al. 2006). Casticin caused cell growth arrest in G2/M and inapoptotic death. As a tubulin-binding agent (TBA), Casticin induced p21, which in turn inhibited Cdk1. Further, casticin appeared to downregulate cyclin A. Following casticin exposure, Bcl-2 depletion occurred in cancer cells, and a sub-G1 accumulation occurred in the cell cycle. A number of features suggested that casticin could be important in cancer therapy as Pgp-overexpressing cells were not resistant to casticin, and its cell killing effect was observed even in p53 mutant or null cell lines.

The chloroform-soluble extract of aerial parts of the *Achillea millefolium* aggregate exerted high tumour cell proliferation inhibitory activities on cervical cancer HeLa and breast cancer MCF-7 cells and a moderate effect on human epithelial carcinoma A431 cells (Csupor-Löffler et al. 2009). In the antiproliferative assay centaureidin was the most effective constituent of the aerial parts of yarrow, exhibiting high cell growth inhibitory activities especially on HeLa (IC_{50} 0.0819 μm) and breast cancer MCF-7 (IC_{50} 0.1250 μm) cells. Casticin and paulitin were also highly effective against all three tumour cell lines (IC_{50} 1.286–4.76 μm), while apigenin, luteolin and isopaulitin proved to be moderately active (IC_{50} 6.95–32.88 μm). Artemetin, psilostachyin C, desacetylmatricarin and sintenin did not display antiproliferative effects against these cell lines.

Achillinin A isolated from the flower exhibited potential antiproliferative activity to adenocarcinomic human alveolar basal epithelial A549, human lung adenocarcinoma RERF-LC-kj and human lung carcinoma QG-90 cells with 50 % inhibitory concentration (IC_{50}) values of 5.8, 10 and 0.31 μM, respectively (Li et al. 2011). Secotanapartholide A isolated from the flower, exhibited moderate cell growth inhibitory activity in vitro against the human cancer cell line MCF7 (IC_{50} = 5.51 μm) (Li et al. 2012a).

Antiinflammatory Activity

A water-soluble protein–carbohydrate complex isolated from the aqueous extract of *Achillea millefolium* flowers, at a dose of 40 mg/kg, exerted antiinflammatory activity as measured by the mouse paw edema test (Goldberg et al. 1969).

The crude plant extract of *A. millefolium* and its flavonoid fraction inhibited human neutrophil elastase (HNE) with IC_{50} values of approximately 20 μg/ml, whereas the dicaffeoylquinic acids fraction was less active (IC_{50} = 72 μg/ml) (Benedek et al. 2007b). The inhibitory activity on matrix metalloproteinases (MMP-2 and -9) was observed at IC_{50} values from 600 to 800 μg/ml, whereas the DCQA fraction showed stronger effects than the

flavonoid fraction and the extract. The scientists concluded that the in-vitro antiphlogistic activity of *Achillea* was at least partly mediated by inhibition of HNE and MMP-2 and MMP-9.

Aqueous extract from *Menyanthes trifoliata* induced a suppressive phenotype of dendritic cells that had reduced capacity to induce Th1 and Th17 stimulation of allogeneic CD4(+) T cells, whereas aqueous extract from *Achillea millefolium* reduced the capacity of dendritic cells to induce a Th17 response (Jonsdottir et al. 2011). Both Th1 and Th17 cells had been implicated in the pathogenesis of inflammatory bowel disease and experimental colitis.

Hepatoprotective Activity

Pretreatment of mice with *Achillea millefolium* crude extract (150–600 mg/kg) significantly prevented D-galactosamine (D-GalN- and lipopolysaccharide (LPS)-induced rise in plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels (Yaeesh et al. 2006). The hepatoprotective effect of the extract was further verified by histopathology of the liver, which showed improved architecture, absence of parenchymal congestion, decreased cellular swelling and apoptotic cells, compared with (d-GalN) and LPS groups of animals. In isolated rabbit jejunum preparations, the extract caused a concentration-dependent (0.3–10 mg/ml) relaxation of both spontaneous and K^+-induced contractions as well as shifting the Ca^{2+} concentration-response curves (CRCs) to the right, similar to that caused by verapamil. These results indicated that the crude extract of *Achillea millefolium* exhibited a hepatoprotective effect, which may be partly attributed to its observed calcium channel blocking activity.

Spasmolytic Activity

The flavonoid fraction of *Achillea millefolium* exhibited spasmolytic activity on isolated terminal guinea pig ilea (Lemmens-Gruber et al. 2006). The aglycones quercetin, luteolin and apigenin exhibited the highest antispasmodic activities with IC_{50} values of 7.8, 9.8 and 12.5 µmol/l, respectively. Rutin and the flavonoid metabolites homoprotocatechuic acid and homovanillic acid showed no significant effects on contractility of the terminal ilea. They concluded that in tea prepared from yarrow, the concentration of the flavonoids was high enough to exert a spasmolytic effect in the gut, which was mainly caused by blockade of the calcium inward current, but additionally also by mediator antagonistic effects. In another study, *Achillea millefolium* hydroalcoholic extract inhibited electrical induced contractions of the isolated guinea pig ileum in a dose-dependent manner with EC_{50} value of 1.5 mg/ml (Babaei et al. 2007).

Choleretic Activity

A fraction of a 20 % methanol yarrow (*Achillea millefolium*) extract enriched in 3,4-, 3,5- and 4,5-DCCA dicaffeoylquinic acids (DCCAs) and luteolin-7-*O*-β-D-glucuronide was found to have choleretic effect in isolated perfused rat liver (IPRL) (Benedek et al. 2006). The fraction caused a dose-dependent increase in bile flow (23–44–47 %). Choleresis was two- to three-fold higher than that of cynarin, the main choleretic compound of *Cynara scolymus*, used as internal standard. The combined effect of DCCAs and luteolin-7-*O*-β-D-glucuronide stimulated bile flow more effectively than the single compound cynarin. Due to their polar structure, these compounds are quantitatively extracted into teas and tinctures.

Estrogenic Activity

A crude extract of the aerial parts of *A. millefolium* exhibited estrogenic activity in-vitro in recombinant MCF-7 cells (Innocenti et al. 2007). After fractionation of the crude extract, nine compounds were isolated and characterized: dihydrodehydrodiconiferyl alcohol 9-*O*-β-D-glucopyranoside, a glycosyl-neolignan; six flavone derivatives, apigenin, apigenin-7-*O*-β-D-glucopyranoside, luteolin, luteolin-7-*O*-β-D-glucopyranoside, luteolin-

4′-*O*-β-D-glucopyranoside, rutin; and two caffeic acid derivatives, 3,5-dicaffeoylquinic acid and chlorogenic acid. Apigenin and luteolin were the most important estrogenic compounds among those tested, for their ability to activate alpha or beta oestrogen receptors (ERalpha, ERbeta) using transiently transfected cells.

Antiulcerogenic Activity

Oral administration of rats with a hydroalcoholic extract of *Achillea millefolium* (30, 100 and 300 mg/kg) inhibited ethanol-induced gastric lesions by 35, 56 and 81 %, respectively (Potrich et al. 2010). Oral treatment with the extract (1 and 10 mg/kg) reduced the chronic gastric ulcers induced by acetic acid by 43 and 65 %, respectively, and promoted significant regeneration of the gastric mucosa after ulcer induction denoting increased cell proliferation, which was confirmed by PCNA (proliferating cell nuclear antigen) immunohistochemistry. The extract prevented the reduction of glutathione levels and superoxide dismutase activity after acetic acid-induced gastric lesions. The results suggested that the antioxidant properties of the hydroalcoholic extract may contribute to its gastroprotective activity.

Aqueous extract of *A. millefolium* aerial parts was found to be effective in protecting the gastric mucosa against acute gastric lesions induced by ethanol and indomethacin and in healing chronic gastric lesions induced by acetic acid with (ED_{50} = 32 mg/kg, p.o.) (Cavalcanti et al. 2006). Safety study showed slight changes in liver weight, cholesterol, HDL-cholesterol and glucose observed in male and female Wistar rats that were not correlated with dose or time of exposure of the animals. The results showed the antiulcer potential of *Achillea millefolium* extract that was accompanied by signs of relevant toxicity even at very long chronic exposure.

Immunomodulatory Activity

Achillea millefolium essential oil and 70 % crude ethanol leaf extract modulated the activation peritoneal macrophages cells from Swiss mice by weakly increasing nitric oxide (NO), at concentrations of 20, 10 and 5 mg/ml, compared to LPS (lipopolysaccharide-potent stimulator of NO production) (Lopes et al. 2003). They also reported *A. millefolium* essential oil was able to stimulate peritoneal macrophages to produce H_2O_2 and TNF-α without causing an overproduction of these compounds in peritoneal macrophages cells from Swiss mice, suggesting that the essential oil could modulate macrophages activation (Lopes et al. 2005).

Three glycosylated phenolic compounds, luteolin 7-*O*-glucoside, apigenin 7-*O*-glucoside and caffeic acid glucoside, were isolated from the methanol extract of aerial parts of *Achillea millefolium* (Yassa et al. 2007), and the immunological properties of different fractions of plant extract were studied on humoral immune system of BALB/c mice using microhaemagglutination test. Only two fractions at 125 and 61.5 mg/kg showed a significant decrease in the anti-SRBC (sheep red blood cell) titer of mice. The immunological properties of the fractions may be attributed to glycosylated derivatives of caffeic acid.

Spasmogenic Activity

A water extract of dried flower heads of *A. millefolium* exerted a direct spasmogenic effect on mouse and human gastric antrum (Borrelli et al. 2012). Among its constituents, choline, but not the flavonoids rutin and apigenin, mimicked the spasmogenic action. The authors concluded that the prokinetic effect of *A. millefolium* extract observed in vivo could provide the pharmacological basis underlying its traditional use in the treatment of dyspepsia.

Vasoprotective Activity

Achillea millefolium extract was found to enhance primary rat vascular smooth muscle cells by partly acting through oestrogen receptors and impairing NF-κB signalling in human umbilical vein endothelial cells (HUVECs) (Dall'Acqua et al. 2011). The results suggested that the extract

may have vasoprotective effect against vascular inflammation.

Antiplasmodial Activity

Among the phenolic compounds isolated from *A. millefolium* methanol extract, apigenin 7-*O*-glucoside and luteolin 7-*O*-glucoside were the most active against both strains of *Plasmodium falciparum* (Vitalini et al. 2011). The chlorogenic acids were completely inactive.

Hemostatic Activity

A glycoalkaloid, achilleine, isolated from the leaves was found to reduce clotting time in rabbits by 37 % (Miller and lee 1954).

Antinociceptive Activity

The hydroalcohol extract of *Achillea millefolium* (500 and 1,000 mg/kg) significantly inhibited abdominal contortions by 65 and 23 %, respectively, whereas *Artemisia vulgaris* (500 and 1,000 mg/kg) inhibited them by 48 and 59 %, respectively (Pires et al. 2009). None of the extracts produced differences in the intestinal transit in mice, nor in the response time in the hot plate or in the immediate or late responses in the formalin test. Both hydroalcohol extracts showed the same flavonoid glycoside as a principal constituent, which was identified as rutin. A high content of caffeic acid derivatives were also found in both extracts.

Hypotensive and Vaso- and Bronchodilatory Activities

The oral administration of *A. millefolium* hydroethanol extract (100–300 mg/kg), dichloromethane fractions (20and 10–30 mg/kg), but not ethyl acetate fraction (10 mg/kg) and butanolic fraction (50 mg/kg) fractions significantly reduced the mean arterial pressure (MAP) of normotensive rats (De Souza et al. 2011). The dichloromethane fractions were found to contain high amounts of artemetin which when administered by either oral (1.5 mg/kg) or intravenous (0.15–1.5 mg/kg) to rats was able to dose-dependently reduce the MAP. Intravenous injection of artemetin (0.75 mg/kg) significantly reduced the hypertensive response to angiotensin I while increasing the average length of bradykinin-induced hypotension. Artemetin (1.5 mg/kg, p.o.) was also able to reduce plasma (about 37 %) and vascular (up to 63 %) angiotensin-converting enzyme activity in-vitro, compared to control group.

The crude extract of *Achillea millefolium* caused a dose-dependent (1–100 mg/kg) fall in arterial blood pressure of rats under anaesthesia (Khan and Gilani 2011). In spontaneously beating guinea pig atrial tissues, the extract exerted negative inotropic and chronotropic effects. In isolated rabbit aortic rings, the extract (0.3–10 mg/ml) relaxed phenylephrine and high K^+-induced contractions. In guinea pig tracheal strips, the extract suppressed carbachol and K^+ - induced contractions. The results indicated that *A. millefolium* extract exhibited hypotensive, cardiovascular inhibitory and bronchodilatory effects and thus elucidated its use in hyperactive cardiovascular and airway disorders, such as hypertension and asthma.

Skin-Rejuvenating Activity

Studies showed that *Achillea millefolium* extract improved expression profile of various epidermal differentiation markers: cytokeratin 10, *trans*glutaminase-1 and filaggrin in cultured skin biopsies as well as increased epidermal thickness (Pain et al. 2011). In-vivo, a 2-month treatment with 2 % *A. millefolium* extract significantly improved the appearance of wrinkles and pores compared with placebo. Results were also directionally better than those of glycolic acid that was chosen as reference resurfacing molecule.

Anxiolytic Activity

Studies in mice showed that *Achillea millefolium* exerted anxiolytic-like effects in the

elevated plus-maze and marble-burying test after acute and chronic (25 days) oral administration at doses that did not alter locomotor activity (Baretta et al. 2012). This behavioral profile was similar to diazepam. The effects of *Achillea millefolium* in the elevated plus-maze were not altered by picrotoxin pretreatment but were partially blocked by flumazenil. Further, *Achillea millefolium* did not induce any changes in [(3)H]-flunitrazepam binding to the benzodiazepine (BDZ) site on the GABA(A) receptor indicating that the anxiolytic-like effects were likely not mediated by GABA(A)/BDZ neurotransmission.

Antimicrobial Activity

Achillea millefolium essential oil showed antimicrobial activity against *Streptococcus pneumoniae*, *Clostridium perfringens*, *Candida albicans*, *Mycobacterium smegmatis*, *Acinetobacter lwoffii* and *Candida krusei*, while water-insoluble parts of the methanol extracts exhibited slight or no activity (Candan et al. 2003). *Achillea millefolium* oils exhibited the antifungal activity against *Candida albicans*, *C. tropicalis*, *C. krusei*, *C. guillermondii*, *C. parapsilosis*, *Cryptococcus neoformans*, *Aspergillus niger*, *A. fumigatus*, *A. flavus* and dermatophytes *Trichophyton rubrum*, *T. mentagrophytes*, *T. mentagrophytes* var. *interdigitale*, *T. verrucosum*, *Microsporum canis*, *M. gypseum* and *Epidermophyton floccosum* (Falconieri et al. 2011). The oils showed the highest activity against dermatophyte strains, with MIC values ranging from 0.32 to 1.25 µl/ml.

Cyclophosphamide Toxicity Amelioration Activity

Studies showed that *Achillea millefolium* inflorescence aqueous extract may be partially protective against cyclophosphamide-induced testicular toxicity in male Wistar rats (Jalali et al. 2012). Cyclophosphamide-treated rats showed significant decreases in the body, testes and epididymides weights as well as many histological alterations. Stereological parameters, spermatogenic activities and testicular antioxidant capacity along with epididymal sperm count and serum testosterone concentration were also significantly decreased by cyclophosphamide. Co-treatment with *A. millefolium* extract caused a partial recovery in above-mentioned parameters.

Anticonflict Behaviour Activity

Molina-Hernandez et al. (2004) found that anticonflict-like behaviour actions of aqueous extract of *Achillea millefolium* flowers in female Wistar rats may vary according to the oestrous cycle phase. Doses of 8.0, 10.0, or 12.0 mg/kg of the extract reduced conflict behaviour during late proestrus. Conversely, during diestrus, only the dose of 12.0 mg/kg reduced conflict behaviour. During late proestrus, control rats displayed reduced conflict behaviour compared with diestrus. Diazepam (2.0 mg/kg; i.p.) reduced conflict behaviour both during late proestrus or diestrus.

Anthelmintic Activity

In-vitro studies revealed significant anthelmintic effects of aqueous extracts and ethanol extracts on live *Haemonchus contortus* worms as evident from their paralysis and/or death at 8 hours post-exposure (Tariq et al. 2008). Aqueous extracts of *A. millefolium* resulted in a mean worm motility inhibition of 94.44 %, while ethanol extracts resulted in mean worm motility inhibition of 88.88 %. The mean mortality index of aqueous extracts was 0.95 while for ethanol extracts it was 0.9. The lethal concentration 50 was 0.05 mg/ml for aqueous extracts and 0.11 mg/ml for ethanol extracts. The in-vivo anthelmintic activity of aqueous and ethanol extracts of *A. millefolium* demonstrated a maximum (88.40 %) nematode egg count reduction in sheep treated with aqueous extracts at 2 g/kg body weight on day 15 after treatment and 76.53 % reduction in faecal egg count for the ethanol extract at the same concentration.

Insecticidal Activity

A methanol extract of *Achillea millefolium* exhibited activity against 24-h-old larvae of *Aedes triseriatus* (Lalonde et al. 1980). The active principle was found to be the antilarval *N*-(2-methlpropyl)-(*E,E*)-2,4-decadienamide. Isolated and synthesized amides at 5 ppm resulted in 98 and 100 % mortality of 24-h-old *A. triseriatus* larvae. The *N*-(2-methylpropyl)-amides of decanoic and (*E*)-2-decenoic acids showed the same order of antilarval activity as *N*-(2-methylpropyl)-(*E,E*)-2,4-decadienamide, but *N*-(2-methylpropyl)sorbamide was inactive.

An ethanol extract of *Achillea millefolium* showed repellant activity against the mosquito, *Aedes aegypti* (Tunón et al. 1994). Of 35 compounds isolated from fractions of the extract, the most active were the nitrogen-containing compound stachydrine; the carboxylic acids, caffeic, chlorogenic and salicylic acids; and the phenolic compound pyrocatechol. They showed a distance and contact-repelling activity similar to the well-known repellent *N*,*N*-diethyl-m-toluamide (DEET) at about the same concentrations. Some further substances with lower activity were characterized for the first time in *A. millefolium*, i.e., adenine, ferulic and mandelic acid and the methyl esters of caprylic acid, linolenic acid and undecylenic acid.

Antileishmanial Activity

Studies showed that *Achillea millefolium* hydroalcoholic extract was effective for treatment of cutaneous leishmaniasis in mice (Nilforoushzadeh et al. 2008). Leishmaniasis is a parasitic disease transmitted by sand flies. The extract was more effective than glucantime. Mean of ulcer size reduction was 43.29 %. The essential oil from the leaves and flowers of *Achillea millefolium* was found to have antileishmanial activity in vitro (Santos et al. 2010). The median inhibitory concentration (IC_{50}) against *Leishmania amazonensis* promastigotes was 7.8 μg/ml, whereas the survival of amastigotes of this pathogen, within peritoneal murine macrophages, was halved by treatment with the oil at 6.5 μg/ml. The mean value for the median cytotoxic concentration of the oil, measured against adherent (uninfected) J774G8 macrophages, was 72.0 μg/ml (i.e., 9.2 and 11.0 times higher, respectively, than the IC_{50} against the promastigotes and intracellular amastigotes). Scanning and transmission microscopy studies showed that the oil caused alterations in shape, size and ultrastructural changes.

Trypanocidal activity

Treatment with *A. millefolium* essential oil inhibited the growth of *Trypanosoma cruzi* epimastigote and bloodstream trypomastigote forms (Santoro et al. 2007) but was less effective than clove oil.

Antifertility (Antispermatogenic) Activity

The ethanol extract (200 mg/kg/day, intraperitoneally, for 20 days) and a hydroalcoholic extract (300 mg/kg/day, orally, for 30 days) of *Achillea millefolium* flowers exerted antispermatogeic effect in Swiss mice (Montanari et al. 1998). The alterations observed were exfoliation of immature germ cells, germ cell necrosis and seminiferous tubule vacuolization. Animals treated with the extracts had an increased number of metaphases in the germ epithelium that might be due to cytotoxic substances or substances stimulating cell proliferation. Studies showed that administration *A. millefolium* extract at a dose of 800 mg/kg by intraperitoneal (IP) injection or through gavage to male Wistar rats for 22 days exerted temporary antispermatogenic effect on treated rats (Takzare et al. 2011). IP resulted in thickened seminiferous tubules on basal membrane, decrease in cell accumulation in seminiferous tubule, severe disarrangement, degenerative cells and severe decrease in sperm count. Oral administration caused thickening of basal membrane and cell disarrangement.

Toxicity/Genotoxicity Studies

A. millefolium, 0.35 and 3.5 mg/ml, did not cause statistically significant inhibition of cellular division in the onion root-tip cells (Teixeira et al. 2003). No statistically significant alterations were found, as compared to untreated controls, in either the cell cycle or the number of chromosome alterations, after treatments with *A. millefolium*, in rat cells or in cultured human lymphocytes. These results regarding the cytotoxicity and mutagenicity of *A. millefolium* provide valuable information about the safety of using them as therapeutic agents. Reproductive evaluation of aqueous crude extract of *Achillea millefolium* administered daily (0.3, 0.6 and 1.2 g/kg/day) during 90 days to male Wistar rats revealed no clinical signs of toxicity (in reproductive organ weights, sperm and spermatid numbers) over the treatment period, and body weight gain was similar in all groups (Dalsenter et al. 2004). A significant increase in the percentage of abnormal sperm in the group treated with the highest dose of yarrow extract was detected with no other important changes in the other reproductive endpoints. Additionally, a 3-day treatment of immature female rats with yarrow extract did not show any uterotrophic effects. Animal studies had shown yarrow to be generally safe and well tolerated but more human clinical studies were warranted (Applequist and Moerman 2011). The claim that yarrow had been shown to be specifically contraindicated during pregnancy was based on a single low-quality rat study, the results of which were incorrectly interpreted.

A. millefolium essential oil exhibited genotoxicity in a heterozygous diploid strain of *Aspergillus nidulans*, with green conidia (de Sant'anna et al. 2009). A statistically significant increasing number of yellow and white mitotic recombinants, per colony, of the diploid strain was reported after oil treatment with 0.19 and 0.25 μl/ml concentrations. The genotoxicity of the oil was associated with the induction of mitotic nondisjunction or crossing over.

The Final report on the Safety Assessment of Yarrow (*Achillea millefolium*) concluded that available published data were insufficient to support the safety of yarrow extract for use in cosmetic products (Anonymous 2001b). The following data were still required: (1) ultraviolet (UV) absorption data, if absorption occurs in the UVA or UVB range, photosensitization data are needed; (2) gross pathology and histopathology in skin and other major organ systems associated with repeated exposures; (3) reproductive and developmental toxicity data; (4) two genotoxicity studies, one using a mammalian system, if positive, a 2-year dermal carcinogenicity assay performed using National Toxicology Program (NTP) methods may be needed; and (5) clinical sensitization testing at maximum concentration of use.

Allergy Problems

Alpha-peroxyachifolid, a soluble component of yarrow was found to cause allergic contact dermatitis (Rücker et al. 1991). Alpha-peroxyachifolid was found to be a strong sensitizer in guinea pig sensitization experiments (Hausen et al. 1991). Other minor sesquiterpene lactones also contribute marginally to the sensitizing activity, while other known yarrow constituents like dehydromatricaria ester and pontica epoxide appeared to play no role.

Traditional Medicinal Uses

Yarrow (*Achillea millefolium* L.) is one of the most widely used plants in folk medicine in the world since antiquity. Yarrow is regarded as antiseptic, antispasmodic, mildly aromatic, astringent, carminative, cholagogue, diaphoretic, digestive, emmenagogue, odontalgic, stimulant, bitter tonic, vasodilator and vulnerary (Grieve 1971; Bown 1995; Chopra et al. 1986). It is has been used for treating wounds, inflammation, pain, liver disorders, gastritis disorders, amenorrhea, bowels, bleeding, hypertension, menstrual pains, dyspepsia, eczema, gum ailments, influenza, fevers and colds, catarrh, chicken pox, smallpox, measles, cystitis, diabetes, kidney diseases, menorrhagia, toothache, thrombosis, ulcers, varicose veins, lung haemorrhage, arthritis and poor vision (Grieve 1971; Chandler at el. 1982a, b; Duke and Ayensu

1985; Chopra et al. 1986; Bown 1995; Chevallier 1996). Yarrow is traditionally used against inflammatory and spasmodic gastrointestinal complaints, digestive problems, respiratory infections, hepatobiliary disorders, blood purification, as an appetite enhancing drug, against skin inflammations and for wound healing due to its antiphlogistic, choleretic and spasmolytic properties and, secondarily, among other uses, for liver disease and as a mild sedative (Benedek and Kopp 2007; Benedek et al. 2008; Applequist and Moerman 2011). The main pharmacologically active principles were shown to be the essential oil (antimicrobial), proazulenes and other sesquiterpene lactones (antiphlogistic), dicaffeoylquinic acids (choleretic) and flavonoids (antispasmodic) (Benedek et al. 2008). Yarrow is used in folk medicine as an emmenagogue (Innocenti et al. 2007).

A. millefolium is employed for the treatment of many different ailments in Iran (Kokkini et al. 2004); in West Azerbaijan, Iran, the infusion of dried flowers is recommended for the treatment of haemorrhoids, dyspepsia, dysmenorrhoea and gastritis (Miraldi et al. 2001); in the Parvati valley, west Himalaya, India, leaves and flowers are employed for gastric problems and fever (Sharma et al. 2004). Yarrow (*Achillea millefolium* L. s.l.) *Achillea millefolium* has a long history of use as traditional herb medicine even in veterinary medicine (Eghdami and Sadeghi 2010). Preparations in the form of infusions, decoctions, or fresh juices have been applied against anorexia, stomach cramps, flatulence, gastritis, enteritis, internal and external bleeding (coughing blood, nosebleed, haemorrhoidal and menstrual bleeding, bloody urine), wounds, sores, skin rash, as well as dog and snake bites. Yarrow has been used internally, usually as a tea, and externally as a lotion, ointment or poultice (Grieve 1971; Chandler et al. 1982a).

Yarrow has been used by native American Indians for treating bruises, burns, neck cramps, sprains and swollen tissues; healing wounds; and providing relief from rashes and itching of various causes (Chandler et al. 1982a). The plant was also a popular febrifuge and enjoyed some use in the treatment of the common colds, bloody urine, indigestion, bowel complaints, earache, headache, sore throat, toothache, spitting blood, haemorrhage and haemorrhoids. A number of its minor uses indicate that the plant is capable of imparting an analgesic (local anaesthetic), abortive and/or antiinflammatory effect and as an emmenagogue, laxative, tonic, stimulant, eyewash, sleep aid, liver aid and kidney aid.

Other Uses

Yarrow can be used as ground cover plant to combat soil erosion as it spreads rapidly and is drought resistant. It is also used as a companion plant as it repels bad insect pests and attracts beneficial predatory insects, such as ladybird beetle and parasitic wasps. The plant has been burnt in order to ward off mosquitoes. The plant and leaves can be used as compost and the leaves soaked in water to prepare a liquid leaf fertilizer for plants. The leaves contain essential oil and have been used as a cosmetic cleanser for greasy skin. The dried flowers and fresh foliage make attractive additions to floral arrangements. Yellow and green dyes are extracted from the flowers. The fragrant seeds have been used to impart a pleasant odour indoors.

Comments

In Australia, yarrow (*Achillea millefolium*) is deemed an environmental weed in Victoria, the ACT, and the southern parts of New South Wales. Though this species is naturalized in many parts of southern Australia, it is only considered to be a serious problem in the alpine and highland regions of southeastern Australia.

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Acmella oleracea

Scientific Name

***Acmella oleracea* (L.) R.K. Jansen**

Synonyms

Anacyclus pyrethraria (L.) Spreng., *Bidens fervida* Lam., *Bidens fusca* Lam., *Cotula pyrethraria* L., *Isocarpha pyrethraria* (L.) Cass., *Pyrethrum spilanthus* Medik., *Spilanthes acmella* auct. non (L.) Murr., *Spilanthes acmella* var. *oleracea* (L.) C.B.Clarke, *Spilanthes acmella* var. *oleracea* (L.) C.B.Clarke ex Hook.f., *Spilanthes fusca* hort.par. ex Lam., *Spilanthes oleracea* var. *fusca* (Lam.) DC., *Spilanthes radicans* Schrad. ex DC. (Illeg.)

Family

Asteraceae

Common/English Names

Brazil Cress, Eyeball Plant, Para Cress, Peek-A-Boo Plant, Perennial Para Cress, Spot Flower, Toothache Plant

Vernacular Names

Brazil: Abecedária, Agrião-Do-Pará, Jambu, Jambú, Jambu-Açu, Jambú Do Rio, Pimenteira (Portuguese)
Burmese: Hankala
Catalan: Creixans Del Para
Chinese: Jin Chou Kou, Liu Shen Cao, Qian Ri Ju, Yin Du Jin Niu Kou
Cuba: Cabrito
Czech: Plamatka
Danish: Parakarse
Dutch: ABC-Kruid, Braziliaanse Cresson, Huzarenknoop, Paratuinkers
Estonian: Harilik Nööpkakar
Fiji: Mbotembotekoro
Finnish: Parakrassi, Spilantes
French: Brede Mafane, Cresson De Para, Spilanthe Des Potagers, Cresson De Para, Cresson Du Brazil Cresson Du Para, Spilanthe Des Potagers
German: Husarenknopfblume, Parakresse, Prickelknöpfchen, Prickelblume
Hungarian: Abécefű, Huszárgomb, Szenyefű
India: Pirazha (Assamese), Akarkar, Pipulka (Hindi), Hemmugalu (Kannada), Leishabi (Manipuri), Acharbomdi, Akalkarra, Pipu-Labo (Marathi), Tefu Mozitang (Naga, Changki), Sarahattika (Sanskrit), Vana-Mugali (Tamil)

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Indonesia: Gletang, Legetan, Sarunen, Saruni (Javanese), Jotang (Sundanese), Gatang (Sumatra)
Italian: Spilante
Japanese: Hokoso, Kibana-Oranda-Senniti, Oranda-Senniti
Korean: Parakuresu
Laos: Kh'aad
Lithuanian: Spilantė, Indienų Kresonas
Madagascar: Brède Mafana, Brèdes Mafanes (French)
Malaysia: Getang, Kerabu, Pokok Getang, Pokok Jotang
Nepal: Bhuin Timur, Lato ghans, Marati, Purpure jhar
Peru: Botoncillo, Boton De Oro, Chimaya, Cobiriqui, Contrayerba, Deflamatoria, Mata Gusanos, Somam, Yerba Del Espanto, Yuyo Quemada
Philippines: Dila-Dilag (Ifugao), Biri (Igorot), Gatang-Gatang, Pilet-Pilet (Sulu)
Portuguese: Agrião-Do-Brasil, Agrião Do Pará, Berro De Pará, Botão-De-Ouro, Botón De Oro, Cabrito, Espilanto, Hierba Del Espanto, Inambu, Jambú, Jambú Do Rio, Jambuaçu, Jamburana, Ñambu, Nhambu, Pimenteira, Pimenteira Do Pará, Remedio De Los Pobres
Reunion Islands: Brède Mafane (French)
Russian: Spilantes, Maslyanyj Kress, Brazilski Kress
Spanish: Jambu
Sri Lanka: Akmaella (Sinhala), Akkirakara (Tamil)
Swedish: Parakrasse, Tandvärksplanta
Thai: Phak Khrat, Phak Phet, Phak tumhu, Phakkhraathuahaeun, Ya tumhu
Vietnamese: Cúc Áo, Cúc Nút Áo, Núc Áo Rau, Rau Cúc Áo

Origin/Distribution

The plant is native to Brazil. It has been introduced across the tropics, and in Africa, escapes from cultivation have been reported. The plant is now grown both in the tropics and subtropics including America, Northern Australia, Africa, Southeast Asia, India and Sri Lanka.

Agroecology

The plant occurs at low to 1,200 m altitudes. It is found in moist, damp environment, in villages, pastures, rice fields and cultivated areas, along ditches, marshy meadows, open waste places, old clearings, on open hillsides and the rocky shores of rivers, and along roadsides. It thrives best in soil rich in compost. It is frost-sensitive but perennial in warmer climates.

Edible Plant Parts and Uses

Leaves and young shoot tips are eaten raw or cooked. In the United States, the leaves are used raw as a pungent flavouring for salads (Bailey 1949) and in India as a cooked vegetable (CSIR 1976) in soups and meats (Jansen 1985). In the Indian Ocean islands (Comoros, Madagascar, Réunion, Mauritius), the main use of the leaves is as a steamed vegetable. Both fresh and cooked leaves are used in the culinary dishes of the indigenous people in Brazil particularly in the provinces of Acre, Amazonas, Pará and Ceará (Benwick 2007). For instance, in the state of Pará, paracress is often consumed with chillies and garlic. Paracress is used in a fried duck-manioc dish called 'tucupí'. Another dish where paracress is used is 'tacacá', a soup thickened with manioc juice that contains dried shrimps and sometimes freshwater fish. In Java, Indonesia, the leaves and young shoots are served raw in 'lalab' served with other vegetables and eaten with a sambal (chilli sauce) (Ochse and Bakhuizen van den Brink 1980). The leaves of another closely related species *S. paniculata* (not *A. oleracea*) are used as cooked vegetables in Assam by the Bodo community (Patiri and Borah 2007) and in Southeast Asia (Roemantyo 1994).

The flowers are also edible (Deane 2007–2012; Benwick 2007; Wetwitayaklung et al. 2008; Toothman 2009; Burdock 2010). In Thailand,

leaves and flower heads are cooked as vegetables and used in curries (Wetwitayaklung et al. 2008). The flowers are used as spice for foods and dentifrice flavouring in Japan (Burdock 2010). Consumption of portions or whole flower buds known as Buzz Buttons, Szechuan Buttons, Sansho Buttons and Electric Buttons have been reportedly used to offset the intense heat of chillies and peppers (Benwick 2007; Toothman 2009). Eating a whole flower bud results in a grassy taste, followed by an extremely strong tingling or numbing sensation and often excessive saliva production and a cooling sensation in the throat. Benwick (2007) reported that a dish of eel basted in a thick, sweet sauce with Szechuan Button flowers and roast pineapple won 'Sushi of the Year' honours in Britain's annual Sushi Awards, sponsored by Eat-Japan. These buds are also used in drinks, cocktails, sorbets (Benwick 2007; Toothman 2009) and an Alaskan halibut curry dish (Toothman 2009). In India, the buds and oleoresins are used as flavouring in chewing tobacco.

Botany

An erect, or decumbent, stout, branched, annual herb, 20–80 cm high. Leaves, opposite, glabrous, simple, broadly ovate to triangular, 5–11 cm long, 4–8 cm wide, base truncate, apex acute, margin serrate (Plate 1). Inflorescence, solitary, axillary or terminal, a globose capitulum up to 2.5 cm across becoming ovoid or conical, with an obtuse or rounded apex (Plates 1 and 2), when young two-coloured with a purplish apex, afterwards uniformly yellow, on long peduncle up to 12 cm long. Involucre shallowly campanulate, involucral bracts 15–18, in 2–3 series, oblong-lanceolate, ciliate. Ray florets very often deficient or if present 3–5 minutes, female, tubular yellowish-green base and yellowish limb. Disk florets numerous up to 600, bisexual, corolla 4–5-merous, up to 3.5 mm long, yellow, occasionally with purplish-red palea in immature capitulum, ovary compressed, style bifid. Achenes flattened ellipsoid, dark brown, 2–2.5 mm long, pappus with two short bristles.

Plate 1 Flower-heads and leaves

Plate 2 Close view of flower heads

Nutritive/Medicinal Properties

Flower Phytochemicals

The structure of spilanthol, the pungent, insecticidal constituent of the flower heads was shown to be *N*-isobutyldeca-2, 6,8-trienamide and

(Jacobson 1957; Yasuda et al. (1980) and to be identical with that of affinin obtained from roots of *Heliopsis longipes* (Jacobson 1957). Two sesquiterpenes, with structures identical to polygodial and eudesmanolide, were isolated from the flower heads of *S. acmella* together with spilanthol (Nagashima and Nakatani 1992b). Spilanthol and three pungent alkamides (2*E*-*N*-(2-methylbutyl)-2-undecene-8,10-diynamide; 2*E*,7*Z*-*N*-isobutyl-2,7-tridecadiene-10,12-diynamide; and 7*Z*-*N*-isobutyl-7-tridecene-10,12-diynamide) (Nakatani and Nagashima 1992) and spilanthol plus six alkylamides were isolated from the flower head (Nagashima and Nakatani 1992a). Three *N*-isobutyl amides spilanthol, undeca-2*E*,7*Z*,9*E*-trienoic acid isobutylamide and undeca-2*E*-en-8,10-diynoic acid isobutylamide were isolated from the dried flower buds (Ramsewak et al. 1999). Three alkamide compounds were identified from the flower head: *N*-isobutyl-2,6,8-decatrienamide (compound 1), undeca-2*E*,7*Z*,9*E*-trienoic acid isobutylamide (compound 2) and (2*E*)-*N*-(2-methylbutyl)-2-undecene-8,10-diynamide (compound 3) (Pandey et al. 2011). The amount of the compounds obtained were 338 mg (compounds 1 and 2) and 188.4 mg (compound 3), respectively. A mixture of C22–C35 normal hydrocarbons was isolated from *S. acmella* flower heads (Baruah and Pathak 1999).

Eight *N*-isobutylamides, two 2-methylbutylamides and one 2-phenylethylamide were detected, with spilanthol as most abundant *N*-alkylamide (88.8 %) in *S. acmella* ethanol flower extract (Boonen et al. 2010a). The *N*-alkylamides included the following: (2*E*,6*Z*,8*E*)-*N*-isobutyl-2, 6, 8-decatrienamide (spilanthol); (2*E*,4*E*,8*Z*, 10*Z*)-*N*-isobutyl-doceca-2,4,8-10-tetraenamide; (2*E*, 7*Z*)-*N*-isobutyl-2,7-tridecadiene-10,12-diyamide; (2*E*,4*Z*)-*N*-isobutyl-2,4-undecadiene-8,10-dynamide; (2*E*,6*Z*,8*E*)-*N*-(2-methylbutyl)-2,6,8-decatrienamide; 2(*Z*)-*N*-isobutyl-2-nonene-6,8-diynamide; *N*-phenylethyl-2,3-epoxy-6,8-nonadiynamide; (2*E*)-*N*-isobutyl-2-undecene-8-10-dynamide; (2*E*)-*N*-(2-methybutyl)-2-undecene-8,10-diyamide; and two unidentified alkylamides. Five *N*-isobutylamides, one 2-methylbutylamide and one 2-phenylethylamide were identified in the ethanol extracts of *Spilanthes acmella* flowers (Sharma et al. 2011). These included (2*E*,6*Z*,8*E*)-*N*-isobutyl-2,6,8-decatrienamide (spilanthol); (2*E*,4*E*,8*Z*,10*Z*)-*N*-isobutyl-dodeca-2,4,8,10-tetraenamide; (2*E*,7*Z*)-*N*-isobutyl-2,7-tridecadiene-10,12-diynamide;(2*Z*)-*N*-phenethyl-2-nonene-6,8-diynamide; (2*E*,4*Z*)-*N*-isobutyl-2,4-undecadiene-8,10-diynamide; (2*E*,7*Z*)-*N*-isobutyl-2,7-decadienamide; and (2*E*,6*Z*,8*E*)-*N*-(2-methylbutyl)-2,6,8-decatrienamide. The following alkylamides were identified from the methanol flower extract of *S. acmella*: spilanthol (0.07 %), (*Z*)-non-2-en-6,8-diynoic acid isobutylamide (0.01 %), (2*E*)-N-isobutylundeca-2-ene-8,10-diynamide (0.01 %) and spilanthic acid 2-methylbutylamide (0.04 %) (Mbeunkui et al. 2011). Supercritical fluid extraction using CO_2 showed *S. acmella* flowers were richer in spilanthol than leaves and stems and presented the highest antioxidant/total phenolic ratio as well as the highest antiinflammatory activity (Dias et al. 2012). Approximately 95 % of the total amount of extracted spilanthol was obtained during the SFE(CO_2) extraction step.

Twenty compounds were identified in the essential oil from *S. acmella* flower heads; limonene (23.6 %), β-caryophyllene (20.9 %), (*Z*)-β-ocimene (14.0 %), germacrene D (10.8 %) and myrcene (9.5 %) were found to be the major constituents of the oil (Baruah and Leclercq 1993).

Leaf Phytochemicals

Ethanol leaf extract of *Acmella oleracea* afforded a larvicidal hexane fraction (LC_{50} = 145.6 ppm) and a nonlarvicidal dichloromethane one (Simas et al. 2013). From the inactive fraction, three amides were identified, deca-6,9-dihydroxy-(2*E*,7*E*)-dienoic acid isobutylamide; deca-8,9-dihydroxy-(2*E*,6*Z*)-dienoic acid isobutylamide; and the known nona-2,3-dihydroxy-6,8-diynoic acid 2-phenylethylamide. From the hexane partition mixture of two acetylenic 2-phenylethylamides, nona-(2*Z*)-en-6,8-diynoic acid 2-phenylethylamide and deca-(2*Z*)-en-6,8-diynoic acid 2-phenylethlylamide were isolated. Studies by Singh and Chaturvedi (2012) showed

that in-vitro tissue cultures of *S. acmella* could be utilized for spilanthol production, an alkylamide used in cosmetics. Significantly higher amount of spilanthol was found in in-vitro plantlet leaves (3294.36 μg/g DW) compared to those taken from field-grown mother plants (2703.66 μg/g DW).

Fourteen volatile compounds isolated from the essential leaf oil of *S. acmella* are as follows: germacrene-D 54.38 %, *trans*-β-caryophyllene 15.58 %, β-elemene 4.53 %, nor-copaanone 2.44 %, bicyclogermacrene 2.15 %, valencene 2.14 %, unidentified 1.66 %, α-humulene 1.53 %, *cis-trans*-α-bisabolene 1.34 %, 2-tridecanone 1.25 %, caryophyllene oxide 1.23 %, neophytadiene 1.21 %, δ-cadinene 1.09 % and β-oplopenone 1.02 % (Kawaree et al. 2008). Three alkamide compounds were identified from the flower head: *N*-isobutyl-2,6,8-decatrienamide (compound 1), undeca-2*E*,7*Z*,9*E*-trienoic acid isobutylamide (compound 2) and (2*E*)-*N*-(2-methylbutyl)-2-undecene-8,10-diynamide (compound 3) (Pandey et al. 2011). The amount of the compounds obtained were 338 mg (compounds 1 and 2) and 188.4 mg (compound 3), respectively.

Plant (Aerial Parts) Phytochemicals

β-Sitosterol, stigmasterol, fatty acid esters of α- and β-amyrin, myricyl alcohol, stigmasterol and stigmasteryl glucoside including β-sitosteryl-3-*O*-β-D-glucoside (Krishnaswamy et al. 1975), and stigmasterol and myricyl alcohol (Tiwari and Kakkar 1990) were isolated from *S. acmella*. In addition to spilanthol [= affinin, (2*E*,6*Z*,8*E*)-deca-2,6,8-trienoic acid isobutylamide], the corresponding 2-methyl-butylamide and two new acetylenic alkamides, namely, (*Z*)-non-2-en-6,8-diynoic acid isobutylamide and (*Z*)-dec-2-en-6,8-diynoic acid isobutylamide, were isolated from *Spilanthes oleracea* (Greger et al. 1985).

Fractionation of the chloroform extract of *S. acmella* aerial parts afforded stigmasterol, stigmasteryl-3-*O*-β-D-glucopyranoside together with a mixture of long-chain hydrocarbon esters (Prachayasittikul et al. 2009). Fractionation of the ethyl acetate extract gave three compounds: 3-acetylaleuritolic acid, vanillic acid and β-sitostenone. The methanol extract fractions provided four compounds: scopoletin, *trans*-ferulic acid, *trans*-isoferulic acid and a mixture of stigmasteryl-3-*O*-β-D-glucopyranoside and β-sitosteryl-3-*O*-β-D-glucopyranoside.

Besides the long known tingling compounds (2*E*,6*Z*,8*E*)-deca-2,6,8-trienoic acid *N*-isobutyl amide (spilanthol) and (2*E*,6*Z*,8*E*)-deca-2,6,8-trienoic acid *N*-(2-methylbutyl) amide, as a minor constituent, a new 2-ketol ester (7*Z*,9*E*)-2-oxo-undeca-7,9-dienyl 3-methylbut-2-enoate (acmellonate) was isolated from the plant (Ley et al. 2006). Acmellonate elicited a weak tingling and numbing effect on the tongue and contributed only to a small extend to the overall flavour of the plant. The following three alkamides were isolated from a hexane extract of the aerial parts of *A. oleracea*: spilanthol; (*E*)-*N*-isobutylundeca-2-en-8,10-diynamide; and (*R*, *E*)-*N*-(2-methylbutyl) undeca-2-en-8,10-diynamide. Spilanthol and undeca-2*E*-ene-8,10-diynoic acid isobutylamide were isolated from the water extract of *S. acmell*a (Spelman et al. 2011). Spilanthol was only detected in *S. acmella* mother plants, flower heads and in-vitro plantlets but was not found in the callus or cell cultures (Tan et al. 2011). However, *N*-isobutyl-2*E*, 4*Z*, 8*Z*, 10*E*-dodecatetraenamide was absent in mother plants but could be detected in the in-vitro plantlets. The antioxidant butylated hydroxytoluene (BHT) and fatty acids, *n*-hexadecanoic acid (palmitic acid) and tetradecanoic acid, were found in each of the sample extracts, namely, mother plant, flower heads, in-vitro plantlets, callus, air-dried cells, freeze-dried cells and fresh cells.

Eighteen compounds were identified from the essential oil of *Spilanthes acmella* (Lemos et al. 1991). The major constituents identified were β-caryophyllene (30.2 %), γ-cadinene (13.3 %) and thymol (18.3 %). More than 45 components were identified from essential oil of the fresh plant of *Spilanthes acmella* from southern India (Jirovetz et al. 2005). The compounds included (*E*)-2-hexenol (25.7 %), 2-tridecanone (13.1 %), germacrene D (11.1 %), hexanol (11.0 %), β-caryophyllene (10.8 %) and (*Z*)-3-hexenol (5.1 %) as significantly dominating compounds.

Additional components responsible for the characteristic aroma impressions were especially C6–C9 derivatives, mono- and sesquiterpenes.

Antioxidant Activity

The volatile leaf oil of *S. acmella* possessed both of the highest antioxidant activity in all three assays, as well as the total phenolic compounds (Kawaree et al. 2008). Antioxidant activity of the leaf essential oil was 276.09 μmol Trolox equivalent/g in the 2,2′-azino-bis (3-ethylbenzo-thiazoline-6-sulfonic acid) diammonium salt (ABTS) assay; the ferric reducing antioxidant power (FRAP) assay was 35,465 μmol/g EC1 (equivalent concentration); lipid peroxidation (β-carotene bleaching assay) was 61.55 % AA (antioxidant activity); and total phenolic content was 308.03 mg gallic acid equivalent/g. Fractions from the chloroform, ethyl acetate and methanol extracts of *S. acmella* aerial parts displayed antioxidant activity in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) and superoxide dismutase assays (Prachayasittikul et al. 2009). The ethyl acetate and methanol extract and fractions exhibited the most potent DPPH radical scavenging activity. No cytotoxic effects of the extracts against KB (human oral carcinoma) and HuCCA-1 (human cholangiocarcinoma) cell lines were evident.

Callus from leaf explants and plant parts (root, stem, leaf) of *S. acmella* were used for quantitative estimation of primary metabolites and antioxidant activity (Tanwer et al. 2010). Methanol extract of stem showed highest superoxide radical scavenging activity (39.54 %), while leaves have showed maximum (76.42 %) DPPH scavenging activity compared to other plant parts and callus. Maximum soluble sugars (51 mg/g DW) in callus, starch (30 mg/g DW) in stem, protein (25 mg/g DW) and phenolic contents (52.3 mg/g DW) in leaves and lipids (80 mg/g DW) in roots were determined.

Vasorelaxation/Spasmolytic Activity

Studies by Wongsawatkul et al. (2008) demonstrated that *S. acmella* extract exerted maximal vasorelaxations in a dose-dependent manner on phenylephrine-induced contraction of rat thoracic aorta. The effect was less than acetylcholine-induced nitric oxide (NO) vasorelaxation. Significant reduction of vasorelaxation was observed in both N(G)-nitro-l-arginine methyl ester (l-NAME) and indomethacin (INDO). In the presence of l-NAME plus INDO, synergistic effects were observed, leading to loss of vasorelaxation of both acetylcholine and the extracts. The extract was found to exhibit vasorelaxation via partially endothelium-induced NO and prostacyclin in a dose-dependent manner. Further, the ethyl acetate extract exerted immediate vasorelaxation (ED_{50} 76.1 ng/ml) and was the most potent antioxidant in the DPPH assay. The chloroform extract showed the highest vasorelaxation and antioxidation in the SOD (superoxide dismutase) assay.

Antiinflammatory Activity

Studies showed that spilanthol, isolated from *S. acmella*, attenuated the lipopolysaccharide (LPS)-induced inflammatory responses in murine RAW 264.7 macrophages partly due to the inactivation of NF-kappaB, which negatively regulated the production of proinflammatory mediators at the transcriptional and translational levels (Wu et al. 2008). Additionally, the LPS-stimulated IL-1beta, IL-6 and TNF-alpha productions were dose dependently reduced by spilanthol.

Aphrodisiac Activity

The orally administered ethanol extracts of the *Spilanthes acmella* flower extract had a dose-dependent positive effect on mounting frequency, intromission frequency and ejaculation frequency of normal male Wistar albino rats (Sharma et al. 2011). The most significant effects were observed at 150 mg/kg treatment, even after a lapse of 7 and 14 days of discontinuance of drug treatment. A dose-dependent effect was also observed on the follicle-stimulating hormone (FSH) and luteinizing hormone (LH) and testosterone serum

levels. In-vitro nitric oxide release was 21.79 μM, which was significantly higher compared to the control group. The aphrodisiac potential of an ethanol *Spilanthes acmella* extract was demonstrated in-vitro and in vivo. *N*-alkylamides might attribute to the improved sexual potential. The results supported traditional use of *S. acmella* as a sexual stimulating agent.

Transdermal/Transmucosal Activity

The *N*-alkylamide spilanthol from *S. acmella* was demonstrated to permeate human skin in a Franz diffusion cell (FDC) system thereby supporting its topical application usage on the skin (Boonen et al. 2010b). Spilanthol from *S. acmella* ethanol extract was demonstrated to permeate porcine buccal mucosa in a Franz diffusion cell experimental setup (Boonen et al. 2010a).

Convulsant Activity

The hexane extract of *Spilanthes acmella* var. *oleracea* when injected intraperitoneally induced full tonic–clonic convulsions in male Wistar rats in a dose-dependent manner indicating the potential for its use as a tool in the development of new models of epilepsy (Moreira et al. 1989).

Diuretic Activity

Spilanthes acmella cold water extract caused marked increase in urinary Na^+ and K^+ levels in rats and a reduction in the osmolarity of urine suggesting that it was mainly acting as a loop diuretic and may also inhibit antidiuretic hormone release and/or action (Ratnasooriya et al. 2004). The results suggested that *Spilanthes acmella* had strong diuretic action. Administration of the petroleum ether, chloroform and alcohol leaf extracts of *S. acmella* to rats caused an increase in total urine volume and electrolytes excretion (sodium Na^+, potassium K^+ and chloride Cl^-) (Yadav et al. 2011b). Among the different extracts, the alcohol extract (500 mg/kg) significantly and markedly increased the urine output. The pattern of diuresis induced by the alcohol extract was almost similar to that produced by the furosemide.

Drug Interaction Activity

The alkylamides present in *S. acmella* showed significant inhibition of cytochrome P450(2E1)-mediated oxidation of *p*-nitrophenol in-vitro at concentrations as low as 25 μM, whereas the caffeic acid derivatives had no effect (Raner et al. 2007).

Gastroprotective Activity

A rhamnogalacturonan polysaccharide containing uronic acid, galactose, arabinose, rhamnose and glucose in a 15:2:1:1:0.5 M ratio and with molecular weight 226,000 g/mol exhibited gastroprotective activity (Nascimento et al. 2013). The rhamnogalacturonan was found to compose of a long chain of →4)-6-OMe-α-D-GalpA-(1→, interspersed with some α-l-Rhap residues, partly substituted by side chains of type II arabinogalactans.

Anti-obesity Activity

The ethanol extract of *S. acmella* flower buds exhibited pancreatic lipase inhibitory activities in a concentration-related manner in the range 0.75–2.0 mg/ml (Ekanem et al. 2007).

Immunomodulatory Activity

The ethanol leaf extract of *S. acmella* (500 mg/kg b.wt. p.o.) exhibited significant peritoneal macrophage stimulation and 25–50 % mortality as compared to control mice, indicating its prominent immunostimulant activity (Savadi et al. 2010). Rats orally administered with the ethanol leaf extract of *S. acmella* showed a significant increase in neutrophil adhesion, haemagglutinating antibody

titre (HAT) and delayed-type hypersensitivity (DTH) response (Yadav et al. 2011a). In rats immunized with sheep red blood cells (RBC), the extract enhanced the humoral antibody response to the antigen and significantly potentiated the cellular immunity by facilitating the footpad thickness response to sheep RBC in sensitized rats. With a dose of 500 mg/kg body weight, the values of neutrophil adhesion, HAT and DTH responses were statistically significant as compared to control. The results demonstrated the immunomodulatory potential of *Spilanthes acmella* in rats.

Anaesthetic and Antipyretic Activities

S. acmella aqueous extracts in concentrations of 10 and 20 % produced 70.36 and 87.02 % anaesthesia, respectively, by the intracutaneous wheal compared to 97.22 % anaesthetic effect produced by 2 % xylocaine (Chakraborty et al. 2010). The mean onset of anaesthesia with the test drug was 5.33 minutes compared to 2.75 minutes for the standard drug in the plexus anesthesia model. In the antipyretic model, the extract in doses of 100, 200 and 400 mg produced dose-dependent reduction in mean temperature at various hours of observation. The results suggested that *S. acmella* aqueous extract had significant local anesthetic and antipyretic activities.

Analgesic Activity

The water extract of *S. acmella* flowers exerted an analgesic effect in rats administered orally with the extract (Peiris et al. 2001). A dose-dependent analgesic activity with a EC_{50} =313 mg/kg was evident when evaluated in hot plate but not in tail-flick test. This analgesic activity had a rapid onset and short duration of action and was not blocked by naloxone, an opioid receptor antagonist. The mid dose of the extract also induced significant sedation as evaluated using rat hole-board technique. It was concluded that the analgesic activity was mediated supraspinally accompanied with sedation.

Antimicrobial Activity

The petroleum ether *S. acmella* flower extract was found to inhibit growth in-vitro of *Fusarium oxysporum*, Fusarium moniliforme, *Aspergillus niger* and *Aspergillus parasiticus* (Rani and Murty 2006). Prasad and Seenayya (2000) reported that *S. acmella* possessed good growth inhibitory activity against red halophilic cocci *Salinicoccus roseus*, *Halococcus turkmenicus* and *Halococcus morrhuae* from salt-cured fish. Studies showed that fractions from the chloroform and methanol extracts of *S. acmella* plant inhibited the growth of many tested organisms, e.g., *Corynebacterium diphtheriae* with minimum inhibitory concentration (MIC) of 64–256 mg/ml and *Bacillus subtilis* with MIC of 128–256 mg/ml (Prachayasittikul et al. 2009). The hexane and chloroform extracts completely inhibited the growth of *Saccharomyces cerevisiae* with MIC 256 µg/ml. The chloroform extract also completely inhibited growth of *Streptococcus pyogenes* II with MIC 256 µg/ml. Further, a methanol fraction also inhibited the growth of *Micrococcus luteus*, *Staphylococcus epidermidis* and *B. cereus* with MIC 128–256 µg/ml.

Insecticidal Activity

Infrared spectra of spilanthol from *Spilanthes* spp. and of a sample of affinin obtained from roots of *Heliopsis longipes* were superimposable, and both materials gave the same high knockdown and kill in tests against houseflies (*Musca domestica*) and mosquito larvae (Jacobson 1957). *S. acmella* extract was shown to be toxic against adults of American cockroach, *Periplaneta americana* (Kadir et al. 1989). *N*-isobutyl-2,6,8-decatrienamide (spilanthol) was found to be the active component. Topical application of spilanthol produced high acute toxicity, and spilanthol was more potent compound compared to three conventional insecticides. The potency was found to be 1.3, 2.6 and 3.8 times more toxic than carbaryl, bioresmethrin and lindane, respectively. Electrophysiological studies indicated immediate

hyperexcitation followed by complete inhibition of the cockroach cercal nerve activity by the extract.

Spilanthes acmella exhibited marked larvicidal effect on the fourth instar larvae of *Culex quinquefasciatus* with an LC_{50} value of 61.43 ppm (Pitasawat et al. 1998).

Three *N*-isobutyl amides spilanthol, undeca-2*E*,7*Z*,9*E*-trienoic acid isobutylamide and undeca-2*E*-en-8,10-diynoic acid isobutylamide were isolated from the dried flower buds (Ramsewak et al. 1999). All were active against *Aedes aegypti* larvae and *Helicoverpa zea* neonates at 12.5 and 250 μg/ml concentrations, respectively. Spilanthol, a major constituent of *S. acmella* ethanol flower extract, found to have potent ovicidal, larvicidal and pupicidal activity (Saraf and Dixit 2002). Maximum 7.5 ppm concentration caused 100 % motility of eggs, larvae and pupae of *Anopheles*, *Culex* and *Aedes* mosquitoes. Spilanthol was more effective even at low doses against eggs and pupae.

The following three alkamides from a hexane extract of the aerial parts of *A. oleracea*, spilanthol; (*E*)-*N*-isobutylundeca-2-en-8,10-diynamide; and (*R*, *E*)-*N*-(2-methylbutyl)undeca-2-en-8,10-diynamide, exhibited insecticidal activity, with spilanthol being the most active (LD_{50}=0.13 μg/mg) against *Tuta absoluta* (Moreno et al. 2012). The alkamides were selective to both beneficial nontarget species, the predator *Solenopsis saevissima* (Hymenoptera: Formicidae) and to the pollinator *Tetragonisca angustula* (Hymenoptera: Apidae, Meliponinae) studied.

Of three *Spilanthes* species, *S. acmella* L.var *oleraceae* Clarke, *S. calva* L. and *S. paniculata* Wall ex DC, *S. acmella* hexane flower extract was the most effective in inducing complete lethality at minimum doses, the respective LC_{50} and LC_{90} values being 4.57 and 7.83 (*Anopheles stephensi*), 0.87 and 1.92 (*Anopheles culicifacies*) and 3.11 and 8.89 ppm (*Culex quinquefasciatus*). This was followed by *S. calva* and *S. paniculata* extracts, respectively (Pandey et al. 2007). Three alkamide from the flower head *N*-isobutyl-2,6,8-decatrienamide; undeca-2*E*,7*Z*,9*E*-trienoic acid isobutylamide; and (2*E*)-*N*-(2-methylbutyl)-2-undecene-8,10-diynamide exhibited larvicidal activity against late III/early IV instar *Anopheles stephensi* larvae (Pandey et al. 2011). A mixture of two acetylenic 2-phenylethylamides, nona-(2*Z*)-en-6,8-diynoic acid 2-phenylethylamide and deca-(2*Z*)-en-6,8-diynoic acid 2-phenylethlylamide, isolated from the hexane fraction of the ethanol leaf extract were active against *Aedes aegypti* mosquito larvae at LC_{50}=7.6 ppm (Simas et al. 2013). They were not toxic to *Artemia salina nauplii* indicating the possibility of using the compounds to control *Aedes aegypti* larvae.

Antiplasmodial Activity

Centrifugal partition chromatography (CPC) fractions from the methanol flower extract, which contained natural mixtures of phytochemicals, demonstrated significantly higher antiplasmodial activity compared to corresponding purified *N*-alkylamides, thus suggesting that interactions between these *N*-alkylamides may potentiate antiplasmodial bioactivity (Mbeunkui et al. 2011). The isolated alkylamides, spilanthol and undeca-2*E*-ene-8,10-diynoic acid isobutylamide, from *S. acmell*a, were shown to have IC_{50}s of 16.5 and 41.4 μg/ml on *Plasmodium falciparum* strain PFB and IC_{50}s of 5.8 and 16.3 μg/ml for the chloroquine-resistant *Plasmodium falciparum* K1 strain, respectively (Spelman et al. 2011). Further, at relatively low concentrations, spilanthol and *S. acmella* water extract reduced the parasitemia 59 and 53 % in mice infected *with Plasmodium yoelii yoelii* 17XNL at 5 and 50 mg/kg, respectively.

Malarial 5 is a traditional Mali drug composed of *Cassia occidentalis* leaves, *Lippia chevalieri* plant and *Spilanthes oleracea* flower heads, administered as a decoction (Gasquet et al. 1993). The drug and its individual plant components were inhibitory in-vitro to *Plasmodium falciparum* with an IC_{50} of 500 μg/ml for the drug and 200–400 μg/ml for *Lippia chevalieri* and *Spilanthes oleracea.* In the in-vivo assay with *P. berghei* in mice, mice treated with 200 mg of lyophilized Malarial 5 over 5 days survived for 2–3 days longer than controls.

Traditional Medicinal Uses

The flowers and leaves of *Spilanthes acmella* have a pungent taste accompanied by tingling and numbness and have been used as a spice for appetizers and as widespread folk medicine for stammering, toothache, stomatitis and throat complaints (Nakatani and Nagashima 1992; Wu et al. 2008). The leaves of *Spilanthes acmella* have been used traditionally as tonic and in the treatment of rheumatism, gout and sialogogue (Savadi et al. 2010). The plant has anaesthetic action and is used for toothache in the East (Burkill 1966). In India, the plant is used as a sialogogoue to increase salivation and stimulation for curing headaches, paralysis of the tongue and affections of the throat. In Java, the dried flower heads are used for sore mouth of sprue. A decoction of the plant can be taken internally as a diuretic and able to resolve stones in the bladder, while a decoction of the roots can be used as a purgative. A decoction of the plant is used as vulnerary and also regarded as an antiscorbutic. The plant is also used as a cure for dysentery and rheumatism and to enhance the immune system. It is used against blood parasites, especially against malaria, both prophylactic and curative.

Other Uses

Acmella oleracea is widely grown as an ornamental (and occasionally as a medicinal) in various parts of the world. In India, the crushed plant is used as a fish poison.

Peptides derived from *A. oleracea* plant extracts are used in a cosmetic composition (in anti-wrinkle cream and antiaging formulations) to help regenerate the dermal matrix and accelerate repair of functional wrinkles (Demarne and Passaro 2005; Belfer 2009). Besides these medicinal uses, the flower heads have been used as a spice for appetizers by the Japanese, and spilanthol-rich extract and essential oil of the plant was used as a flavouring material for dentifrices, mouthwash, chewing gum and breath fresheners (Lion 1985; Shimada and Gomi 1995).

The plant contains *N*-alkylamides (NAAs) which have been regarded to be a promising group of bioactive compounds, which are anticipated to act as important lead compounds for plant protection and biocidal products, functional food, cosmeceuticals and drugs in the next decade (Boonen et al. 2012).

Comments

Several closely *Acmella* species in South America, Africa and Southeast Asia have similar culinary, medicinal and ornamental uses.

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Ageratum conyzoides

Scientific Name

***Ageratum conyzoides* (L.) L.**

Family

Asteraceae

Synonyms

Ageratum album Hort. Berol. ex Hornem., *Ageratum arsenei* B.L. Rob., *Ageratum ciliare* Lour., *Ageratum coeruleum* Desf. (Illeg.), *Ageratum conyzoides* f. *obtusifolia* (Lam.) Miq., *Ageratum conyzoides* var. *pilosum* Blume, *Ageratum cordifolium* Roxb., *Ageratum hirsutum* Poir., *Ageratum hirtum* Lam. (Illeg.), *Ageratum humile* Salisb. (Illeg.), *Ageratum humile* Larrañaga, *Ageratum latifolium* Cav., *Ageratum latifolium* var. *galapageium* B.L. Rob., *Ageratum meridanum* V.M. Badillo, *Ageratum microcarpum* (Benth. ex Benth.) Hemsl., *Ageratum nanum* Hort. ex Sch.Bip. (Illeg.), *Ageratum obtusifolium* Lam., *Ageratum odoratum* Bailly, *Ageratum pinetorum* (L.O. Williams) R.M. King and H. Rob., *Ageratum suffruticosum* Regel, *Alomia microcarpa* (Benth. ex Benth.) B.L. Rob., *Alomia pinetorum* L.O. Williams, *Cacalia mentrasto* Vell., *Caelestina latifolia* (Cav.) Benth. ex Oerst., *Caelestina microcarpa* Benth. ex Benth. (Illeg.), *Caelestina microcarpa* Benth. ex Oerst., *Carelia conyzoides* (L.) Kuntze, *Chrysocoma maculata* Vell., *Eupatorium conyzoides* (L.) E.H.L. Krause (Illeg.), *Eupatorium paleaceum* Sessé & Moc.

Common/English Names

Ageratum, Appa Grass, Bastard Agrimony, Billygoat-Weed, Blue Top, Chick Weed, Cocks Sticks Plant, Conyzoid Floss Flower, Floss Flower, Goatweed, Mother Brinkly, Tropic Ageratum, Whiteweed, Winter Weed

Vernacular Names

Arabic: Bergoman, Berquam, Korink

Bangladesh: Oochunti, Dochunti, Fulkuri (Bengali), Monipuizza Kher (Chakma), Achunai, Chunachu Appa (Marma), Submenum (Tipra)

Benin: Kourotoko, Serekpèki (Bariba), Azongbiwa (Sahouè), Ewé Arougbo, Olokopla, Olokokpè (Yoruba)

Brazil: Catinga-De-Bode, Erva-De-São-João, Mentrasto, Mentrato, Picão-Roxo (Portuguese)

Cameroon: Nyada Elog

Chamorro: Mhéguefa, Tchounamo (Bamileke), Ghé Guefa (Bandjoum), Ntotoo (Eséka), Mumutung (Ewondo), Nyada Eleog (Mbalmayo)

Chuukese: Olloowaisiip

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Columbia: Yerba Hemostatica
Czech: Nestařec Hnidákovitý
El Salvador: Mejorana, Sunsumpate
Fijian: Botebotekoro, Mata Mothemothe, Mbotembotekoro, Sogovanua, Songovanua
French: Agérate, Agerate Conyzoid, Azier François, Baume, Baume Blanc, Baume Mauve, Bouton, Célestine, Eupatoire Bleue, Herbe De Bouc
Gabon: Komba (Apindji), Misi-Ma-Mbya, Nya-Mésidè (Bakèlè), Pôta-Mbwandi (Bakota), Gimbu-Gya-Mukunga (Banzabi), Mambi-Ma-Taba (Bapunu), Kumba (Bavili), Mondjili-Ndjili (Bavové), Marufi-Ma-Taba (Bavungu), Fumele (Bawumpfu), Kéngé-Kengé (Benga), Misi-Mè-Mbwè (Béséki), Kumba-Djuma, Burungu (Eshira), Okè-Kông, Mékwa-Me-Kông, Mekwè-Me-Kông (Fang), Tombi-Djoro (Galoa), Komba-A-Gévindji (Ivéa), Fumangha (Mindumu), Komba-A-Gévindji (Mitsogo), Aludo-Féya (Mpongwè), Tombi-Djoro (Nékomi), Tombé-Djoro (Ngowé), Tombi-Djoro (Orungu)
German: Mexikanischer Leberbalsam
Hawaiian: Maile Hohono, Maile Honohono, Maile Kula, Meie Parari, Mei Rore
Hungarian: Agerátum, Kisfészkű Bojtocska
India: Gendelabon (Assamese), Dochunti, Dochunty, Uchunti (Bengali), Bhakumbar, Dochuntry, Gha Buti, Jangli Pudina, Semandulu, Uchauty, Visadodi (Hindi), Helukasa, Naayi Thulasi, Oorala Gida, Ooralada Gida (Kannada), Appa, Kattappa, Muriyan Pacca (Malayalam), Khongjai Napi (Manipuri), Ghanera Osaadi, Ghaneraosadi, Osaadi, Vosadi (Marathi), Vaihlenhlo, Vailenhlo, Voilenhlo (Mizoram), Vaihlenhlo, Voilenhlo, Pokasunga (Oriya), Visamustih (Sanskrit), Appakkoti, Pumpillu, Pumppillu, Pumpul (Tamil), Pokabanthi, Pokapanthi Povu (Telugu)
Indonesia: Bandotan, Berokan, Wedusan (Javanese), Dus-Bedusan (Madurese), Babadotan, Jukut Bau, Ki Bau (Sundanese)
Kenya: Mucuki Wa Ngigi (Embu), Ilusa (Kakamega), Ilusa (Luhya), Oluoro-Chieng, Orianyacha (Luo), Nasirundu (Marachi), Kundambara (Swahili)
Kwara'Ae: Belohanua
Laos: Nia Kee Lo
Malaysia: Ara Batu, Bunga Lebeh Tikus, Daun Misai Kucing, Rumput Jalang, Rumput Pereh Jarang, Rumput Sekedok, Rumput Tahi Ayam, Selasih Dandi, Senorang Kambing, Si Anggit, Tahi Anjing, Tahi Asu, Tambok- Tambok Jantan, Uda Buda
Mexico: Hierba Dulce
Nigeria: Akwokwo-Nwaosi, Niaika (Ibo), Ufu Opioko, Otogo (Igede), Imi-Esu (Owomode), Imi-Ewure (Yoruba)
Niuean: Sekose Sea, Tekote Tea
Palauan: Ngmak
Philippines: Kulong-Kogong-Babae (Bikol), Kakalding, Pagpagai, Taindikaldi (Bontok), Budbuda (Igorot), Siñgilan (Iloko), Kamumnuag (Ivatan), Bahug-Bahug (Panay Bisaya), Asipukpuk (Pangasinan), Bahu-Bahu (Sulu), Bulak-Manok, Damong-Pallas, Kolong-Kabayo (Tagalog)
Polish: Żeniszek
Polynesia: Meie Parari
Republic of Congo: Mudiadianga (Beembé), Founkou Mpala (Beembe), Konko (Doondo), Lounvouvou (Kikongo), Tsouampari (Téké)
Republic of Guinea: Furu-Furu Kungbèlen (Manika), Kiikala Purèl (Pular), Nyoge Nyaakhi (Susu)
Samoan: A'Amia, Lau Taioti, Tae'Oti
Spanish: Chuva, Huarmi
Swahili: Kimavi Cha Khuku, Kundambara
Swedish: Maile Kula
Tahitian: Maire Vaihi
Tanzania: Kyabakiriao (Buhkoba Rural District), Matawana (Chagga)
Thailand: Saap Raeng Saap Kaa, Yaa Saap Haeng (Chiang Mai), Thiam Mae Haang (Loei), Yaa Saap Raeng (Ratchaburi), Tapsuea Lek (Sing Buri)
Tongan: Te'Ehosi
Uganda: Otikidiel (Padhola)
Vietnamese: Bạch Hoa Hương Thảo, Bông Thúi, Bù Xích, Bù Xít, Cây Cứt Lợn,, Cây Ngũ Sắc, Cây Ngũ Vị, Cỏ Cứt Heo, Cỏ Cứt Lợn, Cỏ Hôi
West Africa: Nri-Ewu (Igbo), Imieshu, Kianzi, Yarnigbei (Yoruba)
Zaire: Kikongo Mpota Ka Saku, Nkaya Bekia Kwa Nsey

Origin/Distribution

The species is native to tropical Central and South America and is now found naturalized pantropically in disturbed areas as weeds. It is common in the warm tropics throughout Africa, Asia and the South Pacific Islands.

Agroecology

It occurs in the warm tropics from sea level to 2,000 m in wet and dry disturbed areas. It is usually found in waste places, gardens, old cultivations, grasslands, low secondary growth forests, forest edges, roadsides, water courses, etc., where there is ample exposure to sunlight (Dung et al. 1996). It also occurs as a major to intermediate weed in rice fields, orchards, plantations, pastures and cultivated vegetable and cropping areas. It thrives best in rich, moist, mineral soils in areas with high air humidity and tolerates shade.

Edible Plant Parts and Uses

The fragrant flowers and foliage are used for scenting edible coconut oil in the southeastern Polynesia (Brown 1935; Facciola 1990). The leaves are eaten in a soup called 'olulu-ogwai' by the Igbo communities in Nigeria (CINE 2007).

Botany

An erect, pubescent, aromatic, slender, annual herb sparingly branching 15–100 cm high. Stems and leaves covered with fine white hairs. Leaves simple, petiolate, green, ovate or rhomboid-ovate, 1–10 cm × 0.5–7 cm, with crenate margin, acute apex and oblong or attenuate base, glandular dorsally (Plates 1 and 2). Inflorescence terminal corymb of 8–15 discoid heads, florets about 75 per head; corolla tubular, white or pale purple

Plate 1 Pale purple flower heads and leaves

Plate 2 Pale blue purple heads

or blue (Plates 1 and 2), 1–1.5 mm long, limb 5-cleft, included in the involucre; style branches exserted. The fruit (achene) linear-oblong, 1.5–2 mm long, black, 5 angled, nearly glabrous with scaly pappus.

Nutritive/Medicinal Properties

The proximate nutrient composition of the edible leaves was reported by CINE (2007) as moisture 42.5 g, energy 181 kcal, protein 6.9 g, fat 0.4 g, carbohydrate 37.5 g, fibre 0.1 g, ash 3.4 g, Ca 345 mg, P 725 g, Fe 10 mg and Zn 4.5 mg. The major amino acids present in free form in the pollens of *A. conyzoides* included arginine,

cystine, glutamic acid, glycine, isoleucine, leucine, methionine, ornithine, tryptophan, amino-n-butyric acid, aspartic acid, proline and tyrosine (Mondal et al. 1998).

Besides nutrients in the leaves (CINE 2007) and amino acids in the pollens, *Ageratum conyzoides* have been reported to contain chromenes, chromones, chromanones, benzofurans, flavonoids including highly methoxylated flavonoids, farnesene derivatives, monoterpenes, triterpenes, sesquiterpenes and phenylpropanoids, sterols, alkaloids and a raft of miscellaneous compounds in plant extracts, volatiles and essential oil extracted from various parts of the plant (Okunade 2003; Kamboj and Saluja 2008).

Essential Oils, Volatiles and Plant Extracts

The essential oil of *A. conyzoides* was found to contain 4–6 major compounds such as ageratochromene (about 53–55 %) and demetoxyageratochromene (about 30–32 %) (Pham and Nguyen 1976). The essential oil of *A. conyzoides* was reported to have complex mixture of 213 compounds of which 43–51 constituents have been reported (Kamboj and Saluja 2008). The constituents identified include 20 monoterpenes 6.4 % [13 monoterpenoid hydrocarbons (5.0 %), 7 oxygenated monoterpenoids (0.08–1.4 %)], 20 sesquiterpenes 5.1 % [16 sesquiterpenoid hydrocarbons (4.3 %), four oxygenated sesquiterpenoids (0.8 %)] and three phenylpropanoids and benzenoids (2.33 %).

Fifty-one constituents—13 monoterpenoid hydrocarbons (5.0 %), 7 oxygenated monoterpenoids (1.4 %), 16 sesquiterpenoid hydrocarbons (4.3 %), 4 oxygenated sesquiterpenoids (0.8 %), 3 phenylpropanoids and benzenoids (2.33 %), 6 chromenes (85.2 %) and 2 chromans (0.9 %)—were identified in the essential oil of *A. conyzoides* leaves in Nigeria (Ekundayo et al. 1988). The essential oils of fresh flowers and a combination of leaves plus stems of flowering and nonflowering *Ageratum conyzoides* in Fiji were found to be rich in sesquiterpenes and ageratochromene (6,7-dimethoxy-2,2-dimethylchromene) and 7-methoxy-2,2-dimethylchromene (Aalbersberg and Singh 1991). The main constituents in the essential oil of *Ageratum conyzoides* from Vietnam were ageratochromene (precocene II), 6-demethoxyageratochromene (precocene I) and β-caryophyllene, accounting for 77 % of the oil (Nguyễn et al. 1989). Two main components 7-methoxy-2, 2-dimethylchromene (precocene I) and β-caryophyllene, a large number of terpenoids and some chromenes were identified in the essential oil of the whole plant (Vera 1993). Two new compounds, coumarin and phytol (a diterpene alcohol), were also identified. The natural occurrence of the two chromans, 6-acetyl-2,2-dimethyl-3,4-dihydro-chromene and its 7-methoxy derivative, was being reported for the first time. Forty-seven components making up of 96.35 % of the oil were identified in the essential oil of *Ageratum conyzoides* from Ghana essential oil of *Ageratum conyzoides* L. from Ghana (Mensah et al. 1993). The major constituents were 6-demethoxyageratochromene (precocene I) (80.29 %) and β-caryophyllene (7.04 %).

Main components of the essential oil of flowers and combination of stem and leaves from Pakistan were β-caryophyllene (14.35 %, 17 %), 6-demthoxy-ageratochromene (30.30 %, 26.60 %) and ageratochromene (34.90 %, 36.90 %), respectively (Riaz et al. 1995). The content of *A. conyzoides* essential oil extracted from the leaves and the roots varied from 0.11 to 0.58 % for the leaves and from 0.03 to 0.18 % for the roots (1996). Oils from leaves and roots show a certain homogeneity of chemical composition. Main constituents were β-caryophyllene (1.2–25.1 %) and precocene I (63.0–92.9 %). β-caryophyllene (10.5 %) and precocene I (81 %) were the major components of the leaf essential oil (Chalchat et al. 1997). Forty constituents comprising 13 monoterpenoids (5.17 %), 17 sesquiterpenoids (13.95 %) and 8 chromenes (71.05 %) were identified in the essential oil of *Ageratum conyzoides* leaves (Kasali et al. 2002).

Twelve components making up of 86–99 % of the essential oil in different plant parts of *Ageratum conyzoides* in Lucknow, namely, flowers, stems, leaves and roots, were identified (Singh et al. 2003). The major constituents were 6-demethoxyageratochromene (precocene I, 13.2–44.3 %)

and ageratochromene (precocene II, 41.1–62.2 %). Total chromene was found maximum in leaves (91.7 %) and minimum in roots. Precocene I (86 %) and β-caryophyllene (8 %) are major components of leaf essential oil (Nébié et al. 2004). The essential oil isolated from the leaves and flowers of *Ageratum conyzoides* in South China was found to contain ageratochromene (precocene II, 25.89 %), the sesquiterpene *β*-caryophyllene (23.79 %), demethoxyageratochromene (precocene I, 14.76 %) and some monoterpene hydrocarbons, with percentages of 2–5.5 % (Sundufu and Shoushan 2004). The essential oil of *A. conyzoides* obtained from 5 different areas in Brazil was found to contain 11 identified compounds and precocene I as the main constituent in the API accession and the precocene II as the main constituent in the other four accessions (De castro et al. 2004). The leaf essential oil of *A. conyzoides* from Brazil consisted exclusively of the chromenes precocene I (95.4 %) and II (4.5 %) (Lima et al. 2005). Forty-six compounds accounting for 97.60 % of the oil of the aerial parts of *Ageratum conyzoides* were identified (Rana and Blazquez 2003). The main compounds were found to be ageratochromene (32.9 %), 6-methoxyquinoline-1-oxide (20.77 %), β-caryophyllene (19.79 %), β-sinensal (5.82 %), β-sesquiphellandrene (1.99 %) and τ-cadinene (1.44 %). The essential oil obtained by hydrodistillation of *A. conyzoides* aerial parts from S. Tomé and Príncipe was characterized by the presence of high percentages of precocene I (34.4 %) and β-caryophyllene (24.6 %), as well as small amounts of precocene II (Martins et al. 2005). *Ageratum conyzoides* essential oil was found to contain precocene II (46.35 %), precocene I (42.78 %), coumarin (5.01 %) and *trans*-caryophyllene (3.02 %) as its major components (Nogueira et al. 2010). Chemical constituents of the essential oil of *A. conyzoides* leaves contained precocene I 74.30 %,(*E*)-caryophyllene 14.23 %, γ-muurolene 3.44 %, bicyclogermacrene 3.14 %, α-humulene 2.80 %, β-cubebene 0.62 %, germacrene D 0.59 %, β-elemene 0.42 %, α-pinene 0.30 % and α-thujene 0.16 % (de Melo et al. 2011).

The main components of the volatiles from the hairy root cultures of *A. conyzoides* were β-farnesene, precocene I, and β-caryophyllene, in different amounts, depending on light conditions and also on the age of cultures (Abdelkadera and George 2011). Precocene I, β-farnesene, precocene II and β-caryophyllene were the main constituents of the volatile oils from the parent plant roots, whereas precocene I, germacrene D, β-caryophyllene and precocene II were the main constituents of the aerial parts of the parent plant.

From the ethanol extract of the whole plant of *Ageratum conyzoides*, a new chromene, 2,2-dimethylchromene 7-methoxy-6-*O*-β-D-glucopyranoside (1), was isolated, together with 13 known compounds, seven of which were being reported for the first time (Adebayo et al. 2011). These were eugenyl-*O*-β-D-glucopyranoside (2), eugenyl-*O*-β-D-apiofuranosyl-(1″ → 6′)-β-D-glucopyranoside (3), 3-(2′-*O*-β-D-glucopyranosyl)-phenyl-2-*trans*-propenoic acid (4), (2*S*)-2,3-*O*-di-(9,12,15-octadecatrienoyl)-glyceryl-6-*O*-(α-D-galactopyranosyl)-(1″ → 6′)-β-D-galactopyranoside) (5), ((9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trienoic acid) (6), 7,3′,5′-tri-*O*-methyltricetin (7), and cirsilineol (8). The other known compounds isolated were precocene II (9), precocene I (10), 6-(1-methoxyethyl)-7-methoxy-2,2-dimethylchromene) (11), 2,2-dimethylchromene-7-*O*-β-D-glucopyranoside (12), 3,5,7,4′-tetrahydroxyflavone (13) and 5,6,7,3′,4′,5′-hexamethoxyflavone (14).

Classes of Phytochemicals

Monoterpenes, Triterpenes, Sesquiterpenes and Phenylpropanoids

Friedelin, a triterpenoid (Hui and Lee 1971); α-pinene, ocimene, eugenol, methyl eugenol, δ-cadinene were reported from whole plant (Rao and Nigam 1973); caryophyllene oxide from aerial plant parts (González et al. 1991b); β-caryophyllene, the major compound and a large number of minor terpenoids from plant essential oil (Vera 1993); β-caryophyllene (14.35 % in flower essential oil, 17 % in leaf and stem essential oil) (Riaz et al. 1995); camphene,

cubebene, elemene, farnesol, β-farnesene, β-myrcene, β-pinene, α-pinene, β-selinene, α-terpinene, β-caryophyllene from aerial plant parts (Dung et al. 1996); β-caryophyllene (10.5 %) from leaf essential oil (Chalchat et al. 1997); sabinene, β-pinene, α-pinene, β-phellandrene, 1,8-cineole, limonene, terpinen-4-ol, α-terpineol, β-caryophyllene, caryophyllene epoxide, sesquiphellandrene from leaf essential oil (Ekundayo et al. 1988); β-caryophyllene, γ-bisabolene from leaf essential oil (Kong et al. 1999); β-caryophyllene (8 %) from leaf essential oil (Nébié et al. 2004).

Chromene, Chromone, Chromanone and Benzofuran

A solid obtained in the dimerization of ageratochromene (6,7-dimethoxy-2,2-dimethyl-1-benzopyran) (II) in the presence of acid was shown to be 5,6,6a,6b,7,12b-hexahydro-1,2,10,11-tetramethoxy-5,5,7,7-tetramethylcyclo-penta [1,2-*c*;5,4,3-*d′e′*]bis[1]benzopyran (IV) (Kasturi et al. 1973a). 6-demethoxyageratochromene, ageratochromene dimer and 6,7,6′,7′-tetramehtyl-3′(4′)-dehydro-3′-4*S*-bichroman were isolated from the plant (Kasturi and Manithomas 1967; Kasturi et al. 1973b). Precocene I and II (Vyas and Mulchandani 1980; Quijano et al. 1982); a highly oxygenated chromone, conyzorigun (Vyas and Mulchandani 1984); two chromones 6-acetyl-2,2-dimethyl-3,4-dihydro-chromene and its 7-methoxyderivative were identified from the leaf essential oil (Ekundayo et al. 1988); chromenes, precocene I and II, dihydrodesmethoxyencecalin, desmethoxyencecalin, 6-vinyl-7-methoxy-2,2-dimethylchromene, desmethylencecalin, dihydro-encecalin and encecalin were also isolated and identified (Ekundayo et al. 1987); 6-vinyl-7-methoxy-2,2-dimethylchromene; 6-(1-methoxyethyl)-7-methoxy-2,2-dimethylchromene; 6-(1-hydroxyethyl)-7-methoxy-2,2-dimethylchromene; 6-(1-ethoxyethyl)-7-methoxy-2,2-dimethylchromene; 6-angeloyloxy-7-methoxy-2,2-dimethylchromene; encecalin, encecanescin from aerial parts (González et al. 1991a). Besides precocene I (7-methoxyageratochromene), precocene II (ageratochromene), an isodihydroeuparin derivative 2-(2′-methylethyl)-5,6-dimethoxybenzofuran; a chromene 2-(1′-oxo-2′-methylpropyl)-2-methyl-6,7-dimethoxy-chromene; a chromone 3-(2′-methylpropyl)-2-methyl-6,8-dimethoxy-chrom-4-one and a chromanone 2-(2′-methylprop-2′-enyl)-2-methyl-6,7-dimethoxy-chroman-4-one were identified from *A. conyzoides* essential oil (Pari et al. 1998). The chromenes precocene I and precocene II were identified from leaf oil (Kong et al. 1999) from aerial parts (Dung et al. 1996) and from leaf essential oil (Nébié et al. 2004). A chromene glucoside, 2,2-dimethylchromene 7-*O*-β-glucopyranoside, and a benzofuran derivative 14-hydroxy-2*H*β,3-dihydroeuparine from the aerial parts were identified (Ahmad et al. 1999). Precocene I (7-methoxy-2,2-dimethylchromene) and precocene II (6,7-methoxy-2,2-dimethylchromene) (20 mg/ml) were extracted from *A. conyzoides* (Sharma and Sharma 2001). Two chromenes, 6-(1′-hydroxylethyl)-2,2-dimethyl chromene and 7-hydroxyl-2,2-dimethylchromene, were reported as constituents of *A. conyzoides* leaf essential oil (Kasali et al. 2002).

The major constituents of the essential oil of different plant parts of *Ageratum conyzoides*, namely, flowers, stems, leaves and roots, were 6-demethoxyageratochromene (precocene I: 13.2–44.3 %) and ageratochromene (precocene II : 41.1–62.2 %) (Singh et al. 2003). Total chromene was found maximum in leaves (91.7 %) and minimum in roots. The chromene derivative encecalol methyl ether and chromene ester encecalol angelate from the dichloromethane extract of *Ageratum conyzoides* (Harel et al. 2011).

Flavonoids

The following flavonoids were isolated from the leaves: kaempferol-3,7-diglucopyranoside (Nair et al. 1977); from the whole plant a flavone 5,6,7,8,3′,4′,5′-heptamethoxyflavone and 5′-methoxynobiletin (Adesogan and Okunade 1979); quercetin, quercetin-3-rhamnopyranoside, kaempferol, kaempferol-3-rhamnopyranoside, kaempferol-3,7-diglucopyranoside (Gill et al. 1978); eupalestin (Vyas and Mulchandani 1984); twelve polyoxygenated flavones were isolated from *Ageratum conyzoides*, ageconyflavone A (5,6,7-trimethoxy-3′,4′-methylenedioxyflavone), ageconyflavone B (5,6,7,3′-tetramethoxy-4′-hydroxyflavone) and ageconyflavone C

(5,6,7,3′,5′-pentamethoxy-4′-hydroxyflavone) (Vyas and Mulchandani 1986). The other nine compounds were identified as linderoflavone B, eupalestin; nobiletin; 5′-methoxynobiletin; 5,6,7,5′-tetramethoxy-3′,4′-methylenedioxyflavone; sinensetin; 56,7,3′,4′,5′-hexamethoxyflavone; 5,6,7,8,3′-pentamethoxy-4′-hydroxyflavone; and 5,6,7,8,3′,5′-hexamethoxy-4′-hydroxyflavone. Two flavonoids, eupalestin and lucidin dimethyl ether, were isolated from the petroleum ether extract of the plant (Calle et al. 1990). Eupalestin; sinensetin; nobiletin; 5′-methoxynobiletin; 5,6,8,3′,4′,5′-hexamethoxyflavone; 5,6,7,3′,4′,5′-hexamethoxyflavone; and 5,6,7,5′-tetramethoxy-3′,4′-methylene dioxyflavone were isolated from aerial parts (González et al. 1991b). A flavone 5,6,7,3′,4′,5′-hexamethoxyflavone (Horie et al. 1993) and another flavone, isolated from *Ageratum conyzoides*, were correctly identified as 8-hydroxy-5,6,7,3′,4′,5′-hexamethoxyflavone (Horie et al. 1995). An isoflavone glycoside 5,7,2′,4′-tetrahydroxy-6,3′-di-(3,3-dimethylallyl)-isoflavone5-O-α-L-rhamnopyranosyl-(1→4)-α-l-rhamnopyranoside was isolated from the stem (Yadara and Kumar 1999). Three flavones, 5,6,7,8,3′,4′5′-heptamethoxyflavone,5,6,7,3′,4′,5′-hexamethoxyflavone, 5,6,8,3′,4′,5′-hexamethoxyflavone, ageratochromene and its two dimers were isolated and identified from the *A. conyzoides* (Hu et al. 2002; Kong et al. 2004). The major constituents of *Ageratum conyzoides* fresh leaves and its essential oil were demethoxyageratochromene, β-caryophyllene, α-bisabolene and *E*-β-farnesene (Kong et al. 2005). 5,6,7,8,3′,4′,5′-heptamethoxyflavone, 5,6,7,8,3′-pentamethoxy-4′, 5′-methy-lenedioxyflavone were isolated from the hexane plant extract (Moreira et al. 2007) and methoxylated flavonoids were isolated from the dichloromethane plant extract (Harel et al. 2011).

Alkaloids

Open chain pyrrolizidine alkaloids, namely, 9-angeloylretronecine, lycopsamine and echinatine, were identified from the plant (Röder et al. 1990; Wiedenfeld and Röder 1991). Trigo et al. (1988) found several alkaloids in the plant, including 1,2-desifropyrrolizidinic and lycopsamine which could have hepatotoxic activity.

Sterols

β-Sitosterol, Δ^{22} stigmasterol, Δ^{22} brassicasterol, dihydrobrassicasterol, Δ^{22} spinasterol, dihydrospinasterol were isolated from the plant (Hui and Lee 1971; Horng et al. 1976; Dubey et al. 1989; González et al. 1991b).

Phenolic and Miscellaneous Compounds

Fumaric and caffeic acid (Nair et al. 1977); three coumarinic compounds including 1-2 benzopyrone (Ladeira et al. 1987); (+)-sesamin González et al. 1991b); a coumarin and phytol (a diterpene alcohol) were isolated from essential oil of the plant (Vera 1993); aurantiamide acetate (Sur et al. 1997); 3,3-dimethyl-5-*tert*-butylindone, and fenchyl acetate from leaf oil (Kong et al. 1999); an unsaturated branched chain fatty acid, (*Z*)-6-methyl-12-heptadecenoic acid (Pari et al. 2000); coumarin from the plant (Moreira et al. 2007); 2*H*-1-benzopyran-2-one (coumarin) from leaves (Alcantara 1985) and coumarin from leaves (Widodo et al. 2008). Xuan et al. (2004) identified three phenolic compounds: gallic acid, coumaric acid and protocatechuic acid in the leaves, stem and roots, and catechin was found only in the stem while *p*-hydroxybenzoic acid was detected in both the leaves and stem. Three additional putative allelochemicals were found in the leaves consisting of *p*-coumaric acid, sinapic acid and benzoic acid. The methylene chloride extract of the air-dried aerial parts of *Ageratum conyzoides* afforded a new natural compound, pyrrolone, 5-ethoxy-1*H*-pyrrol-2(5*H*)-one, together with a known flavonoid (Hussien et al. 2010).

Antioxidant Activity

Extracts of *A. conyzoides* were found to have radical scavenging activity (Adebayo et al. 2010). The water, *n*-butanol and ethyl acetate extract elicited DPPH scavenging activity of 87.80, 85.40, 72.56 and 60.87 %, respectively, while the petroleum ether extract had a low activity of 7.84 %. Kaempferol isolated from the ethyl acetate extract of *A. conyzoides* rapidly scavenged DPPH with an EC_{50} value of 130.07 g/kg highly comparable to the standard

control (vitamin C) with an EC_{50} value of 127.13 8.56 g/kg. Methanol extract of *A. conyzoides* showed the highest antioxidant activity in FRAP and DPPH assay, whereas *A. conyzoides* essential oil showed greater lipid peroxidation inhibition than methanol extract (Patil et al. 2010).

Wound Healing Activity

Methanol extracts of *Ageratum conyzoides* were found to have a better wound healing enhancing action compared with normal saline-treated controls (Oladejo et al. 2003a). Skin wounds of Wistar rats dressed with the extract showed a significant increase in the percentage wound contraction (82.3 %) at day 10 compared with the saline-treated control (55 %). Oladejo et al. (2003b) also reported that on the tenth day post-wound creation in Wistar rats, *Ageratum*-treated skin sections showed fewer inflammatory cells compared with similar honey and control skin sections. Honey and *Ageratum* caused significant greater wound contraction than controls. Healed wounds from the *Ageratum* group had significantly fewer fibroblasts than honey and controls. Dash and Murthy (2011) reported that rats treated with methanol and aqueous leaf extracts of *A. conyzoides* showed faster rate of wound healing compared to other extracts under study. The chloroform extract also produced promising results but the effects were seen to be of lesser magnitude. The petroleum ether extract did not produce significant results. The results supported the use of the leaves of *A. conyzoides* for wound healing activity in folkloric medicine. Topical application of *A. conyzoides* ethanol extract was found to accelerate the rate of wound healing in rats (Arulprakash et al. 2012). The extract increased cellular proliferation and collagen synthesis. Wounds treated with the extract were found to heal much faster, based on the improved rates of epithelialization and wound contraction and on the histopathological results. A 40 % increase in the tensile strength of the treated tissue was observed.

Anticancer Activity

The aqueous root extract of the aqueous extract exhibited antitumour activity against murine ascites Dalton's lymphoma in vivo (Rosangkima and Prasad 2004). Glutathione in the liver and Dalton's lymphoma cells of treated tumour-bearing mice was found to be decreased. The methanol fraction from the ethyl acetate extract of *A. conyzoides* leaves was found to inhibit in-vitro growth of Ehrlich tumour (Momesso et al. 2009).

From the preliminary anticancer screening, the petroleum ether extract of *A. conyzoides* exhibited a significant in-vitro inhibition on human gastric carcinoma (SGC-7901), human colon adenocarcinoma (HT-29), and mouse leukaemia (P-388) cancer cell lines (Adebayo et al. 2010). Similarly, the ethyl acetate extract showed a significant in-vitro inhibition on human non-small cell lung carcinoma (A-549), SGC-7901, HT-29, P-388, human breast carcinoma (MDA-MB-231) and human prostate carcinoma (DU-145) cancer cell lines, while the ethanol extract had a significant inhibitory activity on HT-29 and P-388 cancer cell lines. The results showed that ethyl acetate extract of *A. conyzoides* exhibited the highest cytotoxic activity on human non-small cell lung carcinoma (A-549) and mouse leukaemia (P-388) with IC_{50} values of 0.68 and 0.0003 µg/ml, respectively. The *n*-butanol and water extracts showed no significant inhibition on any of the cancer cell lines.Tri-*O*-methyltricetin(7),precoceneII(9),3,5,7,4′-tetrahydroxyflavone (13) and 5,6,7,3′,4′,5′-hexamethoxyflavone (14) isolated from the ethanol extract of the whole plant exhibited inhibitory activity on the mouse leukaemia P-388 cancer cell line with IC_{50} values of 12.8, 24.8, 3.5 and 7.8 µM, respectively, while compound 9 exhibited inhibitory activity on the human colon adenocarcinoma HT-29 cancer cell line with an IC_{50} value of 61 µM; the others showed no significant cytotoxic activity on the cell lines tested time (Adebayo et al. 2011).

All the fractions of *A. conyzoides* leaf ethanol extract and the petroleum ether fraction of *Parkia biglobosa* were cytotoxic to human lung cancer (SK-MES 1) cell lines which to some extent may support their traditional inclusion in herbal

preparations for treatment of cancer (Adetutu et al. 2012).

Antimicrobial Activity

The ether and chloroform extracts of *A. conyzoides* used in wound healing therapy inhibited in-vitro growth of *Staphylococcus aureus* (Durodola 1977). The methanol extract of the whole plant inhibited growth of *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* (Al-Magboul et al. 1985). The aqueous leaf extract was found to be inhibitory to ringworm pathogens *Epidermophyton floccosum* and *Trichophyton mentagrophytes* (Mishra et al. 1991). *Ageratum conyzoides* ethanol extract exhibited antifungal activity against *Epidermophyton floccosum* with minimum inhibitory concentration of less than 10 mg/ml (Sukandar et al. 1992). The ethanol leaf extract was found to inhibit growth of *Escherichia coli*, *Microsporum canis* and *Trichophyton mentagrophytes* (Vlietinck et al. 1995). *Ageratum conyzoides* essential oil exhibited in-vitro antibacterial activity against 20 bacteria and inhibited in-vitro growth of four fungi *Candida albicans*, *Cryptococcus neoformans*, *Sclerotium rolfsii* and *Trichophyton mentagrophytes* (Pattnaik et al. 1996). The ethanol plant extract inhibited growth of *Streptococcus pyogenes* and *Neisseria gonorrhoeae* (Geyid et al. 2005).

Among 16 tested plants, *Cleome gynandropsis* and *Ageratum conyzoides* aqueous extracts exhibited a significant control of the growth of *Alcaligenes viscolactis*, *Klebsiella aerogenes*, *Bacillus cereus* and *Streptococcus pyogenes* (Perumal Samy et al. 1999). The essential oil of *A. conyzoides* aerial parts showed weak activity against *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus faecalis*, *Proteus vulgaris and Cladosporium cladosporioides* and was inactive against *Escherichia coli*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus niger and A. fumigatus* (Martins et al. 2005). Of all the leaf extracts, *n*-hexane, acidic ethyl acetate, basic ethyl acetate and ethanol, the basic ethyl acetate extract showed the highest antibacterial activity when tested against *Staphylococcus aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Streptococcus haemolyticus* (Wirahardja et al. 2001). Phytochemical analysis showed the presence of alkaloids, flavonoids, polyphenols, saponins, quinines and tannins in the *A. conyzoides* (babadotan) leaves.

A coumarin compound isolated from acetone fraction of *A. conyzoides* leaves exhibited antifungal activity against *Aspergillus niger* with MIC value of 62.5 µg/ml (Widodo et al. 2008). Of ten methanol plant extracts, *A. conyzoides*, *Scleria striatinux* and *Lycopodium cernuum* showed very potent antibacterial activity against *Helicobacter pylori* (Ndip et al. 2007). The lowest MIC for *A. conyzoides* ranged from 0.063 to 1.0 mg/ml and MBC ranged from 0.098 to 12.5 mg/ml. All extracts of the leaf, stem and root of *A. conyzoides* inhibited the growth of the bacterial isolates *Staphylococcus aureus*, *Yersinia enterocolitica*, *Salmonella gallinarum and Escherichia coli* in a concentration dependent manner (Okwori et al. 2007). The hexane extract of the leaf, stem and root elicited 100 % susceptibility; the aqueous leaf extract gave 75 % susceptibility, while methanolic leaf extract gave 50 %. The MIC(s) ranged from 6.25 to 100 mg/ml while the MBC(s) gave a range of 3.13 to 50 mg/ml. Phytochemical analysis of the dried leaves revealed the presence of resins, alkaloids, tannins, glycosides and flavonoids. The dried stems revealed the presence of resins saponins, tannins, glycosides and flavonoids, while the dried roots contained resins, alkaloids saponins and flavonoids.

The growth and aflatoxin production of the toxigenic strain *Aspergillus parasiticus* was completely inhibited by *A. conyzoides* essential oil (Patil et al. 2010). All the studied concentrations of the oil caused a reduction in mycelia growth and decreased aflatoxin production. Volatiles from macerated green leaf tissue of *A. conyzoides* were also effective against *Aspergillus parasiticus*. The strongest antibacterial activity was observed against the bacteria *Staphylococcus aureus* and *Bacillus subtilis*. *Ageratum conyzoides* essential oil inhibited *Aspergillus flavus* growth to different extents depending on the

concentration and completely inhibited aflatoxin production at concentrations above 0.10 μg/ml (Nogueira et al. 2010). Ultrastructural changes were more evident in the endomembrane system, affecting mainly the mitochondria of the fungal cells. Degradation was also observed in both surrounding fibrils. In-vitro studies showed that the ethanol extracts of *Parkia biglobosa* and *A. conyzoides* were inhibitory to *Escherichia coli*, *Staphylococcus aureus*, and methicillin-resistant *Staphylococcus aureus* (MRSA) but not to *Pseudomonas aeruginosa* (Adetutu et al. 2012).

Haematopoietic/Haemostatic Activities

The ethanol leaf extract of *Ageratum conyzoides* administered by gavage to rats was found to increase in a dose-related fashion packed cell volume (PCV) and haemoglobin at the doses of 200, 400 and 500 mg/kg, RBC (red blood corpuscle) for 400 and 500 mg/kg and marginal increases that were not significant for 200 mg/kg (Ita et al. 2007). MCH (mean corpuscle haemoglobin) and MCV (mean corpuscle volume) for 200, 400 and 500 mg/kg doses were not significant. White blood corpuscle (WBC) recorded marginal increases that were not significant. Marginal but nonsignificant decreases in body weight were also observed. The authors concluded that the results indicated haematopoietic potentials of the extract and that it could possibly remedy anaemia. The methanol leaf extract of *A. conyzoides* significantly decreased the bleeding time, prothrombin time and clotting time, respectively, in a dose-dependent manner in albino rats (Bamidele et al. 2010). Conversely, plasma fibrinogen concentration significantly increased. The study suggested the methanol leaf extract of A. *conyzoides* to possess haemostatic activity.

Hypoglycaemic Activity

In streptozotocin-diabetic rats, oral administration of the aqueous leaf extract of *Ageratum conyzoides* elicited a significant reduction of blood glucose level of 9.5 % after 1 hour and 21.3 % after 4 hours (Nyunaï et al. 2006). The aqueous leaf extracts of *A. conyzoides* at 200 and 300 mg/kg showed statistically significant hypoglycaemic and antihyperglycaemic activities in streptozotocin-induced diabetic rats (Nyunaï et al. 2009b). For the oral glucose tolerance test, 100 mg/kg dose only attenuated significantly the rise of blood glucose in normal fasted rats, thus confirming the hypoglycaemic properties of the leaves of *Ageratum conyzoides*. The results validate its use for diabetes in folk medicine. Aqueous leaf extract of *A. conyzoides* had a positive effect on the oxidation-reduction system on streptozotocin-induced diabetic rats and improved glycaemia of diabetic rats (Nyunaï et al. 2009a). The extract lowered lipid hydroperoxides in the groups treated with 100 and 200 mg/kg when compared to the negative control group. Antioxidant power (FRAP) was also higher in the 100 mg/kg group. Further, glycaemia was decreased in the group receiving 200 and 300 mg/kg of the extract.

Gastroprotective Activity

The ethanol extract of *Ageratum conyzoides* was found to have gastroprotective activity (Shirwaikar et al. 2003). Oral administration of the ethanol extract at dose levels of 500 and 750 mg/kg significantly protected gastric lesions by 80.59 and 89.33 %, respectively, as compared to misoprostol (74.43 %) in the ibuprofen model; by 97.09 and 99.24 %, respectively, in the cold stress model as compared to famotidine (77.86 and 92.71 %); and by 86.58 and 92.29 %, respectively, in the alcohol model. The findings suggested that the significant gastroprotective activity could be mediated by its antioxidant activity, Ca^{2+} channel blocking and antiserotogenic properties.

Radioprotective Activity

Administration of alcoholic plant extract of *Ageratum conyzoides* resulted in a dose-

dependent decline in radiation-induced mortality up to a dose of 75 mg/kg, the dose at which the highest number of survivors (70.83 %) was observed (Jagetia et al. 2003). In further studies pretreatment of mice with 75 mg/kg extract reduced the severity of symptoms of radiation sickness and mortality at all exposure doses, that is, 6, 7, 8, 9, 10 and 11 Gy of gamma radiation, and a significant increase in survival was observed compared with the untreated irradiated group. The radioprotection afforded by *Ageratum* extract may be in part due to the scavenging of reactive oxygen species induced by ionizing radiation.

Antiinflammatory Activity

Ageratum conyzoides was found to have fairly good antiphlogistic effect in comparison with hydrocortison, as well as inhibiting action on experimental mice tumour development (Nguyen and Pham 1973). Essential oils from violet and white flower varieties have the same qualitative composition but differ in content of each essential oil type. Treatment of rats with the water-soluble fraction (WSF) obtained from a hydroalcoholic extract of *A. conyzoides* was found to reduce articular incapacitation induced by carrageenan (300 µg) (Magalhães et al. 1997). The neutrophil migration induced by carrageenan (300 µg) injection into rat peritoneal cavities and into 6-day-old subcutaneous air pouches was significantly inhibited by WSF pretreatment (30 and 50 mg/kg; s.c.). At the same dose WSF also inhibited the carrageenan (400 µg/paw)-induced oedema but failed to modify the oedema induced by dextran (100 µg/paw). Additionally, the increase in the cutaneous vascular permeability induced by the potent leucocyte chemotactic agent LTB_4 (39 ng coinjected with 500 ng iloprost, i.d.) was significantly blocked by WSF (30 mg/kg; i.p.). The results suggested that WSF could inhibit the inflammatory reactions induced by neutrophil mobilizing stimuli. The results of another study showed that rats treated with hydroalcoholic extract of *Ageratum conyzoides* leaves (250 mg/kg body weight; p.o.) had a 38.7 % reduction in cotton-pellet granuloma (Moura et al. 2005). The development of chronically induced paw oedema was also reduced significantly by the plant extract. The toxicity study did not show any treatment-related abnormalities in biochemical and hematological parameters. The biochemical analysis from blood samples drawn from group of rats treated orally with 500 mg/kg body weight did, however, present 30.2 % reduction of serum glutamic pyruvic transaminase activity as compared to the corresponding control group. Their results confirmed the antiinflammatory properties of *A. conyzoides*, with no apparent hepatotoxicity. In another study, *A. conyzoides* and *Emilia sonchifolia* alcoholic extracts inhibited 49.85 and 39.47 % of acetic acid-induced pain at the highest dose 2.0 g/kg body weight (BW) in Swiss albino mice (Rahman et al. 2012). These effects were statistically significant as compared to the reference drug, diclofenac sodium (40 mg/kg). *A. conyzoides* reduced 35.48 % and *Emilia sonchifolia* reduced 38.70 % of formalin-induced pain by 2.0 g/kg which were also statistically significant as compared to morphine (0.5 mg/kg). In a time-dependent inhibition of carrageenan-induced paw oedema model in Wistar albino rats, the extracts of *A. conyzoides* and *E. sonchifolia* elicited 50.23 and 48.11 % inhibition of paw oedema at the 4th hour of administration, respectively, and the effects were statistically significant.

Contradictory results were obtained by Yamamoto et al. (1991) in Brazil who found that oral treatment of rodents (rats and mice) with water extract of *A. conyzoides* neither reduced the inflammatory oedema induced by carrageenan or dextran, nor did it reduce the chronic paw oedema induced by complete Freund's adjuvant or formaldehyde in rats. Also the extract did not decrease the reaction to pain stimuli as evaluated by tail flick response in immersion test and writhings induced by 0.8 % acetic acid. In isolated guinea pig ilea, the extract presented an unexpected histamine-like activity characteristic of a partial agonist.

Electrocardiographic Activity

Ageratum conyzoides leaf extract changed the electrocardiogram, atrial impulse velocity, and coronary vessels resistance on isolated guinea pig heart (Garcia and Carvalho 1999). Electrocardiographic alterations were (a) PR interval increased from 80 to 105 ms, (b) QT interval decreased from 170 to 154, (c) heart rate decreased from 170 to 152 bpm, (d) atrial impulse velocity decreased from 51 to 45 cm/s, and (e) the time spent for the impulse to be conducted from the atrium to the His bundle increased from 73 to 100 ms. These effects disappeared after a washout.

Analgesic Activity

The raw leaf juice extract of *A. conyzoides*, injected intraperitoneally at doses of 50 and 100 mg/kg, caused a precocious ataxia, a sedation and a slight ptosis in Wistar rats (Abena et al. 1993). Six hours after injection, those effects disappeared: a reduction of spontaneous motor activity. *Ageratum conyzoides* was one of several plant species found to be a source of potential analgesic compounds when tested in three in-vitro radioligand binding assays (Sampson et al. 2000). The three neuropeptide receptors chosen were bradykinin (BK II), expressed in Chinese hamster ovary cells (CHO), neurokinin 1 (NK 1) expressed in astrocytoma cells and calcitonin gene-related peptide (CGRP) which were all implicated in the mediation of acute pain in the mammalian central nervous system.

Spasmolytic/Anticonvulsant Activities

Ageratum conyzoides root and aerial part extracts were found to induce relaxation on isolated trachea and isolated rat uterus (Achola and Munenge 1998). There was no significant difference between the activities of root and aerial part extracts. The extracts extract inhibited uterine contractions induced by 5-hydroxytryptamine, suggesting that the plant extract exhibited specific antiserotonergic activity on isolated uterus. However, the uterine contraction caused by acetylcholine was unaffected by the plant extract.

Results of another study in isolated rat uterus and intestinal smooth muscles supported the popular use of *A. conyzoides* as a spasmolytic (Silva et al. 2000). The water-soluble fraction of *Ageratum conyzoides* (0.2 and 0.4 mg/ml) increased EC_{50} values and decreased maximum responses to acetylcholine and calcium chloride and at 0.5–3.3 mg/ml also produced direct myorelaxant effect on smooth muscle preparations. Theophylline potentiated the relaxant action of the plant water fraction and also prevented the decrease in maximum response promoted by the fraction in acetylcholine concentration-effect curves. The results appeared to be partially linked to calcium mobilization and also suggest that the water-soluble fraction could act synergistically with theophylline in the inhibition of cyclic AMP phosphodiesterase.

In the maximal electroshock (MES) model, pretreatment with methanol (90 %) extract of *Ageratum conyzoides* exhibited significant reduction in duration of hind-leg extension with 200 mg/kg dose, and the effect was dramatically reduced with 400 mg/kg (Varadharajan and Rajalingam 2011). Similar dose-dependent results were obtained in pentylenetetrazole-induced seizure model in albino Wistar rats by delayed onset of clonic convulsions. The complete protective effect against mortality was reported in both the tests. Acute toxicity of extract was nontoxic up to the recommended dose 2,000 mg/kg body weight orally as per OECD guidelines No. 423.

Hepatoprotective Activity

Studies showed that ethanol leaf extract of *Ageratum conyzoides* afforded protection against acetaminophen and caffeinated acetaminophen hepatotoxicity in rats (Ita et al. 2009). Rats treated with acetaminophen plus caffeine plus leaf extract (250 or 500 mg/kg) had significant reductions in the serum aspartate aminotransferase,

alanine aminotransferase and alkaline phosphate levels compared to the elevated levels in rats treated with only acetaminophen or caffeine or both. Total serum protein was marginally increased in the group treated with acetaminophen plus caffeine plus 250 mg/kg extract and significantly increased in the group treated with acetaminophen plus caffeine plus 500 mg/kg extract.

Diuretic Activity

A. conyzoides leaf water extract exhibited significant diuretic activity in albino Wistar rats (Falang et al. 2012). At the end of 24 hours, 200, 400 and 600 mg/kg of extract produced 7.60, 7.00 and 6.80 ml of urine, respectively. The pH of urine produced by the extract and standard drugs were all alkaline. At a dose of 600 mg/kg body weight, there was significant increase in concentrations of sodium, potassium and chloride ions. This could be important in the treatment of cardiovascular diseases such as hypertension. The results suggested that the leaf extract of *A. conyzoides* had diuretic properties similar to acetazolamide.

Antiprotozoal Activity

The dichloromethane extract prepared from aerial parts of *Ageratum conyzoides* was found to exhibit significant activity (IC_{50} = 0.78 µg/ml) against bloodstream forms of *Trypanosoma brucei rhodesiense*, the etiologic agent of East African human trypanosomiasis (East African sleeping sickness) (Nour et al. 2010). This extract also exhibited appreciable activities against *Leishmania donovani* (Kala-Azar, IC_{50} = 3.4 µg/ml) as well as *Plasmodium falciparum* (Malaria tropica, IC_{50} = 8.0 µg/ml). Five highly methoxylated flavonoids along with the chromene derivative encecalol methyl ether were isolated. While the chromene turned out to be inactive against the tested parasites, the flavonoids showed activity against the protozoan pathogens, some in the lower micromolar range. However, none of these isolated compounds was as active as the crude extract. *Ageratum conyzoides* plant extract was found to have antiplasmodial activity against chloroquine-resistant *Plasmodium falciparum*, causal agent of malarial (Madureira et al. 2002). The aqueous leaf extract of *A. conyzoides* exhibited significant and dose-dependent antiplasmodial activity against *Plasmodium berghei* in mice (Ukwe et al. 2010). All the fractions from the methanol extract showed significant but varying levels of antiplasmodial activity. The LD_{50} was estimated to be greater than 5,000 mg/kg, p.o in mice. Phytochemical screening of the extracts revealed the presence of alkaloids, glycosides, flavonoids, saponins, tannins, reducing sugar, proteins, carbohydrates and resins. The aqueous leaf extract of *A. conyzoides* exhibited significant and dose-dependent antiplasmodial activity against *Plasmodium berghei* in mice (Ukwe et al. 2010). All the fractions from the methanol extract showed significant but varying levels of antiplasmodial activity. The LD_{50} was estimated to be greater than 5,000 mg/kg, p.o in mice. The dichloromethane extract of *Ageratum conyzoides* was recently shown to exhibit considerable activity against *Trypanosoma brucei rhodesiense* (Harel et al. 2011). Isolated compounds, namely, methoxylated flavonoids as well as the chromene derivative encecalol methyl ether were less active than the crude extract. The activity of the extract was found to decrease considerably while stored in solution. The unstable chromene ester encecalol angelate was identified as native constituent of the dichloromethane extract of *Ageratum conyzoides*. Its activity against *Trypanosoma*, *Leishmania* and *Plasmodium* species was quite low, so that it does not represent the chemical principle responsible for the high antiprotozoal activity of the crude extract.

Schistosomicidal Activity

The essential oil of *Ageratum conyzoides* was reported to have schistosomicidal effects in vitro against adult worms of *Schistosoma mansoni* (de Melo et al. 2011). The essential oil was less effective than the positive control (praziquantel) in terms of separation of coupled pairs, mortality,

decrease in motor activity and tegumental alterations. However, the essential oil caused an interesting dose-dependent reduction in the number of eggs of *S. mansoni*. Precocene I (74.30 %) and (*E*)-caryophyllene (14.23 %) were identified as the two major constituents of the essential oil; both compounds were found to be much less effective than the essential oil and praziquantel.

Anticoccidiosis Activity

Studies showed that administration of *Ageratum conyzoides* extract in the drinking fluid to broilers infected with oocysts of *Eimeria tenella*, was efficacious in treating caecal coccidiosis (Nweze and Obiwulu 2009). The faecal oocyst per gram of faeces decreased steadily in all the treatment groups until it became zero. The packed cell volumes, weight and red blood cell counts of the treated birds were significantly higher than those of the infected untreated control. No signs of toxicity were observed during the acute toxicity test. The results confirmed its ethnoveterinary use in the treatment of coccidiosis. *Ageratum conyzoides* leaf extracts were found to have anticoccidial activity in chicken (2012). Pertinent coccidia populations reductions were as follows: 10% water-pulverized leaf extract 96 % ($n = 3,388$), 10 % whole leaf extract 81.7 % ($n = 1,500$), Coxisol 97 % ($n = 1,216$) and Amprocox 85.9 % ($n = 1,600$), the last two being commercials coccidiostats. Pathohistological investigation of treatment with 10 % whole extract of *Ageratum conyzoides* did not find any lesions in the heart, liver, lungs kidney and spleen.

Insecticidal/Larvicidal Activity

The petroleum ether extract of the whole plant induced morphogenetic abnormalities in the formation of larvae of the mosquitoes *Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles stephensi* (Sujatha et al. 1988). Vyas and Mulchandani (1980) reported the action of chromenes (precocenes I and II), isolated from *Ageratum* conyzoides, which accelerated larval metamorphosis, resulted in juvenile forms or weak and small adults. Ekundayo et al. (1988) also demonstrated the juvenilizing hormonal action of precocene I and II in insects, the most common effect being precocious metamorphosis, producing sterile or dying adults. Acetone extracts of *Ageratum conyzoides* showed growth inhibitory and juvenile hormone-mimicking activity to the treated larvae of *Culex quinquefasciatus* (Saxena et al. 1992). Larval pupal intermediates, demalanized pupae, defective egg rafts and adult with deformed flight muscles were few noticeable changes. Biting behaviour was observed to be affected by *Ageratum*, and loss of fecundity was observed in the treated mosquitoes but no sterilant effects could be seen. Adults obtained from larvae exposed to the plant extract produced significantly shorter egg rafts than in control. Petroleum ether extract of the flowers was inhibitory to the *Anopheles stephensi* mosquitoes (Kamal and Mehra 1991). The methanol extract of the whole plant suppressed the population of *Anopheles stephensi* at the preimaginal stage (Saxena and Saxena 1992).

Ageratum conyzoides oil showed larvicidal activity against *Aedes aegypti* with LC_{50} value of 148 µg/l (de Mendonça et al. 2005). *A. conyzoides* also induces morphogenetic abnormalities in the formation of mosquito larvae (*Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles stephensi*). This has been verified using petroleum ether extracts (5 and 10 mg/l) of the whole plants. The larvae showed intermediary stages between larvae–pupae and discolored and longer pupae, as well as incompletely developed adults (Sujatha et al. 1988). Extracts of the flowers of this species showed activity against mosquitoes (*Anopheles stephensi*), in the last instar, showing DL 50 with 138 ppm (Kamal and Mehra 1991).

Ageratum conyzoides plant hexane extract was reported to have activity against *Musca domestica* (González et al. 1991a). The petroleum ether extract of *Ageratum conyzoides* exhibited insecticidal activity against *Musca domestica* (Diptera) third instar larvae, and *Cynthia carye* (Lepidoptera) third, fourth and fifth instar larvae and was also active against *Acanthoscelides obtectus* (Coleóptera) adults (Calle et al. 1990).

The known chromene precocene II was isolated from the extract and found to be highly toxic to *M. domestica* third instar larvae under sunlight exposure, while no larvicidal effect was shown under UV irradiation or in dark. Two flavonoids, eupalestin and lucidin dimethyl ether, were also identified in the extract.

Toxicity Studies

The plant has been reported to contain pyrrolizidine alkaloids (Trigo et al. 1988; Röder et al. 1990; Wiedenfeld and Röder 1991) which have been linked to liver and lung cancers and a range of other deleterious effects (Couet et al. 1996). Preliminary study found that rats that consumed a diet of 50 % *A. conyzoides* leaves for 2 weeks or 25 % *A. conyzoides* for 4 weeks appeared to lose weight compared to control rats that were fed with normal cubed diet for rodents (Sani and Stoltz 1993). Histopathological examination revealed extensive liver lesions characterized by megalocytosis and bile duct cells proliferation. Although the analysis of pyrrolizidine alkaloid-like with hot methanol extraction was low (0.014 %), the pathological changes of liver showed that *Ageratum conyzoides* caused pyrrolizidine alkaloid poisoning in rats.

However, results of recent animal studies suggested that ingestion of *Ageratum conyzoides* leaf extract daily for 21 days may not be hepatotoxic at the doses (200 mg/kg body weight, 400 mg/kg body weight and 600 mg/kg body weight of the extract) investigated (Antai et al. 2009). Treatment of rats with the respective doses of the extract did not significantly alter the serum and liver levels of total protein, ALT, AST and ALP in all test groups. Results of acute and sub-chronic (28-day) oral toxicity studies suggested the hydroalcoholic extract of *A. conyzoides* to be relatively safe when administered orally in rats (Diallo et al. 2010). The limit dose of 5,000 mg/kg did not cause any mortality or signs of acute toxicity in the rats tested during the observation period. In the subchronic tests, the results did not show any treatment-related abnormalities in terms of haematological and biochemical parameters. However, urea was significantly lower in the group treated with 500 mg/kg of *A. conyzoides* extract. The weekly body and organ weight of the rats showed no significant differences between the control and the rats treated with the extract except for liver where there was a significant increase in rats that received 1,000 mg/kg, that is, 3 g as against 2.5 g for the control.

Traditional Medicinal Uses

Ageratum conyzoides was reported as one of several plant species used for prostate problems in folkloric ethnomedicine in Trinidad and Tobago (Lans 2007). *Ageratum conyzoides* is a plant used in traditional medicine for mental and infection diseases, cephalgia, dyspnea, enteralgia and fever (Abena et al. 1993). *A. conyzoides* leaves were reported to be used externally to heal wounds, cuts, scratches or itches and internally, decoctions of roots are taken for treating coughs by the Temuan tribe in Ulu Langat, Selangor, Malaysia (Ong 1990). Decoctions obtained from boiling whole plant parts were used to treat asthma, while leaves obtained from white-flowered types of this species were used to alleviate toothache. In Peninsular Malaysia, the Malays poultice wounds externally with the leaves, which have been heated and oiled (Burkill 1966). For itch, a poultice of the leaves mixed with those of *Phyllanthus pulcher* or *Justicia* is used. Pounded plant material is applied to the abdomen of children for severe diarrhoea. The plant decoction is used for fever and dysentery. The plant has also been reported to be used for urinary disorders. In Java, the leaves are used as a paste mixed with chalk for wounds and a paste of the roots rubbed on the body for fever (Heyne 1927). Crevost and Petelot (1929) reported that the Annamites apply a poultice of the leaves to the hair.

In Vietnam, *Ageratum conyzoides* is used to treat inflammation of the nose, dropsy, wound pimples, eczema and postpartum haemorrhage and to regulate menses allergic sinusitis (Doan and Nguyen 1979; Dung et al. 1996; Vo 1997). The plant was reported to contain essential oils, phenols (eugenol), carotenoids, phytosterols,

tannins and saponins (Vo 1997). In the Philippines the juice of the fresh leaves is pounded, mixed with salt and used as vulnerary (Stuart 2012). Sometimes the leaves are cooked in coconut oil and the medicated oil is applied to wounds. The boiled decoction of stem, roots and flowers are employed for stomach disorders. The plant decoction is used for cough, colds, fever, skin disease and high blood pressure. The plant is also used for bleeding due to external wounds, furuncle, eczema, carbuncle and as poultices for headaches. Plant juice is dropped into the ear to treat otitis media.

In Gabon, the Masango people eat the leaves with cola fruit and salt to treat pain (Akendengue and Louis 1994); the leaves are used to treat cuts and wound, fever, painful menstruation; leaves cooked in palm oil is taken as remedy for sexually transmitted diseases (Raponda-Walker and Sillans 1995). *A. conyzoides* is used to treat fever, measles, postpartum haemorrhage and snake bites in Benin (Adjanohoun et al. 1989), while in Nigeria it is used for skin diseases, wound healing, diarrhoea and pain associated with navel in children (Okunade 2002). A leaf decoction is used to treat human immunodeficiency virus (HIV)/AIDS in Nigeria (Igoli et al. 2005; Kayode et al. 2009); HIV/AIDS, herpes zoster and cryptococcal meningitis in Tanzania (Kisangau et al. 2007); and anguillulosis in the Republic of Guinea (Keita et al. 1999). In the Republic of Congo, leaves juice/extract/decoction are employed to treat headache, rib pain, intercostal pain, body side pain, asthma and inflammatory disorders like rheumatism and arthritis and macerated whole plant is used for treating dyspnea (Adjanohoun et al. 1988). In the Ivory Coast, the plant is used to treat abdominal pain (Diehl et al. 2004). *Ageratum conyzoides* was used to treat epilepsy by traditional healers in Tanzania (Moshi et al. 2005). In Mauritius and Rodrigues, the leaves are used as a diuretic in urinary diseases (Gurib-Fakim et al. 1993), and in Mauritius, the leaves are used to treat diarrhoea, skin infection and gas in the stomach (Gurib-Fakim et al. 1997). In Kwara State, Central Nigeria, leaves are used for *Candida* body infection and grounded leaves mixed with shea butter as an ointment are used to massage inflamed painful area in the neck (Bhat et al. 1990).

In an ethnomedicinal survey of plants in the Rivers State of Nigeria, of 188 plant species, the most important and valuable species were found to be *Ageratum conyzoides* and *Tridax procumbens* (Ajibesin et al. 2012). The plants were commonly used for dermal or digestive problems and fever/malaria. The most used plant part was leaves (42 %), while decoction was the main method of drug preparation (36 %). The tribals of Bangangte in Western Cameroon employed the juice from the plant for peptic ulcer (Noumi and Dibakto 2000). In Madagascar, the leaves are used in tea for diarrhoea and the leaf sap is used as a coagulant (Novy 1997). In India and Central Africa, the plant is used to treat wounds and burns (Durodola 1977). In Kenya, the leaf juice is used to treat eye diseases, macerated leaves used as antiseptic for wounds to stop bleeding and haemorrhagic diarrhoea, mycotic skin infection, furuncle, eczema, carbuncle; leaf and root decoctions are used for coughs; and root decoctions used for chest pains (Noumi 2004, Tsabang et al. 2001). In the Republic of Congo (Brazzaville), leaves and roots are used for headache; leaves are employed for intercostal rib pain and side-body pain, asthma and antiinflammatory problems; macerated plant is used for dyspnea (Adjanohoun et al. 1988). In Benin, grounded leaves are used for infectious diarrhoea, fever, malaria and nausea; aerial plant parts are used for giddiness and postpartum haemorrhage (Adjanohoun et al. 1989).

In Northwest Argentina, the plant extract is drank as a remedy for cough (Hilgert 2001).

In Mexico, the aerial plant part infusion is used in the treatment of diabetes (Andrade-Cetto and Heinrich 2005). *Ageratum conyzoides* has been used in Brazilian folk medicine to treat various ailments such as metrorrhagia, fevers, dermatitis, inflammation, arthritis, rheumatism, diarrhoea and diuretics (Lima et al. 2011). The flowers and leaves are used in the form of an infusion for their analgesic and antiinflammatory properties. In Brazil, the plant is used as an analgesic and antiinflammatory (Elisabetsky and Wannmacher 1993); the leaves are used to treat malaria and yellow fever (Ming 1999); the aerial

parts is used as a tonic, stimulant and emmenagogue (de Melo Junior et al. 2002).

In India, the plant is used to treat leprosy and the essential oil is sued as lotion for purulent ophthalmia (Kasturi et al. 1973a, b). In India, the tribals of Sonaghati of Sonbhadra district, Uttar Pradesh, used the plant to treat tumour and swelling and as an antidote to snakebite and stings (Singh et al. 2002). In Nepal, leaf sap is applied on fresh cuts (Shrestha and Joshi 1993); leaves are applied to cuts and wounds for antihaemorrhagic and antiseptic properties (Bhattarai 1991); leaves and aerial parts for cuts, wounds and to treat stomach upset (Joshi and Joshi 2000).

Other Uses

In Hawaii and Polynesia, the fragrant flowers are used for leis, scent and medicine.

The plant has potential to be used as a biocontrol agent to control weeds, agricultural and veterinary insect pests and plant diseases as it has been reported to contain phytochemicals and allelochemicals that are toxic to plant weeds, insect pests and plant pathogens.

A crude lipid extract from the *Ageratum conyzoides* exerted ovicidal action and induced sterility after topical treatment of both young last instar larvae (L_6) and females of *Dysdercus flavidus* Sign, at emergence by inhibiting ovarian development (Fagoonee and Umrit 1981). The action of the two chromenes precocenes I and II in the crude extract was synergistic. Precocene I and II from *A. conyzoides* exhibited antijuvenile hormone activity against *Sitophilus oryzae*, *Thlaspida japonica and Leptocorisa chinensis* (Lu 1982). Highly toxic properties were exhibited by fractions F and G of the chloroform leaf extract of *A. conyzoides* against *Drosophila melanogaster* and fractions C, D, E, F and G against *Dysdercus cingulatus* (Alcantara 1985). These results were comparable with that obtained for the standard insecticide malathion and relatively high as compared with the natural insecticide rotenone. Purification of fraction D and E afforded 2*H*-1-benzopyran-2-one (coumarin) and a dimer of ageratochromene. Compound 1 was found to be highly toxic to *Drosophila melanogaster* and *Dysdercus cingulatus*. Compound 2 was found to be generally nontoxic to the test insects.

A. conyzoides methanol extract from fresh leaves (250 and 500 ppm) adversely producing a deficiency of juvenile hormone affecting the development of the fourth instar of *Chilo partellus* (Lepidoptera, Pyralidae), a sorghum pest, as evidenced by the presence of a dark stain in the insects' cuticle and immature pupae formation (Raja et al. 1987). Studies found that the leaf extract from *A. conyzoides* at 25 % concentration killed 36.7 % of the population of *Dasynus piperis*, a major pest of black pepper berries (Mustikawati and Nazar 1996). The extract of *Lantana camara* flowers at 10 % concentration killed 30 %, while the extract of *Ageratum conyzoides* flowers at 25 % concentration killed 50 % and aquadest killed 3.3 %. The topical application of the essential oil of *Ageratum conyzoides* to the nymphs of the desert locust *Schistocerca gregaria* showed high nymphal mortality (91 %) (Pari et al. 1998). Essential oil of the plant was toxic to the adults of the cowpea weevil (*Callosobruchus maculatus*) (Gbolade et al. 1999).

An unsaturated branched chain fatty acid (*Z*)-6-methyl-12-heptadecenoic acid from *A. conyzoides* essential oil demonstrated insecticidal and growth regulatory activity against *Schistocerca gregaria* (Pari et al. 2000). Besides mortality, the compound also caused disturbances at the nymphal-adult moult resulting in deformity. In-vitro studies showed that the essential oil of *Ageratum conyzoides* leaves was the most effective insecticide against the maize grain weevil, *Sitophilus zeamais* (LD_{50} = 0.09 % in 24 hours), followed by that of *Lantana camara* (LD_{50} = 0.16 %) and *Chromolaena odorata* (LD_{50} = 6.78 %) (Bouda et al. 2001). The mortality of *S. zeamais* increased with the concentration of the essential oils of the three plants and the duration of exposure of the weevils on the treated maize grains. The hexane and alcohol extracts *of A. conyzoides* showed insecticidal activity against the larvae of the lepidopteran pest *Diaphania hyalinata* (Moreira et al. 2004). Fractionation of the hexane

extract afforded the following active compounds 5,6,7,8,3′,4′,5′-heptamethoxyflavone; 5,6,7,8,3′-pentamethoxy-4′,5′-methylenedioxyflavone and coumarin. The increasing order of susceptibility to coumarin was *Diaphania hyalinata* < *Dione juno juno* < *Tuta absoluta*. The increasing order of toxicity to *D. juno juno* was 5,6,7,8,3′-pentamethoxy-4′,5′-methylenedioxyflavone < coumarin < 5,6,7,8,3′,4′,5′-heptamethoxyflavone. The hexane extract of *A. conyzoides* showed insecticidal activity (Moreira et al. 2007). Three compounds were identified: 5,6,7,8,3′,4′,5′-heptamethoxyflavone, 5,6,7,8,3′-pentamethoxy-4′, 5′-methylenedioxyflavone and coumarin. The *A. conyzoides* extract showed good repellence index (66 %) of *Amblyomma cajennense* nymphs (Cayenne tick) when applied in high concentrations (Soares et al. 2010). Lima et al. (2010) demonstrated that ingestion of maize leaf sections treated with *A. conyzoides* essential oil (0.5 % concentration) by the fall armyworm *Spodoptera frugiperda* caused >70 % mortality. The major component of the essential oil from *A. conyzoides* was found to be precocene (87.0 %).

Aqueous extract of *A. conyzoides* plant was found to reduce larvae emergence of the root-knot nematode, *Meloidogyne incognita* (Shabana et al. 1991). The ethanol extract of *A. conyzoides* leaves was more potent against embryonation (39.6 %) of the parasitic nematode *Heligmosomoides bakeri* than the aqueous extract (53.3 %) at the highest concentration (3.75 mg/ml) (Wabo Poné et al. 2011). Both types of extracts also killed larvae with higher larvicidal activity shown by the ethanol extract.

All the employed concentrations of (2, 4 and 6 % w/v) of aqueous, methanol, and *n*-hexane extracts of *A. conyzoides* inflorescence, leaf, stem and root significantly suppressed the growth of the plant pathogen, *Fusarium solani* (Javed and Bashir 2012). The *n*-hexane extracts of leaf and inflorescence caused highly significant reduction of 84 % in growth of *F. solani* followed by stem and root extracts which caused 80 and 72 % reduction in growth, respectively. The same pattern in growth reduction was observed in methanol and aqueous extracts. Among the four parts of the tested weed, different concentrations of the methanol extract of leaf were found to be highly effective in controlling target fungal species, resulting in up to 78 % reduction in fungal biomass over control followed by inflorescence (74 % reduction), stem (63 % reduction) and root (59 % reduction) at highest used concentration. In case of aqueous extracts, the maximum reduction was observed in leaf extract (72 %) followed by inflorescence, stem and root, respectively.

Volatile oil from *Ageratum conyzoides* was found to have allelopathic activity (Kong et al. 1999). Precocene I, precocene II, β-caryophyllene and 3,3-dimethyl-5-*tert*-butylindone isolated from *A. conyzoides* leaf oil inhibited seedling growth of acceptor plants. Inhibitory activity of the volatile oil was more intense than that of the pure components. Fenchyl acetate and γ-bisabolene had no inhibitory activity, but when mixed with precocene II, they increased the inhibitory activity to growth of acceptor seedling plants. The inhibitory allelopathic effects of *A. conyzoides* volatiles on peanut (*Arachis hypogaea*), redroot amaranth (*Amaranthus retroflexus*), cucumber (*Cucumis sativus*) and ryegrass (*Lolium multiflorum*) increased when plants were grown under nutrient-deficient conditions or in competition with *Bidens pilosa* (Kong et al. 2002). Volatiles from *A. conyzoides* plants infected with *Erysiphe cichoracearum* (powdery mildew fungus) or exposed to *Aphis gossypii* feeding inhibited or killed fungi and insects. Precocenes and their derivatives, monoterpenes and sesquiterpenes, were found to be the major volatile components of *A. conyzoides.*

The residue obtained from an aqueous acetone extract of *Ageratum conyzoides* shoots inhibited the germination and the growth of roots and shoots of *Amaranthus caudatus*, *Digitaria sanguinalis* and *Lactuca sativa* (Kato-Noguchi 2011). The concentration-dependent responses of the test plants suggested that the residue of *Ageratum conyzoides* might contain allelochemical(s). *Ageratum conyzoides* showed potential to be used as a natural herbicide for weed control in paddy fields to reduce the dependence on synthetic herbicides (Xuan et al. 2004).

A. conyzoides exhibited strong inhibition on *Raphanus sativus* (radish) germination and growth in a bioassay with the leaves eliciting a greater suppression than the stem and root. The leaves of *A. conyzoides* applied at 2 t/ha reduced about 70 % of the growth of *Echinochloa crus-galli* var. *formosensis* and completely inhibited emergence of *Monochoria vaginalis* var. *plantaginea* and *Aeschynomene indica* in calcareous soil condition. Application of *A. conyzoides* leaves at 2 t/ha in a paddy field 2 days after transplanting caused about 75 % paddy weed reduction and increased yield by 14 % compared with a herbicide treatment. Three phenolic compounds were identified in the leaves, stem and root including gallic acid, coumalic acid and protocatechuic acid, and catechin was found only in the stem. *p*-Hydroxybenzoic acid was detected in both *A. conyzoides* leaves and stem. Three additional putative allelochemicals were found in the leaves consisting of *p*-coumaric acid, sinapic acid and benzoic acid. The greater number of growth inhibitors found in the leaves might result in the stronger inhibitory activity than the stem and root.

Intercropping *Ageratum conyzoides* in citrus orchards may effectively suppress weeds and control other insect pests and diseases (Kong et al. 2002; Hu et al. 2002; Hu and Kong 2002; Kong et al. 2004, 2005). Investigations showed that the inhibition of major weeds and soil pathogenic fungi in citrus orchards was significantly correlated with the allelochemicals released into the soil by intercropped *A. conyzoides*. Three flavones, 5,6,7,8,3′,4′5′-heptamethoxyflavone, 5,6,7,3′,4′,5′-hexamethoxyflavone,5,6,8,3′,4′,5′-hexamethoxyflavone, and ageratochromene and its two dimers were isolated and identified from the *A. conyzoides* intercropped citrus orchard soil. Three flavones and ageratochromene could significantly inhibit the growth of weeds *Bidens pilosa*, *Digitaria sanguinalis* and *Cyperus difformis* and spores germination of soil pathogenic fungi *Phytophthora citrophthora*, *Pythium aphanidermatum* and *Fusarium solani*. However, two dimers of ageratochromene had no inhibitory actions on them (Kong et al. 2004). Earlier their studies showed flavones produced by and released from *A. conyzoides* could inhibit the major fungal pathogens, such as *Elsinoe fawcettii*, *Colletotrichum gloeosporioides*, *Oidium tingitaninum* and *Capnodium citri* in citrus orchard (Hu et al. 2002). Ten flavones, including one glycoside, from *A. conyzoides* plant were isolated and identified. The inhibitory effect of three flavones 5,6,7,8,3′,4′5′-heptamethoxyflavone, 5,6,7,3′,4′,5′-hexamethoxyflavone,and5,6,8,3′,4′,5′-hexamethoxyflavone was stronger, not only than those of other allelochemicals produced by and released from *A. conyzoides*, but also than that of Carbenzin, a commercial fungicide. The presence of these allelochemicals in soils suggests that they may be able to make a major contribution to control some weeds and diseases in citrus orchards. Hu and Kong (2002) found that the allelopathic potential of *A. conyzoides* decreased because of favourable growing seasons in spring and summer. On the contrary, autumn and winter were unfavourable growing seasons, and the allelopathic potential of *A. conyzoides* increased. In the laboratory, under high or low temperatures and shading conditions, inhibitory effects of allelochemicals of *A. conyzoides* on tested plants intensified significantly at low concentration. It revealed that under unfavourable growing conditions, tested plants resistance to the allelochemicals of *A. conyzoides* decreased. When *A. conyzoides* and tested plants both grew under unfavourable meteorological conditions, allelopathic potential of *A. conyzoides* increased and the tested plants resistant ability to allelochemical decreased. Kong et al. (2005) demonstrated that *A. conyzoides* produced and released volatile allelochemicals into the air in the intercropped citrus orchard, and these volatiles influenced the olfactory responses of predatory mite *Amblyseius newsami*, an effective natural enemy of citrus red mite and citrus red mite *Panonychus citri*. At test temperature (25 °C), *A. conyzoides* fresh leaves, its essential oil, and major constituents, demethoxy-ageratochromene, β-caryophyllene, α-bisabolene, and *E*-β-farnesene, attracted *A. newsami* and slightly repelled *P. citri*. Field experiments demonstrated that spraying *A. conyzoides* essential oil emulsion in an *A. conyzoides* nonintercropped citrus orchard

increased the population density of *A. newsami* from below 0.1 to over 0.3 individuals per leaf, reaching the same level as in an *A. conyzoides* intercropped citrus orchard. However, this effect could not be maintained beyond 48 hours because of the volatility of the essential oil. In contrast, in the *A. conyzoides* intercropped citrus orchard, *A. conyzoides* plants continuously produced and released volatile allelochemicals and maintained the *A. newsami* population for a long time. The results suggested that intercropping of *A. conyzoides* not only made the citrus orchard ecosystem more favourable for the predatory mite *A. newsami*, but also that the volatile allelochemicals released from *A. conyzoides* regulated the population of *A. newsami* and *P. citri*. Gravena et al. (1993) observed lower incidences of mites *Phyllocoptruta oleivora* and *Brevipalpus phoenicis* and higher population densities of predatory phytoseiids in citrus trees with green ground cover of *Ageratum conyzoides* and *Eupatorium pauciflorum* than in trees without weeds.

Comments

Ageratum conyzoides is considered an invasive, noxious environmental weed in Asia, Africa, America, and the Pacific Islands.

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Argyranthemum frutescens

Scientific Name

***Argyranthemum frutescens* (L.) Sch. Bip.**

Synonyms

Anthemis frutescens Voss, *Chrysanthemum floridum* Salisb., *Chrysanthemum foliosum* Brouss. ex DC., *Chrysanthemum frutescens* L., *Chrysanthemum fruticosum* Buch, *Matricaria frutescens* (L.), *Pyrethrum frutescens* (L.) Gaertn., *Pyrethrum frutescens* (L.) Willd.

Family

Asteraceae

Common/English Names

Boston Daisy, Cobbity Daisy, Dill Daisy, Federation Daisy, Marguerite, Marguerite Daisy, Paris Daisy, Paris Marguerite, Summer Daisy, Teneriffe Daisy, White Marguerite

Vernacular Names

Catalan: Margaridera
Czech: Kopretinovec Dřevnatý
Danish: Almindelig Buskmargerit
Dutch: Struikmargriet
Finnish: Marketta (Kasvi)
French: Anthémis, Marguerite
German: Strauchmargerite
Italian: Margherita Delle Canarie
Marjocan: Margalidera Gran, Margalides, Margaridera
Spanish: Margarita
Swedish: Buskmargerit

Origin/Distribution

The species is native to Canary Islands in Macaronesia. It has naturalized in Australia, New Zealand, East Europe, Ukraine and is adventive in Norway, Germany, and Italy.

Agroecology

Marguerite Daisy thrives in areas with a Mediterranean to subtemperate climate. It grows easily in moderately fertile, medium-textured and well-drained soils. It is wind and salt tolerant.

Edible Plant Parts and Uses

The flowers are edible (Rop et al. 2012).

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Botany

A short-lived, perennial herb or subshrub 10–80 (−150 cm) high with a prostrate to erect, branched, glabrous stem. Leaves are alternate, 2–3 pinnately divided, lobes wedge-shaped to linear, ultimate margins serrated rarely entire (Plate 1). Inflorescence a lax irregular cyme often reduced to a solitary capitulum. Involucre hemispherical cup-shaped, phyllaries in 3–4 series, free, persistent in fruit, oblanceolate or ovate to lanceolate-deltate or lanceolate, margins and tips yellow to brown, scarious, tips of inner often expanded; receptacle convex to conic. Ray flowers 12 to >25, ray ovate to linear, female, white, sometimes pink or yellow. Disk flowers 50–80 to >150, bisexual, fertile, corolla white, yellow (pink, red or purple), tubular, 5-deltoid lobed, anther with ovate tips, styler tip truncate, papillate (Plates 1, 2 and 3). Fruit subterete or obovoid achene, faintly 5–8 ribbed without pappus.

Plate 1 Leaves and white-yellow flowers of Marguerite Daisy

Plate 2 Pale purple Marguerite Daisy flowers

Plate 3 Bright pink Marguerite Daisy flower

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Argyranthemum frutescens* had a dry matter content (%w/w) of 9.57 %, crude protein of 6.85 g/kg, and the following elements (mg/kg) fresh mass (FM): P 428.36 mg, K 2617.24 mg, Ca 258.55 mg, Mg 105.26 mg, Na 89.10 mg, Fe 5.15 mg, Mn 7.86 mg, Cu 2.20 mg, Zn 5.49 mg, and Mo 0.30 mg.

Argyranthemum frutescens flowers were found to emit the benzenoid volatile, phenylacetaldehyde. to attract foraging insects like moths (Cunningham et al. 2006).

Leaf extract of *A. frutescens* containing biologically active components such as tetradecanoic acid, pentadecanoic acid, hexadecanoic acid, phytol, linalool, 1,8cineole, and 9, 12, 15octadecanoic acid was found to be effective against the damping-off pathogen of sugar beet, *Sclerotium rolfsii* (Derbalah et al. 2012a).

Antioxidant Activity

Marguerite Daisy was found to have a total antioxidant capacity of 4.24 g ascorbic acid equivalent/kg fresh mass (FM), a total phenolic content

of 2.53 g gallic acid/kg/FM, and total flavonoid content of 1.23 g rutin/kg FM (Rop et al. 2012).

Traditional Medicinal Uses

Marguerite Daisy has been used in the treatment of whooping cough, asthma and nervous excitability. The sticky leaves have been used in wound dressing. An eye lotion for conjunctivitis can be made from the flowers.

Other Uses

The species, cultivars and hybrids are planted as ornamental plants in gardens and parks. The flowers are also used for cut flower arrangements.

The leaves have insecticidal properties. Derbalah et al. (2012b) found that increasing the concentration level of all tested treatments (from 100 to 300 ppm) reduced the emergence of the rice weevil, *Sitophilus oryzae*, even more (concentration dependent) malathion (86 %) followed by *Caesalpinia gilliesii* (79 %) extract and *Chrysanthemum frutescens* leaf extract (73 %), while *Cassia senna* extract was the least effective. The results showed that *C. gilliesii* (100 %) was the most effective treatment against *S. oryzae* adults followed by *C. frutescens* (95.6 %), *Thespesia populnea* var. *acutiloba* (88 %), *Euonymus japonicus* (85 %), *Bauhinia purpurea* (75 %), *C. senna* (80 %), and *Cassia fistula* (70 %), respectively. Malathion (100 %) and *C. gilliesii* (100 %) extract were the most effective treatments on adult's mortality of *S. oryzae* after 2 weeks, while *C. fistula* extract (70 %) was the least effective.

Comments

The species is regarded as environmental weed in South Australia and Western Australia.

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Bellis perennis

Scientific Name

***Bellis perennis* L.**

Synonyms

Aster bellis E.H.L. Krause, *Bellis alpina* Hegetschw., *Bellis armena* Boiss., *Bellis croatica* Gand., *Bellis hortensis* Mill., *Bellis hybrida* Ten., *Bellis integrifolia* DC., *Bellis margaritifolia* Huter, *Bellis minor* Garsault (inval.), *Bellis perennis* var. *caulescens* Rochebr., *Bellis perennis* f. *discoidea* D.C. McClint., *Bellis perennis* var. *fagetorum* Lac., *Bellis perennis* var. *hybrida* (Ten.) Fiori, *Bellis perennis* subsp. *hybrida* (Ten.) Nyman, *Bellis perennis* var. *margaritifolia* (Huter) Fiori, *Bellis perennis* var. *microcephala* Boiss., *Bellis perennis* f. *plena* Sacc., *Bellis perennis* f. *pumila* (Arv.-Touv. & Dupuy) Rouy, *Bellis perennis* var. *pusilla* N. Terracc., *Bellis perennis* f. *rhodoglossa* Sacc., *Bellis perennis* var. *strobliana* Bég., *Bellis perennis* var. *subcaulescens* Martrin-Donos, *Bellis perennis* var. *tubulosa* F.J. Schultz, *Bellis perennis* f. *tubulosa* A. Kern., *Bellis pumila* Arv.-Touv. & Dupuy, *Bellis pusilla* (N. Terracc.) Pignatti, *Bellis scaposa* Gilib. [Invalid], *Bellis validula* Gand. *Erigeron perennis* (L.) Sessé & Moc.

Family

Asteraceae

Common/English Names

Bairnwort, Bainswort, Banewort, Banwood, Billy Button, Bruisewort, Child's Flower Common Daisy, Daisy, Day's Eye, English Daisy, European Daisy, Ewe-Gowan, Field Daisy Flower of Spring, Gowan, Herb Margaret, Lawn Daisy, Little Star, Maudlinwort, Measure of Love, Moon Daisy, Open Eye, Perennial Daisy, Silver Pennies, Woundwort

Vernacular Names

Albanian: Luleshqerre
Brazil: Margarida
Chinese: Chu Ju, Chu Ju Shu
Czech: Sedmikráska Chudobka
Dutch: Madeliefje
Eastonian: Harilik Kirikakar
Esperanto: Beliso, Lekanteto
Finnish: Kaunokainen
French: Fleure De Pâques, Fleure De Pasturage, Pâquerette, Pâquerette Commune, Pâquerette Vivace, Petite Marguerite
Gaelic: Nóinín
German: Angerbleamerl, Augenblümchen, Gänseblümchen, Gemeines Massliebchen, Himmelsblume, Maiblume, Marguerite, Marienblümchen, Massliebchen, Mehrjähriges Gänseblümchen, Mondscheinblume, Mümmeli, Regenblume, Tausendschön, Tausendschönchen
Hungarian: Százszorszép, Vad Százszorszép
Icelandic: Fagurfífill

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Italian: Bellide, Margherite, Margheritina, Margheritina Dei Prati, Pratolina, Pratolina Commune
Norwegian: Tusenfryd
Polish: Margarytka, Stokrotka Pospolita
Portuguese: Bela-Margarida, Bonina, Mãe-De-Família, Margarida, Margarida-Comum, Margarida-Inglesa, Margarida-Menor, Margarida-Rasteira, Margarida-Vulgar, Margaridas, Margaridinha, Margarita, Rapazinho, Rapazinhos, Sempre-Viva
Russian: Margaritka
Slovašcina: Marjetica Navadna, Navadna Marjetica
Slovencina: Sedmokráska Obyčajná
Spanish: Chiribita, Chirivita, Dormilona, Margarita, Margarita Común, Margarita Menor, Maya, Pascueta, Vellorita
Swedish: Bellis, Pytter, Tusensköna
Turkish: Çayır Papatyasi, Koyun Çiçeği, Koyungözü, Koyungözüotu
Welsh: Llygad Y Dydd

Origin/Distribution

The species is native to western, central and northern Europe and middle Asia. It has been introduced to North America and New Zealand. The species is widely naturalized in North America.

Agroecology

B. perennis is a cool climate perennial herbaceous plant grown as a biennial or annual. The plant is found wild in meadows and uncultivated pastures in its native range. It prefers full sun to light shade and organically rich, fertile, consistently moist and well-drained soils. It flowers in spring and declines with summer heat where it is often removed. The plant is intolerant of drought.

Edible Plant Parts and Uses

The leaves and flowers are used as vegetables (Yoshikawa et al. 2008). Flower buds and petals have a mildly bitter taste and can be eaten raw, in salads, sandwiches, soups or as garnish or in tea (Cribb and Cribb 1982; Facciola 1990). Young leaves can be eaten raw in salads or cooked as potherbs (Hedrick 1972; Larkcom 1980; Chiej 1984; Facciola 1990; Bown 1995).

Botany

An herbaceous perennial or annual plant, 10–25 cm high with creeping rhizomes and sparsely strigose scape. Leaves basal and rosulate with long winged petioles; lamina spatulate, 2–6 cm by 1–2.8 cm, with serrated to crenate margins, attenuated base and apex obtuse, sometimes retuse, mucronulate (Plate 1). Capitula terminal, solitary, 2–3 cm across (Plates 1, 2, 3 and 4). Involucre hemispheric or broadly campanulate, 5–6 mm; phyllaries 2-seriate, subequal, oblanceolate, leaflike, surfaces pubescent, margin sparsely ciliate, midvein thin, translucent, apex obtuse, scarious, ciliate. Ray florets white or pinkish or in various shades of red, purple, pink (Plates 1, 2, 3 and 4), lamina about 10×1 mm; disk florets yellow, 2 mm, limb campanulate, about 1.5 mm, sparsely pubescent proximally, lobes erect, triangular, eglandular. Cypselae strigillose 1–2 mm. Pappus absent.

Nutritive Value and Medicinal Properties

The major anthocyanin of red flowers of Bellis perennis was identified as cyanidin 3-*O*-(6-*O*-matonyl-4-*O*-(β-D-glucuronyl)-β-D-glucopyranoside) (Saito et al. 1988). The malonylantho cyanin was more stable in neutral solution than cyanidin 3-glucoside but less stable than cyanidin 3-glucuronylglucoside. The anthocyanins, cyanidin 3-*O*-(4″-*O*-(malonyl)-2″*O*-(β-D-glucuronyl)-β-D-glucopyranoside) and cyanidin 3-*O*-(2″-*O*-(β-D-glucuronyl)-β-D-glucopyranoside) were isolated from the red flowers of *Bellis perennis* cv. 'Super Siberius Crimson' (Toki et al. 1991). A known malonylated cyanidin 3-glucuronyl-glucoside was also obtained as a major pigment, and its structure was revised to the cyanidin

Plate 1 Leaves and terminal white flower head

Plate 2 Dark red flower heads

Plate 3 Close view of pink flower heads

Plate 4 Close view of red flower heads

3-*O*-(6″-*O*-(malonyl)-2″-*O*-(β-D-glucuronyl)-β-D-glucopyranoside). Seven acylated triterpene saponins, perennisosides I–VII, were isolated together with four known saponins, bellidioside A, asterbatanoside D, bernardioside B 2 and bellissaponin BS6 and were isolated from *B. perennis* flowers (Morikawa et al. 2008). The structure of perennisoside I was determined as 23-*O*-acetylbayogenin 28-*O*-α-L-rhamnopyranosyl(1 → 2)[β-D-glucopyranosyl (1 → 3)]-6-*O*-acetyl-β-D-lucopyranoside; the structure of perennisoside II was elucidated as 23-*O*-acetylbayogenin 28-*O*-R-L-rhamnopyranosyl(1 → 2) [β-D-galactopyranosyl (1 → 3)]-6-*O*-acetyl-β-D-glucopyranoside; the structure of perennisoside III was established as 3-*O*-β-D-glucopyranoside of bayogenin 28-*O*-α-L-rhamnopyranosyl(1 → 2) [β-D-glucopyranosyl(1-3)]-6-*O*-acetyl-β-D-glucopyranoside; perennisoside IV was elucidated as 3-*O*-β-D-glucopyranoside of bayogenin 28-*O*-α-L-rhamnopyranosyl(1 → 2)[β-D-galactopyranosyl(1 → 3)]-6-*O*-acetyl-β-D-glucopyranoside; perennisoside V was assigned as 3-*O*-β-D-glucopyranoside of 23-*O*-acetylbayogenin 28-*O*-α-L-rhamnopyranosyl(1-2)[β-D-glucopyranosyl(1-3)]-β-D-glucopyranoside; the structure of perennisoside VI was determined as 3-*O*-β-D-glucopyranoside of 23-*O*-acetylbayogenin 28-*O*-α-L-rhamnopyranosyl(1 → 2)[β-D-galactopyranosyl(1 → 3)]-β-D-glucopyranoside and the structure of perennisoside VII was elucidated as 3-*O*-β-D-glucopyranoside of 23-*O*-acetylbayogenin 28-*O*-R-L-rhamnopyranosyl (1 → 2) [β-D-galactopyranosyl(1 → 3)]-6-*O*-acetyl-β-D-

glucopyranoside. Five new oleanane-type triterpene saponins named perennisosides VIII–XII were isolated from the flowers (Morikawa et al. 2011). Perennisoside VIII was determined to be 3-*O*-β-D-fucopyranosyl-23-*O*-acetylbayogenin {28-*O*-α-L-rhamnopyranosyl-(1 → 2)-[β-D-glucopyranosyl(1 → 3)]-6-*O*-acetyl-β-D-glucopyranosyl} ester; perennisoside IX was determined to be 3-*O*-β-D-fucopyranosyl-23-*O*-acetylbayogenin {28-*O*-α-L-rhamnopyranosyl(1 → 2)-[β-D-galactopyranosyl(1 → 3)]-6-*O*-acetyl-β-D-glucopyranosyl} ester; perennisoside X was determined to be 3-*O*-β-D-glucopyranosyl-(1 → 3)-β-D-glucopyranosyl-23-*O*-acetylbayogenin {28-*O*-α-L-rhamnopyranosyl(1 → 2)-[β-D-glucopyranosyl(1 → 3)]-6-*O*-acetyl-β-d-glucopyranosyl} ester; perennisoside XI was 3-*O*-β-D-glucopyranosyl-(1 → 3)-β-d-glucopyranosyl-23-*O*-acetylbayogenin {28-*O*-α-l-rhamnopyranosyl (1 → 2)-[β-D-galactopyranosyl(1 → 3)]-6-*O*-acetyl-β-D-glucopyranosyl} ester and perennisoside XII was elucidated as bayogenin {28-*O*-α-L-rhamnopyranosyl-(1 → 2)-[β-D-galactopyranosyl (1 → 3)]-[β-D-glucopyranosyl-(1 → 6)]-β-D-glucopyranosyl} ester. Deacylation of perennisosides VIII, IX, X and XI afforded desacyl-perennisoside VIII, desacyl-perennisoside IX, desacyl-perennisoside X and desacyl-perennisoside XI.

Six acylated oleanane-type triterpene oligoglycosides, perennisaponins A, B, C, D, E and F, were isolated from the flowers together with 14 saponins, nine flavonoids and two glycosides (Yoshikawa et al. 2008). Seven new acylated oleanane-type triterpene bisdesmosides designated perennisaponins G, H, I, J, K, L and M and were isolated from the flowers (Morikawa et al. 2010). Several triterpene saponins (Glensk et al. 2001) and five new triterpene saponins perennisosides VIII, IX, X, XI and XII were isolated from *Bellis perennis* flowers (Morikawa et al. 2011).

Bellis perennis flowers were found to contain the following flavonoid compounds: quercetin, apigenin, apigenin 7-*O*-β-D-glucuronide, apigenin 7-*O*-β-D-glucoside, apigenin 7-*O*-β-D-methylglucuronide, apigenin 7-*O*-β-D-(6″-*E*-caffeoyl)-glucoside, isorhamnetin, isorhamnetin 3-*O*-β-D-galactoside, isorhamnetin 3-*O*-β-D-(6″-acetyl)-galactopyranoside, kaempferol, kaempferol 3-*O*-B-D-glucoside and kaempferol 3-*O*-β-D-glucopyranoside (Gudej and Nazaruk 1997; Nazaruk and Gudej 2000; Gudej and Nazaruk 2001; Nazaruk and Gudej 2001). Similar flavonoids were found in cultivated and wild daisy flowers, while differences were noted in the flavonoid composition of the leaves (Nazaruk and Gudej 2001). The flavonoid contents were higher in the flowers than in the leaves. In cultivated and wild daisy flowers, apigenin, apigenin 7-*O*-β-D-glucoside, apigenin 7-*O*-β-D-glucuronide, apigenin 7-*O*-β-d-methylglucuronide, kaempferol, kaempferol 3-*O*-B-D-glucoside, isorhamnetin 3-*O*-β-D-galactoside, isorhamnetin 3-*O*-β-D(6″-acetyl)-galactoside and quercetin were detected. In the flowers of wild growing daisy, apigenin 7-*O*-β-D-(6″-*E*-caffeoyl)-glucoside was detected. In the leaves apigenin, apigenin 7-*O*-β-D-glucoside, apigenin 7-*O*-β-D-glucuronide, kaempferol, kaempferol 3-*O*-β-D-glucoside, isorhamnetin 3-*O*-β-D-galactoside and quercetin were found. Caffeic acid and seven of its derivatives were isolated from leaves *of Bellis perennis* (Scognamiglio et al. 2012). A novel glucuronosyltransferase, BpUGAT, involved in the biosynthesis of flower pigments in the red daisy (*Bellis perennis*) was purified (Sawada et al. 2005). BpUGAT was a soluble monomeric enzyme with a molecular mass of 54 kDa and catalyzed the regiospecific transfer of a glucuronosyl unit from UDP-glucuronate to the 2″-hydroxyl group of the 3-glucosyl moiety of cyanidin 3-*O*-6″-*O*-malonylglucoside. It was highly specific for cyanidin 3-*O*-glucosides cyanidin 3-*O*-6″-*O*-malonylglucoside and UDP-glucuronate.

The essential oil of *B. perennis* leaves and flowers were found to contain polyacetylenes (18–21 %) and terpenoids (Avato and Tava 1995). The major polyacetylenes identified were methyl deca-4,6-diynoate (2,8-tetrahydromatricaria ester) and deca-4,6-diynoic acid. The major polyacetylenes identified from the aerial organs of *Bellis perennis* were methyl deca-4,6-diynoate and deca-4,6-diynoic acid and their structural analogues, deca-4,6-diyne, dimethyl octa-3,5-diyne-1,8-dioate and deca-4,6-diyne-1,10-dioic acid (Avato et al. 1997).

A triterpenoid saponin isolated from *B. perennis* named bellissaponin BS3 was shown to be identical to virgaureasaponin 2 previously isolated from *Solidago virgaurea* (Schopke et al. 1990). Two acylated triterpenoid saponins, bellissaponins BA1 and BA2, isolated from *Bellis perennis* were elucidated as 3-*O*-α-L-rhamnopyranosyl and 3-*O*-β-D-glucopyranosyl-2β,3β,16α,23-tetrahydroxyolean-12-en-28-oic acid-28-*O*-α-L-rhamnopyranosyl (1 → 3)-β-D-xylopyranosyl(1 → 4)-α-L-rhamnopyranosyl(1 → 2)-[*E*-buta-2-enoic acid(1 → 4)]-β-D-fucopyranoside (Schöpke et al. 1991). Four triterpenoid saponins were isolated from the underground parts of *Bellis perennis*. Their structures were elucidated as 3-*O*-β-D-glucopyranosides of 2β,3β,16α-trihydroxyolean-12-ene-28-oic acid-28-α-L-rhamnopyranosyl(1 → 2)-[β-D-glucopyranosyl(1 → 6)]-β-D-glucopyranoside, 2β,3β,23-trihydroxyolean-12-ene-28-oic acid-28-*O*-β-D-xylopyranosyl (1 → 2)-[β-d-glucopyranosyl (1 → 6)]-β-D-glucopyranoside and 2β,3β,23-trihydroxyolean-12-ene-28-oic acid-28-*O*-α-L-rhamnopyranosyl(1 → 2)-[β-D-glucopyranosyl (1 → 6)]-β-D-glucopyranoside and as 3-*O*-α-L-rhamnopyranosyl-2β,3β,23-trihydroxyolean-12-ene-28-oicacid-28-*O*-β-D-glucopyranosyl(1 → 2)-[β-D-glucopyranosyl(1 → 6)]-β-D-glucopyranoside (Schöpke et al. 1992). Four triterpenoid saponins were isolated from the underground parts of *Bellis perennis* and their structures were elucidated as 3-*O*-β-D-glycopyranosides of 2β,3β,16α-trihydroxyolean-12-ene-28-oic acid-28-α-L-rhamnopyranosyl(1 → 2)-[β-D-glucopyranosyl(1 → 6)]-β-D-glucopyranoside, 2β,3β,23-trihydroxyolean-12-ene-28-oic acid-28-*O*-β-D-xylopyranosyl (1 → 2)-[β-D-glucopyranosyl(1 → 6)]-β-D-glucopyranoside and 2β,3β,23-trihydroxyolean-12-ene-28-oic acid-28-*O*-α-L-rhamnopyranosyl (1 → 2)-[β-d-glucopyranosyl(1 → 6)]-β-D-glucopyranoside and as 3-*O*-α-L-rhamnopyranosyl-2β,3β,23-trihydroxyolean-12-ene-28-oic acid-28-*O*-β-d-glucopyranosyl(1 → 2)-[β-d-glucopyranosyl(1 → 6)]-β-D-glucopyranoside (Wray et al. 1992). Six acylated triterpenoid saponins, bellisosides A–F, together with a known saponin, bellissaponin BS2 were isolated from the roots of *Bellis perennis* (Li et al. 2005).

Antioxidant Activity

The antioxidant activity of the flowers using a 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay expressed as IC_{50} values varied from 66.03 to 89.27 μg/ml; it is about 50, 30, 20 and 10 times lower as compared with quercetin, ascorbic acid, Trolox and butylhydroxytoluene, respectively, and about 5 times higher in comparison with apigenin-7-glucoside. The contents of flavonoids in the flowers varied from 0.31 to 0.44 mg quercetin equivalent/100 mg dry weight and from 1.37 to 2.20 mg apigenin-7-glucoside equivalent/100 mg dry weight (Siatka and Kašparová 2010). Total phenolics ranged from 2.81 to 3.57 mg gallic acid equivalent/100 mg dry weight. There is a significant correlation between antioxidant activity and total phenolics. No correlation between total flavonoid contents and antioxidant activity was observed. The aqueous extracts of aerial plant parts showed higher DPPH scavenging activity (85.8 % at 102.5 μg/ml) than the methanol extract (Kavalcioğlu et al. 2010). Reducing power was also observed for both tested extracts, where the formation of linoleic acid peroxides was more for the aqueous extract than the methanol extract.

Anxiolytic and Antidepressant Activities

B. perennis aqueous flower extract was found to elicit biphasic effects on both anxiety-like behavior and learning performance of the rats (Karakaş et al. 2011). In the open field, rats administered the high dose of *B. perennis* aqueous flower extract spent more time at the centre, showed less mobility and velocity. In the elevated plus maze, rats administered the high dose of *B. perennis* caused to spend more time in the open arms, spent less time in the closed arms, were less mobile, were slower and rotated less frequently. In the Morris water maze, rats administered the high dose of *B. perennis* spent more of the time to find the platform.

Oral administration of the crude ethanol flower extract of *B. perennis* elicited anxiolytic and antidepressant-like effects in mice (Marques et al. 2012). In the open field test, there was a significant decrease in the number of crossings at dosages of 50, 100 and 150 mg/kg but no sedative effects at any dosages when compared to controls. In the forced swimming test (FST), the extract dosage of 150 mg/kg was effective in reducing immobility, along with a significant increase in swimming time. The ethanol extract showed strong antioxidant potential in vitro, through the removal capacity against hydroxyl radicals and nitric oxide as well as prevented the formation of reactive substances to thiobarbituric acid (TBARS).

Neuroprotective Activity

Results of animal studies suggested that the ethanol flower extract of *B. perennis* may modulate epileptogenesis and promote anticonvulsant and neuroprotective mechanisms in model of seizures induced by pilocarpine (Marques et al. 2011). Adult Swiss mice treated with pilocarpine exhibited seizures that progressed to status epilepticus; 87.5 % of animals had brain damage in the hippocampus and the damage rate in striatum was 75 %. Pretreatment with the ethanol flower extract produced a significant reduction in these indices.

Antihyperlipidemic Activity

Among seven acylated triterpene saponins isolated from *B. perennis*, perennisosides I and II showed inhibitory effects on serum triglyceride elevation at doses of 25–50 mg/kg, p.o. in olive-treated mice (Morikawa et al. 2008). The methanol extract from *B. perennis* flowers was found to show pancreatic lipase inhibitory activity (IC_{50} 455 μg/ml). From the extract, seven new triterpene saponins named perennisaponins G (IC_{50} 163 μM), H (137 μM), I (147 μM), J (148 μM), K (223 μM), L (81.4 μM) and M (195 μM) were isolated as pancreatic lipase inhibitors (Morikawa et al. 2010).

Anticancer Activity

Six acylated triterpenoid saponins, bellisosides A–F, together with a known saponin, bellissaponin BS2 isolated from *Bellis perennis* roots exhibited cytotoxic activities against HL-60 human promyelocytic leukaemia cells (Li et al. 2005).

Antimicrobial Activity

Triterpenoid glycosides obtained *Bellis perennis* inhibit the growth of human-pathogenic yeasts (*Candida* and *Cryptococcus* species) (Bader et al. 1990). Ester saponin, bellissaponin from *B. perennis*, exerted antifungal effect against *Candida albicans*, *Trichophyton rubrum*, *Trichophyton mentagrophytes* and *Aspergillus niger* (Willigmann et al. 1992). The intensity of growth inhibition was influenced particularly by the carbohydrate chains of the glycosides. Monodesmosidic as well as bisdesmosidic glycosides of polygalacic acid exerted fungicidal effects. Of the major polyacetylenes identified from the aerial organs of *Bellis perennis* methyl deca-4,6-diynoate and deca-4,6-diynoic acid and their structural analogues, deca-4,6-diyne, dimethyl octa-3,5-diyne-1,8-dioate and deca-4,6-diyne-1,10-dioic acid, only deca-4,6-diynoic acid and deca-4,6-diyne-1,10-dioic acid showed antimicrobial activity, being mainly effective against Gram-positive and Gram-negative bacteria (Avato et al. 1997).

Wound Healing Activity

Topically administered ointment prepared from the *n*-butanol fraction of *B. perennis* flowers was found to have a wound healing potential without scar formation in circular excision wound model in rats, verifying the traditional usage of *B. perennis* for wound healing (Karakaş et al. 2012).

Gastric Emptying Inhibition Activity

The methanol-eluted fraction of the methanol extract from *B. perennis* flowers was found to

inhibit gastric emptying in olive oil-loaded mice at a dose of 200 mg/kg, per os (p.o.) (Morikawa et al. 2011).

Antihaemorrhagic Activity

In a double-blind, placebo-controlled, randomized, clinical trial of 40 parturients, treatments with homeopathic *Arnica montana* and *Bellis perennis* were found to reduce postpartum blood loss, as compared with placebo (Oberbaum et al. 2005).

Haemolytic activity

The haemolytic activity of *B. perennis* flower head varied with seasonal changes, being lowest in March, increasing to a maximum in summer months (June, July, August), and then decreasing again (Siatka and Kasparová 2003).

Antiulcerogenic Activity

Oral administration of the aqueous and methanol extracts of *B. perennis* aerial parts (1,100 and 600 mg/kg) reduced gastric ulcers in rats with ethanol-induced gastric ulcers. Both extracts exhibited significant antiulcerogenic activity (Açik et al. 2008).

Skin-Whitening Activity

The phytomedicine Belides (R) obtained from *B. perennis* flowers exhibited a strong inhibitory effect on melanogenesis (John et al. 2005). It was found to contain bioactive constituents such as saponins (triterpene glycosides), polyphenols and polysaccharides. Results of a comparative study conducted with Belides and arbutin, used at equivalent polyphenol concentrations, revealed that Belides was about twice as active as arbutin. Tests carried out on melanoma cells (B16V) showed that Belides controlled transcription of tyrosinase expression, thus inhibiting its synthesis. In addition, Belides significantly decreased the release of the peptide hormone endothelin (ET-1), the binding capacity of alpha-MSH (melanocyte-stimulating hormone) on the melanocortin receptor-1 (MC1-R) and also melanosome uptake mechanisms. Further, results of a pilot study performed on human volunteers demonstrated the in-vivo skin-lightening efficacy of Belides. The authors, thus, recommended the use of Belides in skin-lightening cosmetics and for pigmentation disorders, hyperpigmentation or age spots.

Traditional Medicinal Uses

Since antiquity, *B. perennis* has been used as a diuretic, antispasmodic, antiinflammatory, astringent, antitussive, demulcent, digestive, emollient, expectorant, laxative, purgative, tonic, antipyretic, vulnerary, ophthalmic and homeostatic in traditional medicine (Grieve 1971; Launert 1981; Chiej 1984; Phillips and Foy 1992; Bown 1995; Duke et al. 2002). It has been traditionally used for wounds and was found useful in treating delicate and listless children. It has been used in folk medicine in the treatment of rheumatism and as an expectorant (Schöpke 1991). It has also been employed as a vulnerary and against ecchymoses in veterinary medicine (Avato and Tava 1995). Yazıcıoğlu and Tuzlacı (1995) reported that *B. perennis* was used to relieve stomach ache in Trabzon, Turkey and for treating breast cancer (Chiej 1984). The fresh or dried flowering heads are normally used in infusions, decoctions, ointments and poultices in the treatment of catarrh, rheumatism, arthritis, liver and kidney disorders as a blood purifier, etc. An ointment of the leaves has been applied externally to wounds, bruises and cuts and an aqueous extract used internally to treat inflammatory disorders of the liver. Chewing of leaves was said to cure oral ulcers. A strong decoction of the roots has been recommended for the treatment of scorbutic complaints and eczema, while a mild decoction has been used to ease complaints of the respiratory tract, rheumatic pains and painful or heavy menstruation. The herb has also been widely used in homeopathic therapy.

Other Uses

Bellis perennis is a popular ornamental, widely cultivated in gardens and parks. This daisy is widely steeped in magic and mythology; the daisy is used magically in spells for love and lust and thus associated with the goddess of love Venus (Roman), Aphrodite (Greek) and Freya (Norse). Daisies have traditionally been used for making daisy chains in children's games.

It was shown that the plant possessed antifungal activity in vitro and in-vivo against *Ceratocystis ulmi*, pathogen of Dutch elm disease (Desevedavy et al. 1989).

Comments

The plant may be propagated by seeds or division.

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Calendula officinalis

Scientific Name

***Calendula officinalis* L.**

Synonyms

Calendula aurantiaca Kotschy ex Boiss., *Calendula eriocarpa* DC., *Calendula hydruntina* (Fiori) Lanza, *Calendula officinalis* var. *prolifera* Hort., *Calendula prolifera* Hort. ex Steud., *Calendula* × *santamariae* Font Quer, *Calendula sinuata* var. *aurantiaca* (Klotzsch ex Boiss.) Boiss., *Caltha officinalis* (L.) Moench (nom. illeg.)

Family

Asteraceae

Common/English Names

Bull's Eye, Calendula, Common Marigold, Cowbloom, Death Flower, Drunkard Gold, English Marigold, Garden Marigold, Gold Bloom, Golden Flower of Mary, Herb of the Sun, Holligold, Hollygold, Marigold, Husband's Dial, Kingscup, Marybud, Marygold, May Orange, Poet's Marigold, Poor Man's Saffron, Pot Marigold, Ruddles, Scotch Marigold, Scottish Marigold, Shining Herb, Summer's Bride, Sun's Bride, Water Dragon

Vernacular Names

Albanian: Kalendula Mjekësore
Arabic: Ajamir, Djoumaira
Brazil: Calêndula
Chinese: Chin Chan Hua, Jīn Zhǎn Jú
Croatian: Bileć, Ljekoviti Neven, Mesiček, Ognjac, Vridovno Zelje, Zimorod
Czech: Měsíček Lékařský
Danish: Havemorgenfrue, Morgenfrue
Dutch: Goudsbloem, Tuinggoudsbloem
Eastonian: Harilik Saialill
Esperanto: Kalendulo, Kalendulo Kuraca, Orfloro Kuraca
Finnish: Kehäkukka, Tarhakehäkukka
French: Calendule, Fleur De Souci, Fleurs De Tous Les Mois, Gauche-Fer, Soubi, Souci, Souci Des Jardins, Souci Officinal, Yous Les Mois
German: Goldblume, Ringelblume, Ringelrose, Sonnenwende
Hungarian: Kerti Körömvirág, Körömvirág
Iceland: Morgunfrú
India: Genda, Surajmukhee, Zergul (Hindi), Gulsarfi (Punjabi), Sendigai, Sendigai Poo (Tamil), Banti (Telugu), Gul-E-Ashrafi (Urdu)
Italian: Calendola, Calendula, Calta, Fior D'ogni, Fiorrancio, Fiorrancio Coltivato, Fiorrancio Dei Gardine
German: Butterblume, Dotterblume, Echte Ringelblume, Garten-Ringelblume, Gartendotterblume, Goldblume, Ingelblum, Rinderblume, Ringelblume, Ringelrose, Ringula, Sonnenbraut, Sonnenwende,

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Studentenblume, Totenblume, Warzenkraut, Weckbröseln, Wucherblume
Japanese: Kinsenka, To Kinsenka
Korean: Kumjanhwa
Norwegian: Ringblom
Polish: Nagietek Lekarski
Portuguese: Calêndula, Belas-Noites, Boas-Noites, Maravilhas, Margarida
Russian: Kalendula, Nogot'ki, Nogot'ki Lekarstvennye
Slovaščina: Ognjič Vrtni, Vrtni Ognjič, Zdravilni Ognjič
Slovenian: Nechtík Lekársky, Vrtni Ognjič
Spanish: Botón De Oro,Caldo, Calendula, Cempasúchitl, Corona De Rey, Flamenquilla, Flaminquillo, Flor De Difunto, Flor De Merte, Maravilla, Mejorana, Mercadela, Rosa De Muertos, Virreina
Swedish: Ringblomma, Solsicka, Solsocka
Turkish: Tibbi Nergis
Vietnamese: Cúc Kim Tiền, Hoa Xu Xi, Tâm Tư Cúc, Xu Xi
Welsh: Melyn Mari

Origin/Distribution

The species is a native of the Mediterranean area, but now *Calendula* has naturalized in many temperate countries and is cultivated as ornamentals in warm temperate and sub-temperate areas.

Agroecology

The plant grows well in full sun and tolerate most soils—acidic, sandy, loamy and clayey soils with pH 4.5–8.3—but does best on well-drained, moist, loamy soil. In temperate areas, seeds are sown in spring for blooms that last throughout the summer and well into the fall.

Edible Plant Parts and Uses

Flowers and leaves are edible (Hedrick 1972; Facciola 1990; Roberts 2000). Fresh petals are chopped and added to salads or used as garnish in dishes. The petals can be used in omelette, curry and custard (Roberts 2000). Dried petals have a more intense flavour and are used as a seasoning in soups, cakes, drinks and baked products. An edible yellow dye is obtained from the flowers and used as colorant for butter, cheese, drinks, rice, soups, confectionery and baked products and also used as a substitute for saffron. Calendula was once known as 'poor man's saffron' as its extract was fed to hens to make their egg yolks golden. An herbal tea can be prepared from the flowers and petals. The leaves can be eaten raw in salads.

Botany

The plant is usually grown as an annual, erect or procumbent and branched, stipitate-glandular, with a strong tap root. Leaves are sessile or shortly petiolate, elliptic, obovate, oblong, oblanceolate to spatulate, 3–12 (−16 cm) by 2–5 cm, with entire margins, apex acute, base sometimes clasping, sparsely arachnose on both surfaces (Plates 1 and 2). Flower heads (capitula) borne singly; involucre campanulate to hemispheric; phyllaries linear-lanceolate, pubescent and in two series; ray florets 15–50 (>100) in 1–3 or more series, functionally female, with yellow to orange, linear to oblanceolate corolla; central disc florets 20–60 (>100), hermaphrodite but functionally male, tubular with campanulate throat, corolla yellow, orange (Plates 2 and 3), reddish or purplish. Achene curved and tuberculate or transversely ridged.

Nutritive/Medicinal Properties

Flower Phytochemicals

Carbohydrates

The water soluble polysaccharide fraction obtained from *C. officinalis* inflorescences were found to contain 84.58 % pectic substances, 29.25 % ash, 9.25 % moisture, 25.77 % acidic sugars, 31.25 % reducing sugars and 4.92 % proteins and to have the following monosaccharide composition comprising glucose, galactose, arabinose, xylose, rhamnose and galacturonic

Plate 1 Leaves and a flower bud

Plate 2 Yellow flowers in bloom

acid (Chushenko et al. 1988). Three homogeneous polysaccharides were isolated from *Calendula officinalis* flowers (Varljen et al. 1989). All three polysaccharides contained a (1 → 3)-linked β-D-*galactan* backbone with branching points at C-6. The side chains are composedofshortα-Araf(1 → 3)-Araf,α-l-Rhap-(1 → 3)-Araf or simple α-L-Araf units. The carbohydrate composition of *Calendula officinalis* consisted of free glucose and pectin substances with a low degree of esterification (Khodzhaeva and Turakhozhaev 1993). The monosaccharide composition of the stem comprised rhamnose, galactose and galacturonic acid and the inflorescences have rhamnose, galactose, glucose and galacturonic acid. Pectic substances were also found in the stems and inflorescences.

Plate 3 Close view of flower heads

Terpenoids

From *Calendula officinalis* flowers, five glycosides of oleanolic acid were isolated and their structuresestablishedas3-glucuronide;3-(galactosyl-glucuronide); 3-(galactosyl-glucuronide); 17-glucoside; 3-(galactosyl-(glucosyl)-glucuronide); and 3-(galactosyl-(glucosyl)-glucuronide); 17-glucoside (Kasprzyk and Wojciechowski 1967). A number of alcohols representing different types of pentacyclic triterpenes were identified in *Calendula officinalis* flowers (Kasprzyk and Pyrek 1968). In the group of monohydroxy alcohols, the following were identified: α-amyrin, β-amyrin, taraxasterol and lupeol in addition to previously isolated ψ-taraxasterol. In the group of dihydroxyalcohols, the following were identified: brein and calenduladiol (a new diol of lupeol type) in addition to the previously isolated

arnidiol and faradiol. The presence of four other diols of the α-amyrin, β-amyrin and ψ-taraxasterol types was observed. Alcohols of ψ-taraxasterol type, possessing three and four hydroxyl groups, were also isolated as well as a small amount of oleanolic aldehyde. A new triterpene diol, ursodiol, was isolated from dry *Calendula officinalis* flowers (Sliwowski et al. 1973). Its structure was confirmed as 3,21-di-OH-ursa-12-en. Kasprzyk and Wiłkomirski (1973) isolated a triterpene triol of α-amyrin type from the flowers. A triterpene glycoside, calenduloside F, was isolated from the flowers (Vidal Ollivier et al. 1988).

In *Calendula officinalis* flowers, triterpene monols were found mainly in the chromoplast fraction (68 % of total) with smaller amounts in the cell debris, microsomal and supernatant fractions; the mitochondrial fraction was almost devoid of these compounds (Adler and Kasprzyk 1976). Triterpene diols were present exclusively in the chromoplast fraction, 98 % in the form of the 3-monoesters and 2 % in the form of diesters. The data suggested that the hydroxylation of the triterpene monols to the corresponding diols proceeded in the chromoplasts and the esterified form of the monols was probably the substrate for this reaction.

From *Calendula officinalis* flowers, five pentacyclic triterpene trihydroxyalcohols were isolated and identified as olean-12-ene-3β,16β,28-triol, lup-20(29)ene-3β,16β,28-triol, tarax-20-ene-3β,16β,22α-triol, tarax-20-ene-3β,16β,30-triol and ursa-12-ene 3β,16β,21-triol (Wiłkomirski 1985). Gracza (1987) identified the following terpenoids from the flowering heads: menthone, isomenthone, caryophyllene and an epoxide and ketone derivative, pedunculatine, α- and β-ionone, a β-ionone epoxide derivative and dihydroactinidiolide. Triterpenoids found in the flowers included faradiol monoester, monools ψ-taraxasterol, lupeol, taraxasterol and β-amyrin (Della Loggia et al. 1994). Eleven triterpene alcohols helianol, taraxasterol, ψ-taraxasterol, α-amyrin, β-amyrin, lupeol, taraxerol, cycloartenol, 24-methylenecycloartanol, tirucalla-7,24-dienol and dammaradienol were isolated from the tubular flowers of *Calendula officinalis*, *Carthamus tinctorius*, *Cosmos bipinnatus*, *Chrysanthemum morifolium*, *Helianthus annuus* and *Matricaria matricarioides* (Akihisa et al. 1996). All the flowers shared a common characteristic feature by containing helianol as the most predominant component (29–86 %) in the triterpene alcohol fractions.

From the 1-butanol-soluble fraction of the methanol flower extract of *Calendula officinalis*, four new triterpene oligoglycosides, calendasaponins A, B, C and D, were isolated, together with eight known saponins, seven known flavonol glycosides and a known sesquiterpene glucoside (Yoshikawa et al. 2001). They also isolated two new ionone glucosides (officinosides A and B) and two sesquiterpene oligoglycosides (officinosides C and D) from the flowers of Egyptian *Calendula officinalis* (Marukami et al. 2001). One new triterpenoid of oleanane-series, cornulacic acid acetate (1), along with oleanolic acid acetate was isolated from *Calendula officinalis* flowers (Naved et al. 2005). The structure of (1) was established as 3β-acetoxy-olean-12-en-27-oic acid and oleanolic acid acetate was characterized as 3β-acetoxy-olean-12-en-28-oic acid.

Ten oleanane-type triterpene glycosides, 1–10, calendulaglycoside A (1), calendulaglycoside A6′-*O*-*n*-methyl ester (2), calendulaglycoside A 6′-*O*-*n*-butyl ester (3), calendulaglycoside B (4), calendulaglycoside B 6′-*O*-*n*-butyl ester (5), calendulaglycoside C (6), calendulaglycoside C 6′-*O*-*n*-methyl ester (7), calendulaglycoside C 6′-*O*-*n*-butyl ester (8), calenduloside F 6′-*O*-*n*-butyl ester (9) and calenduloside G 6′-*O*-*n*-methyl ester (10), along with five known flavonol glycosides, 11–15 isorhamnetin-3-*O*-neohesperidoside, isorhamnetin-3-*O*-2-rhamnosyl rutinoside, isorhamnetin-3-*O*-rutinoside,quercetin-3-*O*-glucoside and quercetin-3-*O*-rutinoside, were isolated from the flowers of *Calendula officinalis* (Ukiya et al. 2006).

Lipids

Sterol esters as well triterpene monol and diol esters isolated *Calendula officinalis* flowers were found to contain as alcohol components all the types of sterols and triterpenic alcohols present in the plant (Wojciechowski et al. 1972). Sterols and triterpene monols were esterified with acetic, lauric, myristic and palmitic acids. Triterpene

diols were esterified with lauric, myristic and palmitic acids. The main diol esters were 3-monoesters; diesters were present only in very small amount.

In *C. officinalis* ligulate flowers, it was shown that all free and ester-bound sterols and triterpene monols in both forms occurred in the chromoplast fraction and in the chromoplast-free fraction, whereas all diols were localized only in the chromoplast fraction (Wilkomirski and Kasprzyk 1979). The compositions of the fatty acids esterifying monols and sterols were similar to those esterifying diols in the chromoplasts. However, the fatty acids esterifying extra-chromoplast monols and sterols were different. This result indicated triterpene monol esters to be substrates for the biosynthesis of 3-monoesters of diols. Faradiol esters, namely, faradiol-3-myristic acid ester, faradiol-3-palmitic acid ester and ψ-taraxasterol, were isolated from *C. officinalis* flower heads (Zitterl-Eglseer et al. 1997).

The main compounds of lipophilic extracts of flower heads of *Calendula officinalis* comprised triterpendiol esters, mainly faradiol laurate, faradiol myristate and faradiol palmitate (Zitterl-Eglseer et al. 2001). These faradiol-3-*O*-monoesters were quantified in different parts of *C. officinalis* plants, namely, ray florets, disc florets, involucral bracts, receptacles, leaves and seeds. The contents of the esters were highest in ray florets, approximately ten times lower in disc florets than in the ray florets, and approximately ten times lower in involucral bracts than in the disc florets. In the leaves only traces of the esters could be detected, and in the receptacles no esters could be detected at all. Quantification in the seed was not possible using this method because of interfering fatty compounds.

Dichloromethane extract of dried flowers of *Calendula officinalis* was found to contain eight known bioactive pentacyclic terpenoids and triterpendiol monoesters, namely, faradiol-3-*O*-palmitate, faradiol-3-*O*-myristate, faradiol-3-*O*-laurate, arnidiol-3-*O*-palmitate, arnidiol-3-*O*-myristate,arnidiol-3-*O*-laurate,calenduladiol-3-*O*-palmitate and calenduladiol-3-*O*-myristate (Neukirch et al. 2004). Of the ten varieties of *C. officinalis* investigated, calypso orange florensis produced the highest amounts of the bioactive monoesters, followed by Fiesta Gitana Gelb and may orange florensis. The lipophilic extract from the flowers of calypso orange florensis variety also contained low levels of the newly characterized calenduladiol-3-*O*-laurate.

Marigold also has oleoresins. The solubility of Marigold (*Calendula officinalis*) oleoresin in supercritical CO_2 (SC-CO_2) varied from 4.74×10^{-4} to 17.04×10^{-4} g oleoresin/g CO_2 (Danielski et al. 2007). The use of palm oil as cosolvent for SC-CO_2 extraction of Marigold flower was found to enhance the yield of lutein fatty acid esters by approximately 16 %, with the most suitable concentration being 10 % w/v palm oil (Palumpitag et al. 2011). Under this condition, approximately 87.2 % recovery of lutein fatty acid esters was obtained after 4 hours extraction at 60 °C and 40 MPa. Furthermore, saponification of the Marigold oleoresin for 3 hours with 2 ml of 40 % (w/v) KOH solution per 1 g of oleoresin resulted in the maximum conversion of lutein esters, giving approximately 157.24.4 mg of free lutein/g oleoresin.

Carotenoids

The carotenoid content was higher in orange varieties *of C. officinalis*: 276 mg/100 g fresh flowers for Double Esterel Orange variety and 111 mg/100 g fresh flowers for Radio Extra variety (Pintea et al. 2003). All varieties contain the same pigments (xanthophylls) but there were significant differences for the ratio between individual pigments. The main pigments identified were flavoxanthin, lutein, rubixanthin, β-carotene, γ-carotene and lycopene. The great majority of xanthophylls present had a β-ε structure: flavoxanthin, lutein and luteoxanthin. Zeaxanthin (3,3′-dihydroxy-β, β-carotene) was present in small amount, as well as their epoxides: antheraxanthin, mutatoxanthin and auroxanthin. Other carotenoids present included neoxanthin, lactucaxanthin and α-carotene. Orange varieties contained higher amounts of hydrocarbons, 44.5 % of total carotenoid in Double Esterel Orange, while yellow varieties contain mostly oxygenated derivatives, 97 % of total carotenoids in Double Esterel Jaune. In the orange varieties, a

preferential biosynthesis of hydrocarbons with ψ-ψ and β-ψ structure and of monoxanthophylls with β-ψ (or α-ψ) structure was noted.

In the petals and pollens of *Calendula officinalis*, the main carotenoids were flavoxanthin and auroxanthin while the stem and leaves mostly contained lutein and β-carotene (Bakó et al. 2002).

Carotenoids present in *C. officinalis* cv Alice Orange flowers in percent of total carotenoids (Kishimoto et al. 2005) and in μg/g fresh weight (Kishimoto et al. 2007) were respectively (8′*R*)-luteoxanthine 11 % 186.6 μg; lutein-5,6-epoxide 1.6 % 27.1 μg; (8*R*)-lutein-5,8-epoxide (flavoxanthin) 28.5 %, 483.4 μg; (8*R*,8′*R*)-auroxanthin 7.1 %, 120.4 μg; (9′*Z*)-lutein-5,6-epoxide 5 %, 84.8 μg; lutein 2 % 33.9 μg; antheraxanthin 1 % 17.0 μg; (9*Z*)-lutein 0.6 %, 10.2 μg; (5′*Z*,9′*Z*)-rubixanthin 4 %, 67.8 μg; α-carotene 0.8 %, 13.6 μg; β-carotene 3.4 %, 57.7 μg; (5′*Z*)-rubixanthin 3 %, 50.9 μg; δ-carotene 1.4 %, 23.7 μg; (5*Z*,9*Z*,5′*Z*,9′*Z*)–lycopene 4.1 %, 69.5 μg; γ-carotene 2 %, 33.9 μg; (5′*Z*)-γ-carotene 4.4 %, 74.6 μg; (5*Z*,9*Z*,5′*Z*)-lycopene 3.5 %, 59.4 μg; (5*Z*,9*Z*)-lycopene 4.1 %, 69.5 μg and (all – *E*)-lycopene 8.7 %, 147.6 μg. The carotenoid composition in Alice Yellow flowers were (8′*R*)-luteoxanthin 15.6 %, 195 μg; lutein-5-6-epoxide 3.2 %, 40 μg; (8*R*)-lutein-5,8-epoxide (flavoxanthin) 42.6 %, 532.5 μg; (8*R*,8′*R*)-auroxanthin 10.7 %, 133.7 μg; (9′*Z*)-lutein-5,6-epoxide 8.5 %, 106.2 μg; lutein 5 %, 62.5 μg; antheraxanthin 2.5 %, 31.2 μg; (9*Z*)-lutein 1.5 %, 18.7 μg; and β-carotene 1.0 %, 12.5 μg. Total carotenoids in *C. officinalis* Alice orange was 1696.2 μg/g FW comprising 963.4 μg of yellowish carotenoids and 668.3 μg of reddish carotenoids and total carotenoids in Alice yellow was 1249.9 μg/g FW comprising 119.9 μg of yellowish carotenoids and 1.2 μg of reddish carotenoids (Kishimoto et al. 2007).

Studies showed that solvent had an influence on the stability of carotenoids in oil extracts of *Calendula officinalis* (Bezbradica et al. 2005). The highest degradation rates were observed in extracts prepared with linoleic acid-rich solvents (sunflower oil, soybean oil and grape seed oil), while the lowest were found in oil with saturated fatty acids (Myritol 312®) and paraffin oil. Studies showed that saline irrigation water decreased the fresh and dry weights of *Calendula officinalis* flower heads and pigment contents (total flavonoids and total carotenoids) but increased essential oil yield and its main components (α-cadinol, γ- and δ-cadinene) (Khalid and da Silva 2010). Fresh and dry weights of flower heads and essential oil increased towards the full bloom stage of flowering while pigment content, such as total flavonoids and total carotenoids, increased.

Flavonoids

Eight flavonoids were isolated from *C. officinalis* inflorescence: two aglycones (quercetin, isorhamnetin) and six glycosides (isoquercetin, isorhamnetin 3-*O*-β-D-glucoside, narcissin, calendoflaside, calendoflavoside and calendoflavobioside) (Komissarenko et al. 1988). Seven flavonol 3-*O*-glycosides were isolated from the flowers of *Calendula officinalis* and elucidated as isorhamnetin 3-*O*-glucoside, rutinoside, neohesperidoside, quercetin glucoside and 2 (G)-rhamnosylrutinoside (Vidal-Ollivier et al. 1989). Bilia et al. (2001) identified narcissin, rutin, isoquercitrin, quercetin-3-*O*-rutinosylrhamnoside, isorhamnetin-3-*O*-rutinosylrhamnoside, isorhamnetin-3-*O*-glucosylglucoside and isorhamnetin-3-*O*-glucoside in *C. officinalis* flowers. The triglycoside isorhamnetin-3-*O*-α-l-rhamnopyranosyl-(1 → 2)-*O*-[α-l-rhamnopyranosyl-(1 → 6)]-β-D-glucopyranoside together with the already known glycosides isorhamnetin-3-*O*-β-D-glucopyranoside and isorhamnetin-3-*O*-α-l-rhamnopyranosyl-(1 → 6)-*O*-β-D-glucopyranoside (narcissin) was isolated from *Calendula officinalis* flowers (Masterova et al. 1991). The total content of flavonoids in ligulate ray florets and tubular discflorets inclusively involucre was found to be 0.88 and 0.25 %, respectively.

The following flavonoids isorhamnetin (3′-metoxy-4′,3,5,7-tetrahydroxyflavone), isorhamnetin-3-*O*-glucoside, rutin, quercetin glucoside, quercetin-neohesperoside and quercetin-2G-rhamnosil-rutinoside were isolated from flowers and found to have good antioxidant activity (Albulescu et al. 2004). Two flavonoids

were isolated from the flowers and identified as isorhamnetin 3-*O*-rutinoside (narcissin) quercetin 3-*O*-β-D-glucopyranoside (isoquercitrin) (Kurkin and Sharova 2007). Patulitrin (1) and patuletin (2) were found only in Marigold flowers during and after flowering (Guinot et al. 2008). A water-ethanol mixture gave a high extraction efficiency of both flavonoids.

Essential Oil

Crabas et al. (2003) reported that the essential oil of *Calendula officinalis* obtained from dried flowers in Italy contained methyl hexadecanoate (23.8 %), methyl linoleate (18.6 %), methyl 9,12,15-octadecatrienoate (17.2 %), methyl octadecanoate (4.8 %), methyl tetradecanoate (4.6 %), g-cadinene and cubenol (4.0 %), d-cadinene (3.2 %), a-cadinol (1.8 %) and oplopanone (1.3 %). Essential oil constituents of *C. officinalis* flower head (French source) and Slovakian source without fertilizer application, respectively, were β-pinene 0.45 %, 0.38 %, α-pinene 2.47 %, 2.18 %, myrcene 0.19 %, 0.29 %, phellandrene 2.76 %, 0.74 %, *p*-cymene 2.76 %, 2.22 %, limonene 19.16 %, 18.28 %, 19.61 %, terpinene 0.98 %, 1.578 %, caryophyllene 0.96 %, 1.06 %, 1,18cineole 0.47 %, 0.66 %, linalool 20.88 %, linalyl acetate 36.5 %, 38.64 %, camphor 1.98 %, 5.63 %, borneol 0.96 %, 1.84 %, carvone 0.43 %, 2.54 %, geraniol 2.66 %, 1.9 %, geranyl acetate 0.17 %, 0.17 % and caryophyllene oxide 0.44 %, 1.05 % (Naguib et al. 2005). In another study, essential oil constituents from *Calendula officinalis* flowers from steam distillation were identified as α-copaene 0.9 %, α-ionone 1.5 %, α-humulene 1.2 %, geranylacetone 1.6 %, γ-muurolene 2.3 %, β-ionone 3.2 %, ledene 2.3 %, α-muurolene 5.6 %, γ-cadinene 8.9 %, δ-cadinene 22.5 %, α-cadinene 0.9 %, α-calacorene 2.3 %, caryophyllene oxide 0.5 %, copaene-4-α-ol 0.6 %, β-oplopenone 1.7 %, viridiflorol 2.2 %, ledol 1.3 %, 1,10-di-epi-cubenol 1.6 %, epi-α-muurolol 12.9 %, α-cadinol 20.4 % and cadalene 0.8 % (Gazim et al. 2008). Volatile constituents from *Calendula officinalis* flowers from headspace solid-phase microextraction were β-cyclocitral 2.1 %, α-cubebene 1.8 %, α-copaene 15.1 %, β-cubebene 1.8 %, α-gurjunene 2.7 %, β-caryophyllene 2.7 %, α-ionone 2.3 %, α-humulene 3.9 %, γ-muurolene 5.3 %, β-ionone 3.9 %, α-muurolene 6.2 %, γ-cadinene 25.5 %, δ-cadinene 22.1 % and α-cadinene 2.3 % (Gazim et al. 2008). Volatile constituents from *Calendula officinalis* flowers from headspace cold finger extraction were α-copaene 18.4 %, β-cubebene 3.7 %, α-gurjunene 4.2 %, β-caryophyllene 8.6 %, α-humulene 3.9 %, γ-muurolene 4.7 %, α-muurolene 5.8 %, γ-cadinene 24.9 %, δ-cadinene 18.6 % and α-cadinene 2.3 % (Gazim et al. 2008).

Twenty-four compounds were identified in the fresh flower oil of *C. officinalis*, and the yield was 0.09 % (Okoh et al. 2008). Sesquiterpenoids dominated the fresh flower oil. Major components of the fresh flower oil were α-thujene (26.9 %), T-muurolol (24.9 %) and δ-cadinene (13.1 %).

Coumarins

The ethanol extract of the flowers was found to contain coumarins—scopoletin, umbelliferone and esculetin (Derkach et al. 1987).

Terpenoids, Flavonoids and Phenolic Acids

Triterpenoid esters purified from *C. officinalis* flower heads included faradiol-3-*O*-laurate, faradiol-3-*O*-myristate and faradiol-3-*O*-*palmitate* (Hamburguer et al. 2003). Accompanying minor compounds of the triterpene ester fraction purified included maniladiol 3-*O*-laurate, maniladiol-3-*O*-myristate, ψ-taraxasterol and β-amyrin. Oleanolic acid, β-amyrin, β-amyrin acetate, rutin, narcissin, 3-glucoside of isorhamnetin, quercetin, isoquercitrin, vanillic acid, caffeic acid, chlorogenic acid, protocatechuic acid, *p*-coumaric acid and syringic acid were identified in the flower extract (Matysik et al. 2005). Ten oleanane-type triterpene glycosides were isolated from the flowers: calendulaglycoside A (1), calendulaglycoside A6′-*O*-*n*-methyl ester (2), calendulaglycoside A 6′-*O*-*n*-butyl ester (3), calendulaglycoside B (4), calendulaglycoside B 6′-*O*-*n*-butyl ester (5), calendulaglycoside C (6), calendulaglycoside C 6′-*O*-*n*-methyl ester (7), calendulaglycoside C 6′-*O*-*n*-butyl ester (8), calenduloside F 6′-*O*-*n*-butyl ester (9) and

calenduloside G 6′-*O*-*n*-methyl ester (10) (Ukiya et al. 2006).

Miscellaneous Phytochemicals

Eighteen *n*-paraffins ranging from C_{18} to C_{35} were detected in the petals of *Calendula officinalis* (Komae and Hayashi 1971). The flowers also contained the bitter principle loliolide (calendin) (Willuhn and Westhaus (1987) and a tasteless yellow substance calendulin discovered by Geiger in 1819 (Shoemaker 1891).

Seed Phytochemicals

Fatty acid composition of the seed oil revealed the presence of lauric (3.90 %), myristic (3.58 %), palmitic (14.96 %), stearic (10.13 %), palmitoleic (4.55 %), oleic (16.26 %), linoleic (39.45 %) and linolenic (7.15 %) acids (Saleem et al. 1986). In the seed oil, conjugated acid was present to the extent of 4.5 % whereas the percentage of non-conjugated acid (linolenic acid) was only 2.65 %. The residual meal after the extraction of oil was also studied for its proteins (18 %) and amino acids composition.

The amounts (%) of lipids in *C. officinalis* seeds were: neutral lipids, 15.7 %; glycolipids (GLs), 0.9 %; and phospholipids (PhLs), 0.6 % (Ul'chenko et al. 1998). The lipid yield of extracts from the flowers (EF) was 17.1 % and from the leaves (EL) 9.3 %. The following classes of lipids were found (% by weight) hydrocarbons, 0.9 %; esters of sterols and triterpenols with fatty acids, 0.5 %; triacylglycerols (TAGs), 20.0 % comprising TAGs-I, 59.0; TAGs, 2–11.8 %; TAGs, 3–4.3 %; free fatty acids, trace; hydroxy-TAGs, 0.8 %; free sterols and free triterpenols, 0.4 %; diacylglycerols and monoacylglycerols, 1.2 %; and unidentified components, 1.1 %. The phospholipid complex of Marigold seeds consisted of eight classes, which may be arranged in order of content by weight as follows: PCs (phosphatidylcholines) > PIs (phosphatidylinositols) > *N-acyl-PEs* (*N*-acyl phosphatidylethanolamines) > *N*-acyl-lyso-PEs (*N*-acyl-lyso-phosphatidylethanolamines) > lyso-PIs (lyso-phosphatidylinositols) > PSs (phosphatidylserines) > lyso-PCs (lyso-phosphatidylcholines) > PEs (phosphatidylethanolamines). The glycolipids of the seeds were represented by four components forming the following sequence by mass content: SGs (sterylglycosides) > ESGs (ester sterylglycosides) > MGDGs (monogalactosyldiacylglycerols) > DGDGs (digalactosyldiacylglycerols).

The lipid content of seed of 11 genotypes varied between 13.6 and 21.7 g oil/100 g seeds (Dulf et al. 2013). PUFA contents varied between 60.4 and 66.4 %, while saturates comprising mainly palmitic and long chain saturated fatty acids were found in higher amounts in sterol esters (49.3–55.7 % of total fatty acids). Calendic acid [18:3 (8*t*, 10*t*, 12*c*) (*n*−6)] with contents of 51.47–57.63 % of total fatty acids was the predominant polyunsaturated fatty acid (PUFA) followed by linoleic acid [18:2 (*n*−6)] (28.50–31.86 %), oleic acid [18:1 (*n*−9)] (4.44–6.25 %) and palmitic acid (16:0) (3.86–4.55 %). Small and very small (or trace) amounts (<2 %) of stearic (18:0), β-calendic [18:3 (8*t*, 10*t*, 12*t*) (*n*−6)], elaidic [18:1 (9*t*) (*n*−9)], arachidic (20:0), behenic (22:0), gondoic [20:1 (*n*−9)], α-linolenic [18:3 (*n*−3)], linoelaidic [18:2 (9*t*,12*t*) (*n*−6)], *cis-7-hexadecenoic* [16:1 (*n*−9)], palmitoleic [16:1 (*n*−7)], lauric (12:0), myristic (14:0), pentadecanoic (15:0) and margaric (17:0) acids were also present. Cromack and Smith (1998) reported the seed oil content of around 20 %, of which up to 60 % was calendic acid, a useful industrial feedstock. Chisholm and Hopkins (1967) reported that *Calendula* could accumulate more than 40 % of calendic acid. Ozgul-Yucel found that Turkish calendula seed oil was characterized by high concentration of linoleic acid (43.5 %) and low content of CLNAs (calendic acid (18.3 %) + β-calendic (11.2 %). Angelini et al. (1997) reported 16–46 % levels of calendic acid in the Italian Pot Marigold seed oils.

Crombie and Holloway (1985) found that linoleic and oleic acids were precursors in the biosynthesis of calendic acid in Marigold (*C. officinalis*) seeds but not linolenic acid. (9*S*)-Hydroxyoctadeca-(10*E*,12*Z*)-dienoic acid (α-dimorphecolic acid) was isolated and converted into (*R/S*)-hydroxy- and -hydroperoxy-[9-3*H*]

octadeca-(10*E*,l2*Z*)-dienoic acids but neither labelled specimen was converted into calendic acid by Marigold seed homogenate. Also α-dimorphecolic acid, a minor component of Marigold seed oil, was found to be a terminus rather than an intermediate for calendic acid.

Plant and Leaf Phytochemicals

In the flowers, stem and leaves of *C. officinalis*, 15 amino acids were detected in the free state: alanine, arginine, aspartic acid, asparagine, valine, histidine, glutamic acid, leucine, lysine, proline, serine, tyrosine, threonine, methionine and phenylalanine (Absavoa et al. 1994). Among them, six predominated: arginine, proline, glutamic acid, phenylalanine, lysine and leucine. The leaves contained about 5 % of amino acids, the stems 3.5 % and the flowers 4.5 %. Szakiel et al. (2005) found that Marigold (*C. officinalis*) synthesized significant amounts of oleanane saponins, found not only in flowers but also in all organs of plant. These glycosides comprised two series of structurally related compounds, that is, derivatives of 3-*O*-monoglucoside of oleanolic acid (hence named 'glucosides') and derivatives of 3-*O*-monoglucuronide ('glucuronides'), depending on the first sugar moiety linked to the C-3 hydroxyl group of oleanolic acid, which is either glucose or glucuronic acid. The occurrence of both series of oleanolic acid glycosides occurring in *C. officinalis* was earlier reported by Kasprzyk and Wojciechowski (1967) and Wojciechowski et al. (1971). 'Glucuronides', known as the series I, were designated with letters (F, D, D2, C, B, A) and 'glucosides', forming the series II—with Roman numerals from I to VIII. 'Glucuronides' were found in relatively large amounts (up to 2 % of the dry mass) in flowers and in considerably lower quantity in green organs of the plant. Ruszkowski et al. (2003) found 'glucuronides' in roots of young Marigold plants, while 'glucosides' accumulated mainly in roots of grown and senescing plants and also found in green organs of the plant. However, only glycosides I, II, III, VI and VII were found in Marigold shoots. Oleanolic acid and its 3-*O*-glucuronide derivatives and 3-*O*-glucoside derivatives were found in vacuoles prepared from protoplasts and cell walls obtained from leaf cells of *Calendula officinalis* (Szakiel and Kasprzyk 1989). In both cell compartments 37 % of total cellular oleanolic acid accumulated, 0.6 % occurring as free oleanolic acid (only in vacuoles). Glucuronides accounted for 31.1 % (20.7 % in vacuoles and 10.4 % in cell walls) and glucosides for 5.3 % (2.6 % in vacuoles and 2.7 % in cell walls). Szakiel et al. (1995) found that [3-3*H*]oleanolic acid glycosides formed in the cytosol of *C. officinalis* leaf cells were transported to the extracellular space in the form of pentaglucoside VI (44 %), whereas glucuronides derived from [3-3*H*]oleanolic acid 3-*O*-monoglucuronide (29 %) as well as a part of glucosides (24 %) were transported into the cell walls.

Studies confirmed that plastoquinone occurred only in the chloroplasts, ubiquinone only in the mitochondria and α-tocopherol in both these subfractions of *C. officinalis* leaves (Janiszowska et al. 1976). In *Calendula officinalis* leaves the cyclization of squalene to β-amyrin and its further oxidation to oleanolic acid as well as the biosynthesis of all derivatives of oleanolic acid 3-glucoside and some derivatives of oleanolic acid 3-glucuronoside were found to occur in the microsomal fraction (Janiszowska and Kasprzyk 1977). The final metabolites of oleanolic acid 3-glucoside series, that is, pentaglycosides, were translocated from this fraction, one to the cell wall and plasmalemma fraction and the other to the cytosol. The derivatives of oleanolic acid 3-glucoronoside were synthesized partially in other fractions and accumulated in the different membranous structures of the cell.

Polyphenolic compounds (g/kg dry matter) in the aerial Marigold plant parts were determined as follows: chlorogenic acid 0.55 g, 3,5-DCQA (dicaffeoylquinic acid) 0.78, total caffeoyl derivatives 1.33 g, total dihydroxycinnamic acid derivatives 7.54 g, total flavonoids 5.12 g, total dihydroxycinnamic acid derivatives + flavonoids 12.66 g and total polyphenolic compounds 24.97 g (Fraisse et al. 2011).

Fatty acids C12–C22 were found to be components of acylated steryl glucosides in *Calendula officinalis* (Zdzislaw et al. 1975). As a source of acyl groups for the synthesis of steryl acylglucosides, various phospholipids obtained from the same plant were utilized in the following sequence: phosphatidylinositol greater than phosphatidylethanolamine greater than phosphatidylcholine. It does not utilize triacylglycerols and monogalactosyldiacyl glycerols.

In 3-day and 14-day-old seedlings and leaves of *Calendula officinalis*, the following sterols were identified: cholestanol, campestanol, stigmastanol, cholest-7-en-3-β-ol, 24-methylcholest-7-en-3β-ol, stigmast-7-en-3β-ol, cholesterol, campesterol, sitosterol, 24-methylcholesta-5,22-dien-3β-ol, 24-methylenecholesterol, stigmasterol and clerosterol (Adler and Kasprzyk 1975). Sitosterol was predominant in young and stigmasterol in old tissues. Young tissues contained relatively more campesterol, but in old tissues a $C_{28}\Delta^{5,22}$ diene was present suggesting transformation of campesterol to its $\Delta^{5,22}$ analog, similar to that of sitosterol to stigmasterol. All the identified sterols were present as free compounds and also in the steryl esters, glucosides, acylated glucosides and water-soluble complexes.

Petroleum ether extract of *Calendula officinalis* leaf showed the presence of fatty acids, and chloroform extracts showed the presence of triterpenes and sterols (Chakraborthy 2010). Flavonoids, carbohydrates, amino acids, and saponins were present in methanol extract, and saponins, phenolic substances, and tannins were present in the water extract of *Calendula officinalis*.

Thirty and twenty-one compounds were identified in the fresh leaf and dry leaf oils of *C. officinalis* and the yield was 0.06 and 0.03 %, respectively (Okoh et al. 2008). Sesquiterpenoids dominated the fresh leaves (59.5 %) while the monoterpenes dominated the oil in the dry leaves (70.3 %). The fresh leaf oil was dominated by T-muurolol (40.9 %), α-thujene (19.2 %) and δ-cadinene (11.4 %), while the dry leaves oil was found to be rich in 1,8-cineole (29.4 %), γ-terpinene (11.6 %), δ-cadinene (9.0 %), β-pinene (6.9 %) and α-thujene (6.3 %).

The yield in *Calendula officinalis* leaf essential oil showed a maximum at the full flowering stage (0.97 %) and a minimum during the pre-flowering stage (0.13 %) (Okoh et al. 2007). The compositions also showed different patterns at different phases of the vegetative cycle. Sesquiterpenes (α-cadinene, α-cadinol, T-muurolol and epi-bicyclosesquiphellandrene) and monoterpenes (limonene, 1,8-cineole and *trans*-β-ocimene) showed the highest correlations with the age of the plant. Aiming the use of essential oil as a food ingredient, the most interesting stage is the post-flowering period, the essential oil at this time being rich in α-cadinene, α-cadinol, t-muurolol, limonene and 1,8-cineole, with *p*-cymene present at lower levels. The total yields of the essential oils at the different stages of the vegetative cycle increased with the age of the plant and ranged between 0.13 % (3rd week) and 0.97 % (12th week, flowering); α-cadinene is an important flavouring agent in baked foods, candy and chewing gum and also used as a fragrance in cosmetics and detergents. T-muurolol and α-cadinol are important antimicrobial agents. The essential oil at 12 week was dominated by geraniol (44.5 %), α-cadinol (24.20 %), δ-cadinene (23.8 %), T-muurolol (22.50 %), 1,8-cineole (22.10 %), cadina-1,4-diene (12.20 %), germacrene D (11.50 %), α-cadinene (10.7 %) and calarene (5.70 %). Other minor components included α-pinene (2.90 %), limonene (2.6 %), α-cubebene (1.7 %), α-humulene (1.7 %), β-pinene (1.4 %), nerolidol (1.3 %), sabinene (0.9 %), endobourbonene (1.0 %), β-caryophyllene (0.9 %), α-ylangene (0.8 %), palustron (0.7 %), epi-bicyclosesquiphellandrene (0.5 %), β-selinene (0.3 %), alloaromadendrene (0.2 %), α-bourbonene (0.2 %), muurolene (0.10 %), terpene-4-ol (0.10 %), *p*-cymene (0.10 %), carvacrol (0.10 %), α-thujene (0.10 %) and α-gurjunene (0.10 %). These compounds occurred in trace amounts: δ-3-carene, nonanal, 3-cyclohexene-1-ol, α-phellandrene, bornyl acetate, sabinyl acetate, α-copaene, β-cubebene, aromadendrene and oplopenone.

Root Phytochemicals

A new series of glycosides of oleanolic acid was found in the roots of old *Calendula officinalis* plants (Wojciechowski et al. 1971). These compounds were derivatives of 3-glucoside of oleanolic acid and were different, from those previously isolated from the flowers, derivatives of 3-glucuronoside of oleanolic acid. The sugar components of eight representatives of the new series are glucose and galactose in following ratios: in glucoside I, 1:0; in II, 1:1; in III, 1:2; in IV, 2:1; in V, 3:1; in VI, 3:2; in VII, 4:1; and in VIII, 4:1. The sugars in I–VII were attached only in position 3 of oleanolic acid, but in VIII one glucose molecule was joined to 28-carboxyl of oleanolic acid. Glucoside I was identified as 3-monoglucoside and II as 3-(4′-galactosyl)-glucoside of oleanolic acid. Besides these compounds, 6′-methyl ester of 3-glucuronoside of oleanolic acid was also found in the roots.

A monoside 3-*O*-β-D-glucopyranoside of oleanic acid and a bioside (calenduloside A) with the structure 3-galactosylglucosyloleanolic acid (Vecherko et al. 1969, 1971b) and calenduloside B with the structure *O*-β-D-galactopyranosyl-(1 → 4)-*O*-β-D-glucopyranosyl-(1 → 3)-oleanoloyl-(28 → 1)-α-D-glucopyranoside (Vecherko et al. 1971a); oleanolic acid 3-{[galactopyranosido-(1 → 3)] [glucopyranosido–(1 → 2)]-β-D-glucopyranoside} (calenduloside C) and 28-acyl-β-D-glucopyranoside of calenduloside C (calendulososide D) (Vecherko et al. 1975); glucopyranosyl oleanolate 3-*O*-β-D-glucuronopyranoside (calenduloside F) (Vecherko et al. 1973), oleanolic acid 3-*O*-β-D-galactopyranosyl-(1 → 3)-β-D-glucuronoside (calenduloside G) and 28-acyl-β-D-glucopyranoside of calenduloside G (calenduloside H) (Vecherko et al. 1974) were isolated from the roots of *C. officinalis*. Calenduloside B, trioside of oleanolic acid, was isolated from the roots (Iatsyno et al. 1978).

Chemical studies have revealed the presence of various classes of compounds, the main being triterpenoids, flavonoids, coumarins, quinones, volatile oil, carotenoids and amino acids in *C. officinalis* plant parts (Muley et al. 2009; Khalid and da Silva 2012). The extract of this plant as well as pure compounds isolated from it had been demonstrated to possess multifold pharmacological activities: antioxidant, antiinflammatory, antiedematous, immunostimulant, anticancer, lymphocyte and wound healing, hepatoprotective, antibacterial and antifungal, anti-HIV, spasmolytic and spasmogenic, cytotoxic, genotoxic and antigenotoxic, inhibition of heart rate and antiviral, among others.

Antioxidant Activity

Superoxide radicals and hydroxyl radicals were observed in decreasing concentrations in the presence of increasing concentrations of *C. officinalis* butanolic fraction with IC_{50} values of 1 and 0.5 mg/ml, respectively, suggesting a possible free radical scavenging effect (Cordova et al. 2002). Lipid peroxidation in liver microsomes induced by Fe^{2+}/ascorbate was 100 % inhibited by 0.5 mg/ml of the fraction (IC_{50} = 0.15 mg/ml). Its total reactive antioxidant potential (TRAP) (in μM Trolox equivalents) was 368.14 and its total antioxidant reactivity (TAR) was calculated to be 249.19 μM. The results suggested the butanolic fraction of *C. officinalis* to have significant free radical scavenging and antioxidant activity.

The methanol and water extracts of wild Marigold, *Calendula arvensis* (GWM) and cultivated Marigold, *Calendula officinalis* (CM), in a concentration range of 0.10–0.90 mg/ml, scavenged all types of investigated radicals in dependence on their applied concentrations (Ćetković et al. 2004). Generally, CM extracts possessed higher scavenging and antioxidant activity than GMW extracts, while methanol extracts exhibited lower activities than water extracts. Water extracts of CM had the best antioxidant properties; 0.75 mg/ml extracts completely eliminated hydroxyl radical, which was generated in the Fenton system. The same concentration of this extract scavenged 92 % DPPH and 95 % peroxyl radical during lipid peroxidation. Antioxidant properties were in correlation with the contents of total phenolic compounds (14.49–57.47 mg/g) and flavonoids (5.26–18.62 mg/g) in extracts. The electron spin

resonance (ESR) spectroscopy data demonstrated that methanol and water extracts of CM possessed similar free radicals scavenging and antioxidative activity as synthetic antioxidants BHA. Total antioxidant capacity (%) (DPPH scavenging activity) of *C. officinalis* aerial plant parts was 1.52 % and contribution from the main caffeoyl derivatives was as follows: chlorogenic acid 3.15 %, 3,5-DCQA (dicaffeoylquinic acid) 6.90 % and total caffeoyl derivatives 10.05 % (Fraisse et al. 2011).

Calendula officinalis flower top extract was found to scavenge superoxide radicals generated by photoreduction of riboflavin and hydroxyl radicals generated by Fenton reaction and inhibited in-vitro lipid peroxidation (Preethi et al. 2006). Concentrations needed for 50 % inhibition (IC_{50}) were 500, 480 and 2,000 mg/ml, respectively. The extract scavenged ABTS radicals and DPPH radicals with IC_{50} of 6.5 and 100 mg/ml, respectively. The extract also scavenged nitric oxide (IC_{50} = 575 mg/ml). Oral administration of *Calendula* extract inhibited superoxide generation in macrophages in vivo by 12.6 and 38.7 % at doses of 100 and 250 mg/kg body weight. Oral administration of the extract to mice for 1 month significantly increased catalase activity and produced significant increase in glutathione levels in the blood and liver. Glutathione reductase was found to be increased, whereas glutathione peroxidase was found to be decreased after extract administration. The results indicated *Calendula officinalis* possessed significant antioxidant activity in-vitro and in-vivo.

The propylene glycol extract of *Calendula officinalis* exerted its anti-ROS (reactive oxygen species) and anti-RNS (reactive nitrogen species) activity in a concentration-dependent manner during polymorphonuclear leukocytes burst, with significant effects being observed at even very low concentrations: 0.20 μg/ml without L-arginine, 0.10 μg/ml when L-arginine was added to the test with phorbol 12-myristate 13-acetate and 0.05 μg/ml when it was added to the test with *N*-formyl-methionyl-leucyl-phenylalanine (Braga et al. 2009). Electron paramagnetic resonance (EPR) spectroscopy confirmed these findings, 0.20 μg/ml being the lowest concentration of *C. officinalis* extract that significantly reduced 2,2-diphenyl-1-picrylhydrazyl (DPPH). *Calendula officinalis* propylene glycol extracts were found to have protective effect against oxidative DNA damage and lipid peroxidation induced by high polyunsaturated fatty acid (PUFA) intake in young growing pigs (Frankic et al. 2009). It elicited a numerical trend towards the reduction of plasma malondialdehyde and urinary isoprostane (iPF2α-VI) excretion. Its effect was comparable with that of vitamin E. The extract from flower tops showed less antioxidant potential than the extract from petals. They concluded that the amount of *C. officinalis* extracts proposed for internal use by traditional medicine protected the organism against DNA damage induced by high PUFA intake.

Methanol enabled more efficient extraction of flavonoids from *C. officinalis* flowers than the other solvents isopranol and ethanol tested (Butnariu and Coradini 2012). From cv Petran and cv Plamen flowers, methanol extracted, respectively, 2.04 and 2.142 mg/100 g FW of carotene pigments (lycopene, lutein), 10.358 and 5.222 mg/100 g FW of total photosynthetic pigments (chlorophyll a, b), total flavonoid content 96.17 and 90.37 mg quercetin equivalent (QE)/100 ml and total phenolic content of 134 and 153.23 mg GAE/100 ml. The highest antioxidant activity correlated to the polyphenol content was obtained for extracts prepared using methanol. For the methanol extract of cv Petran and cv Plamen, the DPPH radical scavenging activity was2.64 and 2.97 mmol Trolox/g and the ferric reducing antioxidant power (FRAP) was 0.29 and 1.55 mmol Fe^{2+}/g.

Studies by Ozkol et al. (2012) showed that administration of *Calendula officinalis* extract protected rats against subacute cigarette smoke-induced cell injury. Marigold extract decreased the elevated levels of malondialdehyde, reduced glutathione and protein carbonyl caused by cigarette smoke. Further, Marigold extract increased the diminished levels of glutathione peroxidase (GPx), superoxide dismutase activities and β-carotene and vitamins A and C caused by cigarette smoke.

Bernatoniene et al. (2011) confirmed dry *Calendula officinalis* extract to be an effective scavenger of H_2O_2 radicals in in-vitro studies with the mitochondria of rat cardiac muscles. *Calendula* extract incorporated into hydrophilic cream containing complex emulsifier provided significant antioxidant effect due to the content of carotenoids, polyphenols and flavonoids and good emulsion quality. Cream with the best properties (0.9 % of *Calendula* extract) contained 0.73 mg/100 g of total carotenoids expressed as β-carotene.

Anticancer/Antiproliferative Activities

Laser Activated Calendula Extract (LACE) showed a potent in-vitro inhibition (70–100 %) of tumour cell proliferation when tested on a wide variety of human (leukaemias, melanomas, fibrosarcomas and cancers of the breast, prostate, cervix, lung, pancreas and colorectal) and murine tumour cell lines (Jiménez-Medina et al. 2006). Mechanisms of inhibition were identified as cell cycle arrest in G0/G1 phase and caspase-3-induced apoptosis. In contrast, the same extract showed an opposite effect when tested on human peripheral blood lymphocyte (PBL) and NKL (natural killer) cell line, in which in-vitro induction of proliferation and activation of these cells was observed. The intraperitoneal injection or oral administration of LACE in nude mice inhibited in-vivo tumour growth of Ando-2 melanoma cells and prolonged the survival day of the mice. Two triterpene glycosides from the flowers, calenduloside F 6′-*O*-*n*-butyl ester (9) and calenduloside G 6′-*O*-*n*-methyl ester, exhibited potent cytotoxic effects against colon cancer, leukaemia and melanoma cells (Ukiya et al. 2006).

Simultaneous administration of *C. officinalis* flower extract to tumour-bearing male C57BL/6 mice reduced the lung B16F-10 melanoma tumour nodules by 74 % with 43.3 % increase in life span (Preethi et al. 2010). Elevated levels of hydroxyproline, uronic acid, hexosamine, serum sialic acid and γ-glutamyl transpeptidase in the metastatic controls were significantly lowered in the *C. officinalis*-treated animals. The extract also inhibited expression of MMP-2, MMP-9, prolyl hydroxylase and lysyl oxidase and activated TIMP-1 and TIMP-2 and downregulated proinflammatory cytokines. The results indicated antimetastatic effects of *Calendula officinalis* flowers through the inhibition of key enzymes were involved in processes of metastasis.

Studies demonstrated that chamomile and Marigold (*Calendula officinalis*) tea exerted selective dose-dependent cytotoxic action against target cancer cells; cytotoxicity of Marigold tea was higher than chamomile (Matić et al. 2013). However, the cytotoxic effect of chamomile tea was very weak to healthy peripheral blood mononuclear cells (PBMC), while the effect of Marigold tea on PBMC was more pronounced. Marigold tea exerted highly selective antitumor effect especially to melanoma Fem-x cells in comparison to the action to normal healthy PBMC. Chemical analyses showed that dominant phenolic compounds in examined infusions and decoctions were flavonoid glycosides and hydroxycinnamic acid derivatives. Ethanol extracts of *C. officinalis* and other Asteraceae species were found to have antileukemic properties and to induce J-45.01 human acute T leukaemia cell death via apoptosis. The correlation between antileukemic activity and total polyphenol content was determined (Wegiera et al. 2012).

Three major flavonoid fractions separated from *C. officinalis* flower methanol extract did not exhibit inhibitory effect on the parent and tamoxifen-resistant T47D human breast cancer (Ostad et al. 2004). Quercetin increased cell proliferation of the resistant T47D cells in the presence of tamoxifen but no effect was detected by using quercetin itself. Also it was found that isorhamnetin did not have any proliferative or antiproliferative activity on the both cell lines.

Wound Healing Activity

Studies on surgically induced skin wound in Wistar albino rats showed that application of % unguentum containing fractions C1 and C5, isolated from *Calendula officinalis* flowers of in combination with allantoin, significantly stimulated

physiological skin regeneration and epithelialization (Klouchek-Popova et al. 1982).

In-vitro studies showed that chick chorioallantoic membrane (CAM) treated with a freeze-dried aqueous extract of *C. officinalis* flowers were positive for hyaluronan, a tissue glycosaminoglycan associated with neovascularization; no hyaluronan was found in control CAMs (Patrick et al. 1996). The numbers of microvessels in calendula-treated CAMs were statistically and significantly higher than in the control CAMs. Although the extract contained water-soluble compounds such as flavonoids, the exact nature of the active angiogenic component(s) was yet to be identified.

Studies showed that rats with experimentally induced burns treated with *Calendula officinalis* flower extract showed significant improvement in healing when compared with the control untreated animals (Preethi and Kuttan 2008). The indicators of the wound healing such as collagen hydroxyproline and hexosamine contents were significantly augmented in the treated group indicating accelerated wound healing in the treated animals. The acute phase proteins haptoglobin and orosomucoid which were elevated due to burn injury were lowered significantly in 200 mg/kg body weight extract-treated animals. The antioxidant defense mechanism, which was decreased in the liver during burn injury, was enhanced in treated animals. The lipid peroxidation was significantly lowered in the treated group when compared to control animals. Tissue damage marker enzymes alkaline phosphatase, alanine and aspartate transaminases were significantly lowered in the treated groups in a dose-dependent manner. The histopathological analyses of skin tissue also confirmed the increased healing potential of the extract after burn injury. Another study reported that rats with excision wounds treated with *Calendula officinalis* flower extract had 90 % wound closure compared with 51.1 % in the control group on the eighth day of wounding (Preethi and Kuttan 2009b). The days needed for reepithelialization were 17.7 for the control animals; extract treatment at a dose of 20 or 100 mg/kg body weight reduced the period to 14 and 13 days, respectively. A significant increase was observed in the hydroxyproline and hexosamine content in the extract-treated group compared with the untreated animals. *Calendula* extracts were found to have wound healing effect using the scratch assay (Fronza et al. 2009). The hexane and ethanol extracts of *Calendula officinalis* stimulated proliferation and migration of Swiss 3 T3 albino mouse fibroblasts at low concentrations, for example, 10 μg/ml enhanced cell numbers by 64.35 and 70.53 %, respectively. Inhibition of proliferation showed that this effect was mainly due to stimulation of migration. The triterpenoids, faradiol myristate and palmitate gave comparable stimulation rates at an almost 50 μg/ml concentration, indicating that they contributed partially but not most significantly to the wound healing effects of *Calendula* preparations.

Studies by Parente et al. (2012) found that the ethanol extract, the dichloromethane and hexanic fractions of *C. officinalis* flowers presented anti-inflammatory and antibacterial activities as well as angiogenic and fibroplastic properties acting in a positive way on the inflammatory and proliferative phases of the healing process as through the chorioallantoic membrane and cutaneous wounds in rat models. The angiogenic activity of *C. officinalis* flower ethanol extract and dichloromethane and hexanic fractions was evidenced in both experimental models using 36 rats and 90 embryonated eggs to evaluate healing and angiogenic activities through the induction of skin wounds and the chorioallantoic membrane, respectively (Parente et al. 2011). They verified that this effect was not directly related to the expression of vascular endothelial growth factor (VEGF) and it could be associated to other pro-angiogenic factors. Their data suggested the healing activity of *C. officinalis* could be related, among other factors, to its positive effect on angiogenesis, characterized by the induction of neovascularization. In a prospective nonrandomized pilot study of 25 patients (10 men and 15 women) with venous ulcers, 7 week treatment with the herbal-based ointment Herbadermal® comprising extracts of garlic, St. John's wort and calendula elicited 99.1 % epithelialization without significant effects on the microbial flora

(Kundaković et al. 2012). Based on this, they recommended the herbal-based ointment as topical treatment for wound healing because of its epithelializing, anti-erythematous and antiedematous properties.

Hepatoprotective and Nephroprotective Activities

Animal studies showed that the flower extract of *C. officinalis* had a protective effect against CCl_4-induced acute hepatotoxicity and cisplatin-induced nephrotoxicity (Preethi and Kuttan 2009a). The activities of serum marker enzymes of liver injury like glutamate pyruvate transaminase (SGPT), glutamate oxaloacetate transaminase (SGOT) and alkaline phosphatase (ALP) which were elevated by CCl_4 injection were found to be significantly reduced by the pretreatment of the flower extract at 100 and 250 mg/kg body weight. The lipid peroxidation in liver, the marker of membrane damage and the total bilirubin content in serum were also found to be at significantly low level in the extract pretreated group. The elevated kidney urea and creatinine levels in cisplatin-treated animals were significantly lower in the flower extract pretreated groups (100 and 250 mg/kg body weight). Moreover, cisplatin-induced myelosuppression was ameliorated by the flower extract pretreatment. Treatment with the extract produced enhancement of antioxidant enzymes—superoxide dismutase and catalase and glutathione.

Antidermatitic/Radioprotective/Skin Therapeutic Activities

In a phase III randomized trial of *Calendula officinalis* (126 patients) compared with trolamine (128 patients) Calendula treatment was found to reduce acute dermatitis during irradiation for breast cancer (Pommier et al. 2004). The occurrence of acute dermatitis of grade 2 or higher was significantly lower with the use of calendula (41 %) than with trolamine (63 %). Moreover, patients receiving calendula had less frequent interruption of radiotherapy and significantly reduced radiation-induced pain. *Calendula* was considered to be more difficult to apply, but self-assessed satisfaction was greater. Body mass index and adjuvant chemotherapy before radiotherapy after lumpectomy were significant prognostic factors for acute dermatitis. Marigold (*Calendula officinalis*) and rosemary cream preparations were found to be effective against experimentally induced irritant contact dermatitis in healthy volunteers (Fuchs et al. 2005). In a prospective assessment phase III study, *Calendula officinalis* was shown to be superior to trolamine for the prevention of radio-epithelitis (Chargari et al. 2009). In another study of topical products used in the prevention of radiodermatitis, to support care delivery to women with breast cancer during teletherapy, de Andrade et al. (2012) found that *Calendula*, corticosteroids and Xclair have shown significant protective effects against radiodermatitis. Data from a randomized and double-blind study of 66 infants with diaper dermatitis suggested that topical application of aloe vera cream and *Calendula officinalis* ointment could serve as safe and effective treatment for the treatment of diaper dermatitis in infants (Panahi et al. 2012).

The hydroalcoholic extract of *C. officinalis* was found to contain polyphenol, flavonoid, rutin and narcissin contents of 28.6, 18.8, 1.6, and 12.2 mg/g, respectively (Fonseca et al. 2010). The extract exhibited in-vitro dose-dependent antioxidant activity against different radicals. Cytotoxicity experiments demonstrated that the extract was not cytotoxic for L929 and HepG2 cells at concentrations less than or equal to of 15 mg/ml. However, in concentrations greater than or equal to 30 mg/ml, toxic effects were observed. Further, oral treatment of hairless mice with 150 and 300 mg/kg of the extract maintained GSH levels close to nonirradiated control mice. In addition, this extract affected the activity/secretion of matrix metalloproteinases 2 and 9 (MMP-2 and -9) stimulated by exposure to UVB irradiation. The gel formulation [Formulation 3 (F3)] found to be the most effective for the topical delivery of *Calendula officinalis* extract, which was detected as 0.21 μg/cm(2) of narcissin and as 0.07 μg/cm(2) of the rutin in the viable

epidermis of hairless mice exposed to ultraviolet (UV) B irradiation (Fonseca et al. 2011). This formulation was able to maintain glutathione reduced levels close to those of nonirradiated animals but did not affect the gelatinase-9 and myeloperoxidase activities increased by exposure to UVB irradiation. In addition, F3 reduced the histological skin changes induced by UVB irradiation that appeared as modifications of collagen fibrils.

Results of studies by Mishra et al. (2012a) suggested that calendula oil cream can be used to protect the skin from UV radiations in form of sunscreen cream and to maintain the natural pigmentation of the skin. The essential oil of *Calendula officinalis* flowers in cream formulation exhibited good activity sun protection factor (SPF) (SPF = 14.84). In another paper they reported that treatment with creams containing 4 and 5 % of *Calendula officinalis* essential oil caused a significant decrease in the malonyldialdehyde level, whereas the levels of catalase, glutathione, superoxide dismutase, ascorbic acid and the total protein level were significantly increased after 1 month of daily UVB irradiation treatment when compared to untreated control groups (Mishra et al. 2012b). The results suggested that the cutaneous application of the essential oil of *Calendula* prevented UVB-induced alterations in the level of antioxidants in skin tissue.

In a multicentre, controlled, parallel-group study, menopausal women with vaginal dystrophy were randomized to vaginal gel EG (containing isoflavones, *Lactobacillus sporogenes*, *Calendula officinalis* extract and lactic acid) (103 women) or no topical treatment (NT, 83 women) for 4 weeks (Tedeschi et al. 2012). The severity of itching, burning, vulvovaginal erythema, vaginal dryness and dyspareunia were significantly reduced during EG treatment compared with the NT group.

Marigold therapy (*Tagetes* and *Calendula* species) had been used for over 30 years in the United Kingdom and had been evaluated by numerous randomized double-blind placebo-controlled studies for various skin problems on the lower extremity (Hadfield et al. 2008; Khan 2008). Various species of Marigold had been reported to be naturally antiviral, keratolytic and antiinflammatory when applied topically to the affected area. In particular, through numerous research, controlled and case studies by M Taufiq Khan and M Tariq Khan specific extracts had been developed that were directly applied by the podiatric physician to the patient: an antiviral paste (for verruca), an antiinflammatory paste (for bursitis and tendonitis), a keratolytic paste (for hyperkeratosis) and an antifungal paste (for nails). Marigold therapy had been reported to provide a noninvasive and gentle treatment for difficult to treat plantar verruca, painful hyperkeratotic lesions and inflamed bursa secondary to hallux abducto valgus.

Calendula officinalis flowers and *C. officinalis* extracts are used as skin conditioning agents in cosmetics. Using the threshold of toxicological concern (TTC) approach, Re et al. (2009) evaluated their safe use in cosmetic and personal care products. For each of its known constituents, the concentration in the plant, the molecular weight and the estimated skin penetration potential were used to calculate a maximal daily systemic exposure which was then compared to its corresponding TTC class value. Owing to the variability of composition of plant extracts, back calculation was used to determine the maximum acceptable concentration of a given constituent in an extract of *C. officinalis*. Akhtar et al. (2011) evaluated the effects of newly formulated topical cream of *Calendula officinalis* extract on the mechanical parameters of the cheek skin in healthy human volunteers by using the cutometer, a device that is designed to measure the mechanical properties of the skin in response to the application of negative pressure. After 8 weeks, the instrumental measurements produced by formulation reflected significant improvements in hydration and firmness of skin.

Antiinflammatory Activity

Russian studies reported that preparations of calendula alleviated the signs of chronic inflammatory conjunctivitis and other chronic ocular inflammatory conditions in laboratory animals (Marinchev et al. 1971; Mozherenkov and Shubina 1976).

The triterpenoids were shown to be the most important antiinflammatory principles of *C. officinalis* flower CO_2 extract (Della Loggia et al. 1994). Among them, the faradiol monoester appeared to be the most relevant principle for the activity of the extract, due to its quantitative prevalence. The unesterified faradiol, not present in the extract, was the most active of the tested compounds and equalled indomethacin in activity, whereas the monools ψ-taraxasterol, lupeol, taraxasterol and β-amyrin were less active than the free diol. Isorhamnetin glycosides isolated from *Calendula officinalis* were found to inhibit the activity of lipoxygenase in vitro (Bezákova et al. 1996). All of the triterpene alcohols helianol, taraxasterol, ψ-taraxasterol, α-amyrin, β-amyrin, lupeol, taraxerol, cycloartenol, 24-methyl-enecycloartanol, tirucalla-7,24-dienol and dammaradienol isolated from the tubular flowers of *Calendula officinalis*, *Carthamus tinctorius*, *Cosmos bipinnatus*, *Chrysanthemum morifolium*, *Helianthus annuus* and *Matricaria matricarioides* exhibited marked antiinflammatory activity against 12-*O*-tetradecanoylphorbol-13-acetate-induced inflammation (1 μg/ear) in mice, and their 50 % inhibitory dose was 0.1–0.8 mg/ear (Akihisa et al. 1996). Faradiol esters, namely, faradiol-3-myristic acid ester and faradiol-3-palmitic acid ester, isolated from *C. officinalis* flower heads showed nearly the same dose-dependent anti-oedematous activity in the inhibition of Croton oil-induced oedema of the mouse ear, and no significant synergism appeared with their mixture (Zitterl-Eglseer et al. 1997). The free monol, ψ-taraxasterol, had a slightly lower effect and showed the same effect as an equimolar dose of indomethacin. Furthermore, faradiol was more active than its esters and than ψ-taraxasterol. The major antiinflammatory triterpenoid esters purified from *C. officinalis* flower heads were faradiol-3-*O*-laurate, faradiol-3-*O*-myristate and faradiol-3-*O*-palmitate (Hamburguer et al. 2003). Accompanying minor compounds of the triterpene ester fraction purified included maniladiol 3-*O*-laurate, maniladiol-3-*O*-myristate, ψ-taraxasterol and β-amyrin.

Three new terpenoid derivatives derived by systematic chemical modifications of faradiol from *C. officinalis* flowers, the C(16) benzyl ether 15, the C(30) aldehyde 24 and the C(30) primary alcohol 25 showed significantly improved antiinflammatory potencies in the inhibition of croton oil induced ear oedema in mouse (Neukirch et al. 2005). In evaluation of oleanane-type triterpene glycosides 1–9 isolated from the flowers for inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1 μg/ear) in mice, calendulaglycoside A (1), calendulaglycoside A 6′-*O*-*n*-methyl ester (2), calendulaglycoside A 6′-*O*-*n*-butyl ester (3), calendulaglycoside B (4), calendulaglycoside B 6′-*O*-*n*-butyl ester (5), calendulaglycoside C (6), calendulaglycoside C 6′-*O*-*n*-methyl ester (7), calendulaglycoside C 6′-*O*-*n*-butyl ester (8) and calenduloside F 6′-*O*-*n*-butyl ester (9), all except compound (1), exhibited marked antiinflammatory activity, with ID_{50} values of 0.05–0.20 mg/ear (Ukiya et al. 2006).

Oral administration of 250 and 500 mg/kg body weight *Calendula officinalis* flower extract produced significant inhibition (50.6 and 65.9 %, respectively) in paw oedema of animals induced by carrageenan and 41.9 and 42.4 %, respectively, with inflammation produced by dextran (Preethi et al. 2009). In chronic antiinflammatory model using formalin, administration of 250 and 500 mg/kg body weight *Calendula* extract produced an inhibition of 32.9 and 62.3 %, respectively, compared to controls. TNF-alpha production by macrophage culture treated with lipopolysaccharide (LPS) was found to be significantly inhibited by *Calendula* extract. Furthermore, elevated levels of proinflammatory cytokines IL-1beta, IL-6, TNF-alpha and IFN-gamma and acute phase protein, C-reactive protein (CRP), in mice induced by LPS injection were inhibited significantly by the extract. LPS-induced cyclooxygenase-2 (Cox-2) levels in mice spleen were also found to be inhibited by the extract. The results showed that potent antiinflammatory response of *C. officinalis* extract may be mediated by the inhibition of proinflammatory cytokines and Cox-2 and subsequent prostaglandin synthesis.

In a study of 103 children aged 6–18 years diagnosed with otalgia associated with acute otitis media (AOM), Otikon, an ear drop formulation of

naturopathic origin (containing *Allium sativum*, *Verbascum thapsus*, *Calendula flores* and *Hypericum perforatum* in olive oil), was found to be as effective as anesthetic ear drops and was proven appropriate for the management of AOM-associated ear pain (Sarrell et al. 2001). In a subsequent double-blind trial in an outpatient community clinic involving a total of 171 children aged 5–18 years with otalgia and otitis media, they found the herbal formulation Naturopathic Herbal Extract Ear Drops (NHED) (comprising *Allium sativum*, *Verbascum thapsus*, *Calendula flores*, *Hypericum perforatum*, lavender and vitamin E in olive oil) to be beneficial. Results were better in the NHED group than in the controls (Sarrell et al. 2003).

Calendula officinalis, rich in quercetin, carotenoids, lutein, lycopene, rutin, ubiquinone, xanthophylls and other antioxidants, at 2–3 %, completely inhibited human matrix metalloproteinase 2 (MMP-2) activity and human gingival fibroblast-mediated collagen degradation more than the corresponding concentration of quercetin (Saini et al. 2012). They attributed this to additional components in *Calendula* other than quercetin.

Cell Growth Stimulating Activity

The heptane, ethyl acetate and methanol extracts of *Calendula officinalis* flowers, were found to stimulate cell growth when introduced to a human skin fibroblast (HSF) cells culture and a culture of human breast cancer cells (T47D), cell culture collection ECACC number 85102201 (Matysik et al. 2005). The ethyl acetate but not the heptane and methanol extracts in concentrations above 25 μg/ml stimulated cell proliferation and cellular metabolism by increase of mitochondrial dehydrogenase activity. However, concentrations exceeding 75 μg/ml were toxic for cells.

Exfoliative Cheilitis Therapeutic Activity

Roveroni-Favaretto et al. (2009) described a case of recurrent exfoliative cheilitis in an 18-year-old man that responded to treatment with a standardized topical preparation of *Calendula officinalis.*

Hypoglycaemic, Gastric Emptying and Gastroprotective Activities

The methanol extract and its 1-butanol-soluble fraction from *Calendula officinalis* flowers were found to show a hypoglycaemic effect, inhibitory activity of gastric emptying and gastroprotective effect (Yoshikawa et al. 2001). From the 1-butanol-soluble fraction, four new triterpene oligoglycosides, calendasaponins A, B, C and D, were isolated and were shown to exhibit potent inhibitory effects on an increase in serum glucose levels in glucose-loaded rats, gastric emptying in mice and ethanol- and indomethacin-induced gastric lesions in rats. Some structure-activity relationships are discussed. They further isolated two new ionone glucosides (officinosides A and B) and two sesquiterpene oligoglycosides (officinosides C and D), from the flowers of Egyptian *Calendula officinalis* (Marukami et al. 2001).

Hypotensive and Sedative Activity

Animal studies found that high doses of *Calendula* exhibited sedative effect and also reduced blood pressure (Bojadjiev 1964). For this reason, it might not be safe to combine calendula with sedative or blood pressure medications.

Antipyretic and Analgesic Activities

Crude ethanol extract of *C. officinalis* displayed significant antipyretic (74.95 % inhibition at a dose of 300 mg/kg) and analgesic (27.42 % inhibition at a dose of 40 mg/kg) in rat models (Ahmad et al. 2000). The extract not only reversed induced hyperthermia but also affected normothermia in rats. The extract at a dose of 20 mg/kg was as potent in its analgesic properties as acetylsalicylic acid at 40 mg/kg.

Antiulcerogenic Activity

Calendulozide B, trioside of oleanolic acid, isolated from *C. officinalis* roots was shown to have antiulcerogenic activity (Iatsyno et al. 1978). In oral doses of 5, 10, 20 and 50 mg/kg, it exerted an antiulcerous action in three experimental ulcer models (caffeine-arsenic induced, butadion induced and pylorus ligation induced) and also exhibited antiphlogistic and sedative action. It was devoid of effects on the cardiovascular system, the tone of intestinal smooth muscles, the diuretic renal function, the electrolytes excretion with urine or on the biligenic function of the liver. It had no local irritation properties, manifested a relatively low haemolytic activity and an insignificant toxicity both with its one-time and chronic administration.

In a clinical trial of 24 patients with chronic nonspecific colitis, treatment of an herbal combination of *Taraxacum officinale*, *Hipericum perforatum*, *Melissa officinalis*, *Calendula officinalis* and *Foeniculum vulgare* abrogated spontaneous and palpable pains along the large intestine in 95.83 % of the patients by the 15th day of their admission to the clinic Chakurski et al. 1981). Defecation became daily in the patients with obstipation syndrome. In another clinical trial, 137 patients (78 with duodenal ulcer and 59 with gastroduodenitis) were treated only with the herbal combination of *Symphytum officinalis* and *Calendula officinalis* and 33 (21 with duodenal ulcer and 12 with gastroduodenitis) were treated with the herbal combination together with antacid (Chakŭrski et al. 1981) As a result from the treatment, the spontaneous pains disappeared in 90 % of the patients in the group with antacid, and in the group without antacid, the dyspeptic complaints decreased over 85 %, but in the patients treated with herbs and antacid, these complaints disappeared several days earlier. The palpitation pains, in both groups, disappeared in more than 90 % of the patients within the same time. Gastric acidity, in both groups, showed a statistically insignificant tendency to decrease prior and post treatment. The ulcer niche, in both groups, was healed in almost the same percentage of the patients.

In a clinical study of patients with venous leg ulcers, after 3 weeks of treatment with an ointment of *C. officinalis* extract, of 21 patients treated, total ulcer surface area decreased by 41.7 % and 7 patients had complete epithelialization (Duran et al. 2005). In the control group of 13 patients, treated with saline solution dressings, total ulcer surface area decreased by 14.52 % and four patients had complete epithelialization. The preliminary results suggested the positive effects of the Marigold extract ointment on venous ulcer epithelialization. Studies showed that treatment of dogs with of acetic acid-induced ulcerative colitis resolved the damages of ulcerative colitis (Mehrabani et al. 2011). Loose stools, diarrhoea, gross bleeding and loss of body weight happened after administration of acetic acid, and crypt damage, loss of epithelium, infiltration of inflammatory cells and depletion of goblet cells were observed histologically.

Strychnos nux-vomica (nux vomica) and *Calendula officinalis* are used in highly diluted form in homeopathic medicine to treat patients suffering from gastritis and gastric ulcers. Results of studies suggested both drugs prepared in ethanol solution to be potent inhibitors of *Helicobacter pylori* induced gene expression (Hofbauer et al. 2010). Addition of nux vomica and *Calendula officinalis* in a 43 % ethanol solution produced a significant reduction of *H. pylori*-induced increase in gene expression of heparin-binding epidermal growth factor (HB-EGF) in gastric epithelial cell line KATO-III (reduced to 53.12 and 75.32 % vs. control), respectively. This effect was only observed when the drugs were primarily prepared in ethanol, not in aqueous solutions.

Antigingivitis Activity

Polysorb-immobilized *Calendula* was found to be highly effective in the treatment of chronic catarrhal gingivitis (Krazhan and Garazha 2001). Two patients with a diagnosis of lichen planus presenting as desquamative gingivitis who had undergone previous treatments for this condition with no significant results were treated by a handling gel containing clobetasol, nystatin, *Calendula*

officinalis, and pectin in custom trays (Machado et al. 2010). Both patients had remission of symptoms while using the trays, and after they stopped the treatment, the symptomatic outbreaks were delayed and presented as less severe symptoms in the 2 years follow-up. The treatment is aimed primarily at reducing the length and severity of symptomatic outbreaks of desquamative gingivitis.

Antimicrobial Activity

Hydroacetonic extract from fresh *C. officinalis* plant inhibited the growth of *Staphylococcus aureus* at a concentration of 1 mg/ml in vitro (Dumenil et al. 1980). *Calendula* extract tested on biofilms of infant dentifrices did not demonstrate antimicrobial effects in vitro against *Actinomyces viscosus*, *C. albicans*, *Lactobacillus casei*, *Streptococcus mitis*, *Streptococcus mutans*, *Streptococcus oralis*, *Streptococcus sanguis*, and *Streptococcus sobrinus* (Modesto et al. 2000). *Melissa officinalis* and *C. officinalis* flower extracts exhibited low inhibiting activity (MIC > or = 2,048 mg/l) against all the tested periodontopathic bacteria species with the exception of *Prevotella* sp. (Iauk et al. 2003). Oleanolic acid isolated from Marigold (*Calendula officinalis*) inhibited bacterial growth and survival, influenced cell morphology and enhanced the autolysis of Gram-positive bacteria, suggesting bacterial envelopes were the target of its activity (Szakiel et al. 2008). The sap of *Calendula* racemes demonstrated the most profound antimicrobial effect while that of the roots was the least effective (Radioza and Iurchak 2007). *Calendula* species inhibited all tested pathogenic microorganisms, especially *Pseudomonas syringae*, *Pseudomonas fluorescens*, *Xanthomonas campestris* and *Agrobacterium tumefaciens*. Chloroform, ethanol and water extracts of *C. officinalis* leaves exhibited in-vitro antibacterial activity against Gram-positive *Bacillus subtilis*, *Staphylococcus aureus*, and Gram-negative bacteria *Escherichia coli* and *Klebsiella pneumonia*, whereas significant activity was not observed with petroleum ether extract (Chakraborthy 2008). All the extracts did not show any antifungal activity.

Calendula officinalis flower extract showed high in-vitro inhibitory activity against *Aspergillus niger*, *Rhizopus japonicus*, *Candida albicans*, *Candida tropicalis* and *Rhodotorula glutinis* (Kasiram et al. 2000). The inhibitory effects of extracts were very close and identical in magnitude and were comparable with that of standard antibiotics used. The ethanol, water and n-butanol *C. officinalis* aerial plant parts extracts were found to be effective against most of the human pathogenic microorganisms: *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterococcus* sp., coagulase (+) *Staphylococcus* sp., coagulase (−) *Staphylococcus* sp., *Candida albicans* and *Candida parapsilosis* (Goyal and Mathur 2011). The methanol extract of *C. officinalis* petals exhibited better antibacterial activity against most of the clinical bacteria tested than the ethanol extract (Efstratiou et al. 2012). Both methanol and ethanol extracts showed excellent antifungal activity against tested strains of fungi, comparable to fluconazole.

In a trial of 18 patients to compare the antimicrobial effect of mouthwashes (6 patients per mouthwash) containing *Calendula officinalis*, *Camellia sinensis* and 0.12 % chlorhexidine digluconate on the adherence of microorganisms to suture materials after extraction of unerupted third molars, all three mouthwashes exhibited antimicrobial activity against the adherence of microorganisms to sutures (Faria et al. 2011). However, *C. officinalis* and *C. sinensis* were not as efficient as chlorhexidine digluconate. The hydroethanol herbal extract of *C. officinalis* was one of several herbal extracts that showed high growth inhibition of *Campylobacter jejuni*, the most common cause of enteric infections, particularly among children, resulting in severe diarrhoea (Cwikla et al. 2010).

Antiviral Activity

Tinctures of *C. officinalis* flowers inhibited replication of herpes simplex virus, influenza A2 and influenza APR 8 viruses in-vitro (Bogdanova et al. 1970). However, an aqueous extract was

inactive (May and Willhun 1978). A 5 % hot aqueous extract of *Calendula* flowers inhibited replication of tick-borne encephalitis virus after intraperitoneal administration to mice (Fokina et al. 1991).

Studies found that the organic extract from *Calendula officinalis* flowers caused a significant dose- and time-dependent reduction of human immunodeficiency virus type 1 (HIV-1) reverse transcription (RT) activity in the in-vitro MTT/tetrazolium-based assay (Kalvatchev et al. 1997). An 85 % RT inhibition was achieved after 30 minutes. In addition, in the presence of the organic extract (500 µg/ml), the uninfected human lymphocytic Molt-4 cells were completely protected for up to 24 hours from fusion and subsequent death, caused by cocultivation with persistently infected U-937/HIV-1 cells. Ten oleanane-type triterpene glycosides isolated from the flowers, calendulaglycoside A (1), calendulaglycoside A6′-*O*-*n*-methyl ester (2), calendulaglycoside A 6′-*O*-*n*-butyl ester (3), calendulaglycoside B (4), calendulaglycoside B 6′-*O*-*n*-butyl ester (5), calendulaglycoside C (6), calendulaglycoside C 6′-*O*-*n*-methyl ester (7), calendulaglycoside C 6′-*O*-*n*-butyl ester (8), calenduloside F 6′-*O*-*n*-butyl ester (9) and calenduloside G 6′-*O*-*n*-methyl ester (10), exhibited moderate inhibitory effects against the Epstein-Barr virus early antigen (EBV-EA) activation induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA), (IC_{50} values of 471–487 mol ratio/32 pmol TPA) (Ukiya et al. 2006).

Calendula officinalis aqueous extract was found to have an immunomodulation effect against three different live viruses in broiler chickens (Barbour et al. 2004). There was a reduction in immune response to IB (infectious bronchitis) virus at 42 days of age, to ND (Newcastle disease) virus at 29 and 42 days of age, and to IBD (infectious bursal disease) virus at 14, 29 and 42 days of age in the *Calendula-treated* birds in comparison with controls. This immune reduction in *Calendulas*-treated birds was associated with insignificant reduction in the bursal weight index at 42 days of age and an improvement in mean weights at 21 and 41 days of age.

Immunomodulatory Activity

Polysaccharide fractions with molecular weights in the range of 25,000–500,000 and higher isolated from *C. officinalis* and several other plants showed significant immunostimulating activities in granulocytes and carbon clearance tests (Wagner et al. 1985). Three polysaccharides isolated from *Calendula officinalis* flowers showed immunostimulating activity in several in-vitro immunological test systems (Varljen et al. 1989). Studies found that the ethanol extract of *C. officinalis* exhibited no direct mitogenic effect on human lymphocytes or thymocytes (Amirghofran et al. 2000). They showed a complete inhibitory effect on the proliferation of lymphocytes in the presence of PHA (SI (simulation index) range 0.01–0.49). Treatment of mixed lymphocytes with 0.1–10 µg/ml of *C. officinalis* (SI range 1.34–1.80) strongly increased the cell proliferation.

Calendula officinalis extract was one of several herbal extracts that was shown to be not inferior to *Echinacea purpurea* tincture in terms of stimulation of humoral immune response, phagocytic and bactericidal activity of peritoneal macrophages in mice but exceeded effect of *E. purpurea* on phagocytic activity of peripheral blood neutrophils (Borsuk et al. 2009).

Antimutagenic Activity

All 13 saponins isolated *Calendula officinalis*, *C. arvensis* and *Hedera helix* were found to be nontoxic and non-mutagenic for doses of 400 µg in the *Salmonella*/microsomal assay (Elias et al. 1990). Chlorophyllin inhibited the mutagenic activities of benzo-[a]pyrene (BaP) (1 µg) and a mutagenic urine concentrate from a smoker (5 µl) in a dose-dependent manner.

Genotoxic/Antigenotoxic Activity

A fluid extract of *Calendula officinalis* exhibited dose-dependent genotoxic properties when assayed for mitotic segregation in the heterozygous diploid

D-30 of *Aspergillus nidulans* (Ramos et al. 1998). Mutagenicity testing with the *Salmonella*/microsome assay in strains TA 1535, TA 1537, TA 98 and TA 100 was negative in a plate incorporation protocol, with concentrations ranging from 50 to 5,000 μg/plate. The extract was also negative in the mouse bone marrow micronucleus test at 1 g/kg per os. Pérez-Carreón et al. (2002) found that in the unscheduled DNA synthesis (UDS) assay in liver cell cultures, diethylnitrosamine (DEN) at 1.25 μM elicited a maximal increase of 40 % (3) H-thymidine ((3)HdTT) incorporation, and both aqueous (AE) and aqueous-ethanol (AEE) extracts of *C. officinalis* flower completely reverted the DEN effect at around 50 ng/ml and between 0.4 and 16 ng/ml, respectively. In the absence of DEN, these two polar extracts induced UDS at concentrations of 25 μg for AE and 3.7 μg/ml for AEE to 100 μg/ml in rat liver cell cultures. Concentrations producing genotoxic damage were three orders of magnitude above concentrations that conferred total protection against the DEN effect. Thus, at the lower end, ng/ml concentrations of the two polar extracts AE and AEE conferred total protection (antigenotoxic) against the DEN effect, and at the higher end, g/ml concentrations produced genotoxic effects.

No genotoxic or mutagenic effect was observed in blood and bone marrow samples from mice after 2 weeks of treatment with ethanol (250 or 500 mg/kg) or aqueous (90 mg/kg) extracts of *C. officinalis* prior to treatment with saline or methyl methanesulfonate (Leffa et al. 2012). Additionally, both extracts showed an antigenotoxic effect by Comet assay, repairing the DNA damage caused by methyl methanesulfonate. In the micronucleus test, only aqueous extract of *C. officinalis* revealed a protective effect to genetic material. The results suggested that all the extracts of *C. officinalis* contained protective substances that decreased damage to genetic material.

Hepatoprotective Activity

In a rat hepatocarcinogenesis model, *Calendula officinalis* flower extracts exhibited both protective and cytotoxic effects dependent on the concentration used presenting a phenomenon known as hormesis (Barajas-Farias et al. 2006). The protective effect was observed at 0.1 mg/kg concentration, increased at 0.5 mg/kg and reached its maximum at 2.5 mg/kg, when it decreased the area and number of altered foci by 55 and 49 %, respectively, in comparison with rats treated only with carcinogen, *N*-nitrosodiethylamine. Ten and 20 mg/kg doses produced a notorious increment in the area and number of altered hepatic foci, and at 40 mg/kg of extract the increment was 40 and 53 %, respectively.

Cardioprotective Activity

Animal studies showed that *C. officinalis* ameliorated myocardial ischemic reperfusion injury (Ray et al. 2010). Rat hearts perfused with *C. officinalis* prior to subjecting the heart to ischaemia and achieved cardioprotection by stimulating left ventricular developed pressure and aortic flow as well as by reducing myocardial infarct size and cardiomyocyte apoptosis. Cardioprotection appeared to be achieved by changing ischaemia reperfusion-mediated death signal into a survival signal by modulating antioxidant and antiinflammatory pathways as evidenced by the activation of Akt and Bcl2 and depression of TNF-α.

Spasmogenic and Spasmolytic Activities

The crude aqueous-ethanol extract of *Calendula officinalis* flowers was found to contain both spasmolytic and spasmogenic constituents, exhibiting these effects through calcium channel blocking and cholinergic activities (Bashir et al. 2006). In isolated rabbit jejunum, the extract caused a dose-dependent (0.03–3.0 mg/ml) relaxation of spontaneous and K^+-induced contractions, suggestive of calcium channel blockade. In a few preparations, a mild non-reproducible spasmogenic effect was observed at lower doses, followed by relaxation. Activity-directed fractionation revealed that the spasmolytic activity of

the plant was concentrated in its organic fractions. The aqueous fraction exhibited a marked atropine sensitive spasmogenic effect but was found to be devoid of any spasmolytic effect. The study provided a scientific base for its traditional use in abdominal cramps and constipation.

Uterotonic Activity

A crude water extract of *C. officinalis* was found to enhance the uterine tonus in isolated rabbit and guinea pig uterine horn (Shipochliev 1981).

Estrogenic Activity

Two Polish studies in early 1960s reported that calendula flower extracts exhibited some estrogenic activity in ovariectomized mice (Banaszkiewicz and Mrozikiewicz 1962; Banaszkiewicz et al. 1962).

Insecticidal Activity

A study on human volunteers showed that the essential oils of myrtle and Marigold (*Calendula officinalis*) exhibited repellency against *Anopheles stephensi*, vector of malaria disease, but was generally lower than DEET, a synthetic repellent (Tavassoli et al. 2011). The protection time of 50 % essential oils of Marigold and myrtle were respectively 2.15 and 4.36 hours compared to 6.23 hours for DEET 25 %. The median effective dose (ED_{50}) of essential oils was 0.1105 and 0.6034 mg/cm^2, respectively, for myrtle and Marigold.

Antiparasitic Activity

Glycosides of oleanolic acid, isolated from Marigold, inhibited the development of L3 *Heligmosomoides polygyrus* larvae, the infective stage of the intestinal parasitic nematode (Szakiel et al. 2008). Furthermore, both oleanolic acid and its glycosides reduced the rate of L3 survival during prolonged storage, but only oleanolic acid glucuronides affected nematode infectivity.

Molluscicidal Activity

Studies found that the *Calendula micrantha officinalis* flower ethanol extract higher molluscicidal activity against *Lymnaea cailliaudi*, Fascioliasis-transmitting snail, than the leaf extract with LC_{50} of 35 and 52.17 ppm, respectively (Abd-El-Megeed 1999). The mortality rate of exposed snails was increased by prolongation of the exposure time. The molluscicidal effect resulted in enhancing energy utilization and nutrient consumption since glucose, lipids, proteins and triglycerides were greatly reduced. The stomach and digestive gland of the treated *L. cailliaudi* snails were greatly altered. Natural rubber used as a binding matrix for *Calendula officinalis* was found to be a source of molluscicidal saponin (Helaly et al. 1999). The amount of saponin released was affected by the environmental temperature and the type of fillers present in the formulations.

Allergy Problem

Members of the Compositae including *C. officinalis* had been suspected of sensitization or elicitation of Compositae dermatitis (Paulsen 2002). Sesquiterpene lactones were the most important allergens, but there were a few cases of sensitization from a coumarin, a sesquiterpene alcohol and a thiophene.

Toxicity Studies

Animal studies by Lagarto et al. (2011) found that the acute and subchronic toxicities of *C. officinalis* extracts were low. In the subchronic study with doses of 50, 250 and 1,000 mg/kg/day administered in drinking water, several of the blood elements were significantly affected in male and female Wistar rats after 90 days, haemoglobin, erythrocytes, leukocytes and blood

clotting time. For blood chemistry parameters, ALT, AST and alkaline phosphatase were affected. Histopathological examination of tissues showed slight abnormalities in hepatic parenchyma that were consistent with biochemical variations observed. In the acute study (dose of 2,000 mg/kg) there were no mortality and signs of toxicity.

Jeschke et al. (2009) conducted a prospective observational study of prescribing patterns of remedies containing Asteraceae extracts and adverse drug reactions (ADR) in Germany from these remedial extracts. Their study involved herbal medicines, containing extracts of Asteraceae such as *Echinacea* spp., *Arnica montana*, *Matricaria recutita* and *Calendula officinalis* and involved 38 physicians, 55 % of whom were general practitioners and 45 % were specialists. During the study period, a total of 50,115 patients were evaluated and 344 ADRs for conventional and complementary remedies were reported. The most frequently prescribed Asteraceae was *Matricaria recutita* (23 %), followed by *Calendula officinalis* (20 %) and *Arnica montana* (20 %). No serious ADRs for Asteraceae-containing remedies were reported. The majority of reported ADRs for Asteraceae-containing remedies were classified as uncommon. The proportional reporting ratios (PRRs) for Asteraceae-containing remedies with respect to all other prescriptions was 1.7 for the system organ class 'skin and subcutaneous tissue disorders' (six ADRs) and 1.0 for 'gastrointestinal disorders' (three ADRs). Neither result was significant. Their results indicated treatment with Asteraceae-containing remedies was not associated with a high risk of adverse drug reactions (ADRs).

In the acute toxicity test, the hydroalcohol extract of *Calendula officinalis* failed to cause death in the animals after administration of oral doses up to 5.0 g/kg (Silva et al. 2007). Oral treatment with the extract at 0.025, 0.25, 0.5 and 1.0 g/kg did not induce hematological alterations when compared with the control group. In the biochemical parameters, there was an increase in blood urea nitrogen and in alanine transaminase levels. Morphological examination of the brain, kidney and heart did not show any alteration. However, inflammatory sites were found in the lung and liver, which were associated, respectively, with oral gavage and a possible hepatotoxic effect. The extract was nontoxic in rats, although there was evidence of renal and liver overload. Subsequent studies by Silva et al. (2009) showed that the treatment of Wistar rats with hydroalcohol extract of *Calendula officinalis* flowers did not affect male reproductive parameters. Besides, it was nontoxic in the preimplantation and organogenic periods (early and middle periods) of pregnancy. However, the extract induced a decrease in the maternal weight gain when administered during the foetal period.

The Cosmetic Ingredient Review (CIR) Expert Panel in their final report concluded that *Calendula officinalis*-derived cosmetic ingredients were safe for use in cosmetics in the practices of use and concentration given in the amended safety assessment (Andersen et al. 2010). *C. officinalis* extract, *C. officinalis* flower, *C. officinalis* flower extract, *C. officinalis* flower oil, and *C. officinalis* seed oil are cosmetic ingredients derived from *C. officinalis*. These ingredients may contain minerals, carbohydrates, lipids, phenolic acids, flavonoids, tannins, coumarins, sterols and steroids, monoterpenes, sesquiterpenes, triterpenes, tocopherols, quinones, amino acids and resins. These ingredients were not significantly toxic in single-dose oral studies using animals. The absence of reproductive/developmental toxicity was inferred from repeat-dose studies of coriander oil, with a similar composition. Overall, these ingredients were not genotoxic. They also were not irritating, sensitizing or photosensitizing in animal or clinical tests but may be mild ocular irritants.

Traditional Medicinal Uses

Calendula officinalis is used medicinally in Europe, China and India among several other places in the world (Muley et al. 2009) and is one of the most common and versatile herbs in western herbal medicine and popularly used as domestic medicine (Grieve 1971; Chevallier

1996). The whole plant, in particular the flowers and the leaves, are deemed antiphlogistic, antiseptic, antispasmodic, aperient, astringent, cholagogue, diaphoretic, emmenagogue, stimulant and vulnerary (Uphof 1968; Grieve 1971; Chiej 1984; Chevallier 1996). *Calendula officinalis* has been widely used from time immemorial in Indian and Arabic cultures as an antiinflammatory agent to treat minor skin wound and infections, burns, bee stings, bites, sunburn, sprains, wounds, sore eyes, ulcers, varicose veins and cancer (Grieve 1971; Chiej 1984; Ray et al. 2010). Pot Marigold is taken internally in treating fevers and chronic infections (Grieve 1971; Chevallier 1996) and used internally in order to speed the healing of wounds (Castro 1996) and prevent suppuration (Grieve 1971). The leaves, blossoms and buds are used to make a homeopathic remedy (Castro 1996). Leaves eaten as salad were considered useful in the treatment of scrofula in children. The petals are used in herbal tea taken to ease varicose veins. The crushed stems are applied to warts and corns. Pot Marigold is also used as a bactericide, antiseptic and antiinflammatory.

Other Uses

Potted Marigolds are grown all over the world for ornamental purposes and also as medicinal herbs in many cultures. Calendula flowers can be used as cut flowers. In eastern countries, Marigold flowers are used in garlands for social and religious purposes. The flowers also provide a yellow dye used for fabrics, cosmetics and food. Potted Marigold plant extracts are widely used in cosmetics presumably due to presence of compounds such as saponins, flavonoids, resins and essential oils. Potted Marigold is also an important dietary and medicinal source of carotenoids such as lutein, lutein esters, zeaxanthin, auroxanthin and flavoxanthin.

Calendula officinalis can be grown as an intercrop or use as soil amendments to deter insect and soil pests. Studies found that intercropping with pot Marigold (*C. officinalis*) afforded the most effective pest control on white cabbage (Jankowska et al. 2009). Populations and ovipositing activities of cabbage pests, namely, cabbage aphid *Brevicoryne brassicae*, flea beetles *Phyllotreta*, small white butterfly *Pieris rapae*, large white butterfly *Pieris brassicae*, cabbage moth *Mamestra brassicae* and larvae and pupae of the diamondback moth *Plutella xylostella*, were significantly reduced. Studies found that when used as a soil mulch (compost), the plant can significantly reduce root-knot nematode, *Meloidogyne incognita*, population in quito orange (*Solanum quitoense*) plantings (Betancourth García et al. 2011). Pérez et al. (2003) found that amending soil with *C. officinalis* flowers significantly reduce reproduction rate of *Meloidogyne artiellia* on chickpea compared to the non-amended treatment.

Comments

C. officinalis is widely grown in Europe, now mainly as an ornamental. It is widely cultivated in the CIS (Commonwealth of Independent States comprising Belarus, Russian Federation and Ukraine) republics, Holland, and in Germany as an herbal medicine.

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Centaurea cyanus

Scientific Name

***Centaurea cyanus* L.**

Synonyms

Centaurea concinna (Boiss. & A. Huet.) Trautv., *Centaurea concinna* Willd. ex Steud., *Centaurea cyaneum* St.-Lag., *Centaurea cyanus* var. *denudata* Suksd., *Centaurea hoffmanniana* Asch., *Centaurea lanata* Roxb., *Centaurea pulcherrima* Wight ex DC., *Centaurea pulchra* DC., *Centaurea rhizocephala* Trautv., *Centaurea segetalis* Salisb., *Centaurea umbrosa* Reut., *Cyanus arvensis* Moench, *Cyanus cyanus* Hill, *Cyanus dentatofolius* Gilib., *Cyanus vulgaris* Delarbre, *Jacea segetum* (Hill) Lam., *Leucacantha cyanus* (L.) Nieuwl. & Lunell.

Family

Asteraceae

Common/English Names

Bachelors Button, Blue Bottle, Blue Cap, Blue poppy, Blueblow, Bluebonnets, Bluebottle, Boutonniere Flower, Cornflower, Cyani Flower, Garden Cornflower, Hurtsickle

Vernacular Names

Brazil: Escovinha, Fidalguinhos
Czech: Chrpa Modrá, Chrpa Modrák, Chrpa Polní
Danish: Kornblomst
Dutch: Korenbloem
Eastonian: Rukkilill
Esperanto: Cejano, Centaŭreo Grenkampa, Grenfloro
Finnish: Ruiskaunokki, Ruiskukka
French: Barbeau, Barbeau Bleu, Bleuet, Bleuet Des Champs, Casse Lunette, Centaurée Bleue, Centaurée Bleuet, Centaurée Bluet
Gaelic: Gormán
German: Blauchrut, Blaue Kornblume, Blaumütze, Cyane, Hunger, Hungerblume, Kaiserblume, Kornbeisser, Kornblume, Kornfresser, Kornmutter, Kornnelke, Kornnägeli, Kreuzblume, Rockenblume, Roggenblume, Schanelke, Sichel-blume, Sträpsen, Tremisse, Trämpsen, Zachariasblume, Ziegenbein
Hungarian: Búzavirág, Kék Búzavirág, Vetési Búzavirág
Icelandic: Akurprýði, Garðakornblóm, Kornblóm
Italian: Fiordaliso, Fiordaliso Vero
Japanese: Yaguruma-Giku
Norwegian: Åkernellik, Knoppurt, Kornblom, Kornblomst
Polish: Bławatek, Chaber Blawatek, Kolendra Siewna
Portuguese: Ambreta, Centáurea, Ciano, Fidalguinhos, Lóios, Lóios-Dos-Jardins, Loucos-Dos-Jardins, Saudades

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Romanian: Albastrele
Slovašcina: Escovinha, Fidalguinhos
Slovencina: Nevädza Poľná
Spanish: Aciano, Azulejo, Centaura Azul, Pincel
Swedish: Blågubbar, Blåklint, Blåklätt, Klint
Turkish: Maviçiçek, Peygamber Ciçeği
Welsh: Glas Yr Ŷd, Penlas Yr Ŷd

Origin/Distribution

Cornflower is indigenous to Europe, where it occurs as a weed in fields.

Agroecology

It is found especially on porous, nutrient-rich soils with pH 6.6–7.6 in grain fields, rye fields, fallow land, wasteland and roadsides in its native range. It thrives in full sun but has high average daily water requirement.

Edible Plant Parts and Uses

The flowers are eaten cooked or raw as vegetables in salads or as garnish (Facciola 1990; Bown 1995; Rop et al. 2012). An edible blue dye is obtained from the flowers, used for coloring sugar and confections. The young shoots are also eaten (Chiej 1984).

Botany

A robust, herbaceous annual, 20–85 cm with grey-green, distally branched, weakly tomentose, slender stem. Leaves gray-tomentose, alternate, basal leaves linear-lanceolate, 3–10 cm, with entire margins sparsely toothed and acute apices, petiolated, cauline leaves linear, sessile with entire margins. Flower heads (capitula) rounded or flat-topped cymbiform arrays, 2.5–3.5 cm diameter, on long peduncles surrounded by campanulate involucral bracts. Phyllaries green, ovate to oblong, tomentose to subglabrous, margins and erect appendages white to dark brown or black fringed with slender teeth (Plate 1). Capitula's ray florets 25–35, violet blue–blue (Plate 1) (sometimes pinkish or white), obliquely funnel-shaped, tip lobed, those of sterile florets raylike and enlarged, 20–25 mm those of fertile florets 10–15 mm; disc florets violet blue, tubular, in the centre of capitula. Stamens 5. Pistil of 2 fused carpels. Fruit elliptic, flattish, yellowish, fine-haired, 3.5–4 mm (0.14–0.16 in.) long cypsela, tip with short, stiff unequal bristles.

Plate 1 Opened and unopened cornflowers

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Centaurea cyanus* had a dry matter content (%w/w) of 9.75 %, crude protein of 6.73 g/kg and the following elements (mg/kg fresh mass (FM): P 534.48 mg, K 3568.77 mg, Ca 246.18 mg, Mg 138.49 mg, Na 74.28 mg, Fe 6.89 mg, Mn 2.29 mg, Cu 0.89 mg, Zn 7.59 mg and Mo 0.49 mg.

From the aerial plant parts, six flavonoid aglycons (quercetin, kaempferol, isorhamnetin, apigenin, luteolin, hispidulin), 8 flavonoid glucosides (quercetin 7-*O*-β-D-glucoside (quercimeritrin), isorhamnetin-7-*O*-β-D-glucoside, kaempferol 7-*O*-β-D-glucoside, apigenin 4′-*O*-β-D-glucoside, apigenin 7-*O*-β-D-glucoside (cosmossiin), luteolin 7-*O*-β-D-glucoside (cynaroside), apigenin 7-apioglucoside (apiin), luteolin 7-apioglucoside (graveobioside)) and four hydroxycinnamic acids (caffeic, chlorogenic, neochlorogenic and

isochlorogenic acids) were isolated (Litvinenko and Bubenchikova 1988). Also, amino acids arginine, serine, methionine, proline, glutamic acid, tryptophan, alanine, phenylalanine and threonine were detected. Apigenin-4′-*O*-(6-*O*-malonil-glucoside)-7-*O*-glucuronide, methyl-apigenin and methyl-vitexin,cyanidin-3-*O*-succinyl-glucoside-5-*O*-glucoside/centaurocyanin (the marker compound), cyanidin-3,5-diglucoside/cyanidin, quercetin-3-*O*-gluco-rhamnoside/rutoside, isorhamnetin-7-*O*-glucoside, naringenin and naringenin-7-*O*-gluco-rhamnoside were also reported from cornflower (Pirvu et al. 2012).

The following phenolic compounds were found in the flowers: *cis* and *trans*-caffeic acids, protocatechuic and chlorogenic acids, *p*-hydroxybenzoic, *p*-coumaric, vanillic, syringic, ferulic, salicylic and benzoic acids, as well as *cis*-sinapic acid, *trans*-sinapic acids or *o*-hydroxyphenylacetic acid and *p*-hydroxyphenylacetic acids (Murav'eva and Bubenchikova 2007; Pirvu et al. 2012) and coumarins: 7-hydroxy-6-methoxycoumarin (scopoletin) and 7-hydroxycoumarin umbelliferone (Bubenchikova 1990).

Blue cornflower pigment protocyanin was found to have a complex of six molecules each of anthocyanin (centaurocyanin, cyanidin 3-*O*-(6-*O*-succinylglucoside)-5-*O*-glucoside) and flavones glycoside (apigenin 7-*O*-glucuronide-4′-*O*-(6-*O*-malonylglucoside), with metals one ferric iron, one magnesium and two calcium ions (Shiono et al. 2005; Takeda et al. 2005). *Centaurea cyanus* flowers were found to contain phenylpropanic compounds, flavonoids and anthocyanins and tannins (Chiru 2009). Anthocyanins were found to confer diuretic, antiinflammatory and healing properties. Red flowers were found to have four to five times more anthocyanins and also phenolic compounds than blue flowers.

The methanol extract of the seeds of *Centaurea cyanus* afforded four indole alkaloids: moschamine, *cis*-moschamine, centcyamine and *cis*-centcyamine (Sarker et al. 2001). Epoxylignans, berchemol and lariciresinol 4-*O*-β-D-glucopyranoside were found in the seeds of *C. cyanus* (Shoeb et al. 2004).

Volatiles emitted from mechanically damaged *C. cyanus* leaves included predominantly (100–1,000 μg) *cis*-3-hexenyl acetate; *cis*-3-hexenol, β-caryophyllene and germacrene D; *trans*-β-farnesene (38–100 μg) and 1–37 μg of *trans*-2-hexanal, hexyl acetate, hexanol, *trans*-2-hexenol, α-copaene, β-cubebene, γ-amorphene/γ-muurolene, α-muurolene, unknown sesquiterpene, bicyclogermacrene, δ-cadinene and geranylacetone (Beck et al. 2008). *C. cyanus* had been reported to attract the weevil, *Ceratapion basicorne*, a candidate for biological control.

Antioxidant Activity

Cornflowers were found to have a total antioxidant capacity of 6.81 g ascorbic acid equivalent/kg fresh mass (FM), a total phenolic content of 4.76 g gallic acid/kg/FM and total flavonoid content of 1.81 g rutin/kg FM (Rop et al. 2012).

Antiinflammatory Activity

Different pharmacological experiments (inhibition of carrageenan, zymosan and croton oil-induced oedemas, inhibition of plasma haemolytic activity, induction of anaphylatoxin activity) showed that polysaccharides extracted from *C. cyanus* flower heads had antiinflammatory properties and interfered with complement (Garbacki et al. 1999). Additionally, these polysaccharides were found to be mainly composed of galacturonic acid, arabinose, glucose, rhamnose and galactose. The findings rationalized the use of cornflower flowers in European phytotherapy for the treatment of minor ocular inflammations.

Cytotoxicity Activity

Four indole alkaloids, moschamine, *cis*-moschamine, centcyamine and *cis*-centcyamine, isolated from the seeds exhibited cytotoxicity as determined by brine shrimp lethality bioassay (Sarker et al. 2001). Crude extracts of *Centaurea cyanus* exhibited cytotoxicity in *Artemia salina* and human fibrosarcoma cells, and were found to contain guaianolides (Bruno et al. 2005). The inflorescence and root ethanol extracts of *C. cyanus*

elicited antileukemic properties and induced cell death via apoptosis (Wegiera et al. 2012).

Serotoninergic and COX Inhibitory Activities

Moschamine, a safflomide-type phenylpropenoic acid amide found in *C. cyanus*, was found to exhibit serotoninergic and COX inhibitory activities (Park 2012). At the concentration of 10 µmol/l, moschamine was able to inhibit forskolin-stimulated cAMP formation by 25 %, via inhibiting serotonin receptors in the OK cells. The inhibition was repressed by two 5-HT1 antagonists (Nan-190 and spiperone), suggesting that moschamine may suppress cAMP formation via binding to 5-HT1 receptors in the cells. Also, moschamine being a very potent compound inhibited COX-I by 58 % and COX-II by 54 %, at the concentration of 0.1 µmol/l.

Antiulcerogenic Activity

The crude aqueous, ethanol and acetone extracts of *C. cyanus* flower head and aerial parts were found to have potent gastroprotective effect using the stress-induced ulcer model in rats (Pirvu et al. 2012). The polyphenol fraction of the acetone extract contained high levels of polysaccharides and minerals (over 60 %) and modest level of quercetin, apigenin and caffeic acid derivatives (<1 %).

Traditional Medicinal Uses

Cornflower has been used in herbal medicine for a long time (Grieve 1971; Launert 1981; Chiej 1984; Chopra et al. 1986; Bown 1995; Chevallier 1996) but is seldom used nowadays (Chiru 2009). The dried flowers are antipruritic, antitussive, astringent, mildly diuretic, emmenagogue, ophthalmic, very weakly purgative and tonic. An infusion can be used in the treatment of dropsy, constipation, kidney ailments, or as a mouthwash for ulcers and bleeding gums. The infusion is also taken as a bitter tonic and stimulant for the liver, improving digestion as well as improving resistance to infections. An eye wash prepared with cornflower blossoms is employed as an antiinflammatory for eye ailments, conjunctivitis, as well as to relieve strained, tired, or puffy eyes. Blue blossoms infused in water are held to have both curative and calming action for nervous disorders. Eye wash is reputed to strengthen weak eyes. Traditionally it is said to work best on blue eyes while *Plantago major* (great plantain) was used for brown eyes. The seeds are employed as a mild laxative for children. Cornflower leaves are used to create a cleansing facial steam for dry sensitive skin. A decoction of the leaves is antirheumatic.

Other Uses

The cornflower is considered to be a good companion, in small quantities, for cereal crops and a good plant for bees, butterflies and moths. Flowers are popularly used in fresh and dried floral arrangements. A blue dye is obtained from the petals when mixed with alum; the dull impart a lovely color to linen but the dye is not permanent. Extracts of the plant are used in hair shampoos and rinses.

In folklore, cornflowers were worn by young men in love; if the flower faded too quickly, it was taken as a sign that the man's love was not returned.

Comments

The blue cornflower is the national flower of Estonia and also one of the national flowers of Germany.

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Chrysanthemum morifolium

Scientific Name

***Chrysanthemum morifolium* Ramat.**

Synonyms

Anthemis artemisifolia Willd., *Anthemis grandiflora* Ramat., *Anthemis stipulacea* Moench, *Chrysanthemum hortorum*, *Chrysanthemum hortorum* W. Mill., *Chrysanthemum maximoviczianum* Ling, *Chrysanthemum maximoviczianum* var. *maximoviczianum*, *Chrysanthemum morifolium* var. *genuinum* Hemsley, *Chrysanthemum morifolium* var. *morifolium*, *Chrysanthemum morifolium* var. *sinense* (Sabine) Makino, *Chrysanthemum procumbens* Blume, *Chrysanthemum sabini* Lindl., *Chrysanthemum sinense* Sabine ex Sweet, *Chrysanthemum sinense* Sabine, *Chrysanthemum sinense* var. *hortense* Makino ex Matsum., *Chrysanthemum sinense* var. *sinense*, *Chrysanthemum stipulaceum* (Moench), *Dendranthema grandiflorum* (Ramat.) Kitam., *Dendranthema morifolium* (Ramat.) Tzvelev, *Dendranthema sinensis* (Sabine) Des Moul., *Matricaria morifolia* (Ramat.) Ramat., *Pyrethrum sinense* (Sabine) DC., *Pyrethrum sinense* var. *sinense*, *Tanacetum morifolium* (Ramat.) Kitam., *Tanacetum sinense* (Sabine) Sch. Bip.

Family

Asteraceae

Common/English Names

Chrysanthemum, Mum, Mums, Florists Chrysanthemum, Florist's Daisy, Garden Mums

Vernacular Names

Brazil: Crisântemo, Crisântemo-Da-China, Crisântemo-Do-Japão, Monsenhor
Chinese: Chu Hua, Huangjuhua, Ju Hua, Qui Hua
Costa Rica: Crisántemo
Czech: Listopadka Velkokvětá
French: Chrysanthème
German: Chrysantheme, Garten-Chrysantheme
Honduras: Crisantemo, Margarita, Rosa De Novia
India: Gundandi (Hindi), Chandramukhi (Manipuri)
Indonesian: Bunga Krisan
Japanese: Kangiku, Ryouri-Giku, Shokoyu-Giku
Korean: Guk Hwa
Malaysia: Kek Hwa, Bunga Chrysanthemum
Nicaragua: Margarita
Philippines: Manzanilla (Iloko), Rosas De Japon (Spanish), Rosas De Japon (Tagalog)
Russian: Chrisantema Šelkovicelistnaja, Kitajskaja, Krupnocvetovaja
Spanish: Crisantemo
Swedish: Krysantemum
Thai: Khek-Huai
Vietnamese: Bạch Cúc, Cúc Hoa Trắng, Đại Cúc

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Origin/Distribution

Garden Chrysanthemum is native to China. It has been introduced as an ornamental to Europe, North and South America, Asia, Australia and South Africa.

Agroecology

Chrysanthemum prefers mild cool climates and is grown in areas with mean temperature of 16–24 °C. They are frost sensitive, and low temperature below 10 °C is detrimental for plant growth, development and flowering. Optimum temperature for flowering has been reported to be in the range of 18–21 °C (De Jong 1978; Karlsson et al. 1989). Langton and Horridge (2006) found that chrysanthemum flowered earlier when grown in a 24 °C day/14 °C night temperature regime compared with alternating between continuous 114 and 24 °C conditions on 2-day or 14-day cycles. Karlsson et al. (1989) suggested that chrysanthemum flowering was dependent upon an interaction between day and night temperature, as well as the incident daily photosynthetic photon flux. They also found that a night temperature between 17 and 18 °C yielded the largest flowers and the shortest time to flower in 'Bright Golden Anne', regardless of day temperature or irradiance level.

van der Ploeg et al. (2007) divided chrysanthemum cultivation into a long-day (LD) period, during which the plants grow vegetatively, and a short-day (SD) period. During this latter period, flower initiation and further development takes place. The number of days from the start of SD to harvest is referred to as the reaction time, and this trait is very sensitive to temperature, showing a definite temperature optimum (De Jong 1978). Chrysanthemums are short-day (SD) plants; the natural photoperiod of about 12 hours is suitable for good flowering of most cultivars (Kofranek 1980; Kahar 2008). Kahar (2008) found that shortening the day length from about 12 hours under natural photoperiod to 8 hours with and without incandescent lighting did not really improve flowering time and flower quality of *C. morifolium* cv. Reagan Sunny.

Garden chrysanthemum thrives best in fertile, moist, well-drained slightly acidic soil rich in organic matter in full sun but will grow in less ideal conditions.

Edible Plant Parts and Uses

The flowers and young leaves are edible (Read 1946; Uphof 1968; Tanaka 1976; Facciola 1990). Leaves are cooked or boiled and used as greens or as fritters. They are tangy, bitter and mildly peppery in flavour. The leaves can also be used to flavour vinegar. An aromatic tea is also made from the leaves. The flowering heads and petals are parboiled, seasoned with vinegar or soya sauce, and served as a salad with tofu. They can also be prepared as tempura, pickled, dried or added to soups. In Chinese cuisine, chrysanthemum petals are mixed into a thick snake meat soup to enhance the flavour. In Japan, small chrysanthemum flowers are used as garnish in sashimi. A tangy aromatic tea is made from the flowers or flower petals, commonly called chrysanthemum tea, and is drunk without or with little sugar or honey. In Korea, a rice wine flavoured with chrysanthemum flowers is called 'gukhwaju'. Chrysanthemum flowers are also widely used as a food supplement and are considered a health food by many consumers (Chu et al. 2004; Lai et al. 2007).

Botany

An herbaceous perennial grows to 1 m high with erect or ascending sometimes procumbent, sparsely branched stem with dense pubescent foliage. Leaves olive-green, aromatic, weakly pubescent to subglabrous on both surfaces on 1–2 cm long petioles. Lamina ovate to oblong ovate in outline, 4–10 cm by 3–5 cm wide, deeply cut (pinnatifid) to shallowly pinnatipartite into short, obtuse, terminal and lateral lobes (Plates 1 and 2), truncate to subcordate at the base, upper leaves entire and smaller. Capitula 3–6 cm across, numerous on 5 cm long pubescent peduncles in lax corymbs. Involucre 10–22 mm in diameter, 4–5 seriate, phyllaries outer ones deltoid-ovate,

Plate 1 Garden chrysanthemum leaves and immature flower buds

Plate 3 Close view of chrysanthemum (anemone flower type)

Plate 2 Garden chrysanthemum plants in full bloom

middle ones ovate, innermost elliptic, broader at apex. Ray florets yellow to variously coloured (pink, white, orange, lavender, purple, red, rust, bronze, olive-green) in cultivars with entire or triserrate oblong ligules (Plates 2, 3, 4, 5, 6, 7 and 8). Disc florets yellow to pale greenish-yellow with 5-toothed corolla tube. Cypsela obovoid, 1.5–2 mm, light brown.

Nutritive/Medicinal Properties

Flower Phytochemicals

Four kinds of normal saturated hydrocarbons, C_nH_{2n+2} ($n = 19$–22), namely, nonadecane, eicosane, heneicosane and docosane; and campesterol, stigmasterol, β-sitosterol, α-amyrin, palmitic acid, linoleic acid, stearic acid, behenic acid and lignoceric acid were detected in *Chrysanthemum morifolium* petals (Takahashi et al. 1975). Also 11 free amino acids, arginine, aspartic acid, threonine, serine, glycine, proline, glutamic acid, alanine, leucine, isoleucine and valine, were identified. Two hydroxy taraxastane-type triterpenes, faradiol and heliantriol C, were isolated from the ligulate flowers of *C. morifolium* (Yasukawa et al. 1998). Content of chlorogenic acid found in the flowers were 0.060–0.467 % (Li et al. 1999). Three flavonoids in *C. morifolium* were identified as acacetin-7-*O*-β-D-glucoside, apigenin-7-*O*-β-D-glucoside and luteolin-7-*O*-β-D-glucoside (Liu et al. 2001). From *C. morifolium*, eight compounds were isolated and identified as chrysoeriol (1), apigenin (2), luteolin (3), quercetin (4), chrysoeriol-7-*O*-β-d-glucoside (5), apigenin-7-*O*-β-D-glucoside (6), luteolin-7-*O*-β-D-glucoside (7) and tilianin-7-*O*-β-D-glucoside (8) (Jia et al. 2003).

From the nonsaponifiable lipid fraction from the methanol flower extract, 24 triterpene diols and triols were isolated, of which three were new compounds: (24*S*)-25-methoxycycloartane-3β,24-diol, (24*S*)-25-methoxycycloartane-3β,24,28-triol, and 22α-methoxyfaradiol (Ukiya et al. 2001). Faradiol (9) and heliantriol C (19), present in the nonsaponifiable lipid fraction and as the 3-*O*-palmitoyl esters in the *n*-hexane soluble fraction, were the most predominant triterpene diol and triol constituents. Fifteen pentacyclic triterpene diols and triols, consisting of six taraxastanes,

Plate 4 (**a**, **b**) Chrysanthemum (spider flower type)

Plate 5 Chrysanthemum (decorative flower type)

Plate 6 Chrysanthemum (single daisy-like flower type)

Plate 7 Chrysanthemum (cushion or azalea mums flower type)

faradiol, heliantriol B0, heliantriol C, 22α-methoxyfaradiol, arnidiol and faradiol α-epoxide; five oleananes, maniladiol, erythrodiol, longispinogenin, coflodiol and heliantriol A1; two ursanes, brein and uvaol; and two lupanes, calenduladiol and heliantriol B2, were isolated from the nonsaponifiable lipid fraction of the edible flower extract of *C. morifolium* (Ukiya et al. 2002). The flavonoids acacetin, apigenin, luteolin and quercetin were isolated from the ethyl acetate fraction of the flower methanol extract (Miyazawa and Hisama 2003). The amount of luteolin was found to be lower than that of luteolin-β-D-glucoside (Hu et al. 2004). Two dicaffeoylquinic acids,

Plate 8 Green-flowered chrysanthemum (anemone flower type)

3,5-dicaffeoyl-epi-quinic acid and 1,3-dicaffeoyl-epi-quinic acid, were isolated from *Chrysanthemum morifolium* together with six known dicaffeoylquinic acid derivatives and three flavonoids (Kim and Lee 2005). Two flavonoid glycosides were isolated from the flowering heads and their structures elucidated as luteolin 4′-methoxy-7-*O*-(6″-*O*-*acetyl*)-β-D-glucopyranoside and acacetin 7-*O*-(3″-*O*-acetyl)-β-D-glucopyranoside (Zhang et al. 2006). The flowers were found to contain D-mannitol and saccharide (Cheng et al. 2008).

Sixteen xanthophylls were isolated from chrysanthemum petals among which. Among them, (3S,5S,6R,3'R,6'R)-5,6-dihydro-5,6-dihydroxylutein (1) and five di-Z geometrical isomers of lutein-5,6-epoxide, i.e., 9Z,13'Z (2), 13Z,9'Z (3), 9'Z,13'Z (4), 9Z,13Z (5), and 9Z,9'Z (7), had never before been identified as natural products (Kishimoto et al. 2004). All of the carotenoids isolated from chrysanthemum, except for (9*Z*)-violaxanthin, are β, ε-carotene (α-carotene) derivatives.

Total anthocyanins and total carotenoids in μg/g fresh weight in *C. morifolium* cv. Dark Dramatic (orange flowers) were 792.7 and 343.4 μg, respectively; cv. Florida Marble (yellow flowers) was 144.9 μg and cv. Vodka Lime (yellow flowers) was 121.9 μg (Kishimoto et al. 2007). Eleven compounds were identified in the flowers; luteolin (1), quercetin (2), acacetin 7-*O*-β-D-(3″-acetyl)-glucopyranoside (3), luteolin 7-*O*-β-D-(6″-acetyl)-glucopyranoside (4), hesperetin 7-*O*-β-D-glucopyranoside (5), acacetin 7-*O*-β-D-glucopyranoside (6), diosmetin 7-*O*-β-D-glucopyranoside (7), apigenin 7-*O*-β-D-glucopyranoside (8), hesperidin (9), linarin (10) and luteolin 7-*O*-β-D-glucopyranoside (11) (Wang et al. 2008c). The common chemical constituents in the essential oil of the five Hangjuhua cultivars were juniper camphor (10.51–13.28 %), methyl β, β-dimethylbenzenepropanoic acid ester (1.51–4.89 %), 1,3,3-trimethylcyclohex-1-ene-4-carboxaldehyde, borneol, α-curcumene, α-bisabolol, *cis*-caryophyllene, benzyl benzoate, 2,4-decadienal and heneicosane (Guo et al. 2008). Juniper camphor was found to be a characteristic constituent in the essential oil of Hangjuhua. A *p*-hydroxyphenylacetyl flavonoid, diosmetin 7-(6″-*O*-*p*-hydroxyphenylacetyl)-*O*-β-D-glucopyranoside, was isolated from the flowers together with five known flavonoids, luteolin, diosmetin, diosmetin 7-*O*-β-D-glucopyranoside, diosmin and scolimoside, and four known caffeoylquinic acid derivatives, macranthoin F 3,5-dicaffeoylquinic acid, 1,3-dicaffeoyl-epi-quinic acid and chlorogenic acid (Xie et al. 2009).

Thirty-three volatiles were extracted and identified in dry chrysanthemum flowers comprising mainly unsaturated organic compounds, such as monoterpenes, sesquiterpenes and their oxygenous derivatives; triterpenoids; and aliphatic compounds (Wang et al. 2008a). The compounds included the following: camphene (112.7 μg/g), pinene (106.3 μg/g), bornyl acetate (67.3 μg/g), 3-carene (62. μg/g), eucapyptol (52.1 μg/g), 1,7,7-trimethyl-bicyclo[2.2.1]hept-2-ene (41.3 μg/g), camphor (29.4 μg/g), caryophyllene oxide(20.0μg/g),4-methylene-1-(1-methylethyl)-cyclohexene (13.5 μg/g), 2,2,3-trimethyl-3-cyclopentene-1-acetaldehyde (10.9 μg/g), 1-methyl-4-[1-methylethyl]-1,4-cyclohexadiene (9.2 μg/g), borneol (4.2 μg/g), 6,6-dimethyl-2-methylene-bicyclo[2.2.1]heptan-3-one (4.2μg/g),(1*S*)-6,6-dimethyl-2-methylenebicyclo [3.1.1]heptane (3.4 μg/g), bicyc[3.1.1]hept-2-en-4-ol,2.6.6-trimethyl-,acetate (3.1 μg/g), 6,6-dimethyl-2-methylenecyclo[3.1.1]heptane (2.7 μg/g), 4-methyl-1-[1-methylethyl]-3-cyclohexen-1-ol (1.8 μg/g), 2-methyl-5-(1-methylethyl)-bicyclo [3.1.0]hex-2-ene (1.7 μg/g), oct-1-enyl acetate (1.7 μg/g), 1-methyl-4-[1-

methylethylidene]-cyclohexene (1.6 μg/g), 2-methyl-butanoic acid 2-methylbutylester (1.6 μg/g), 4-camphene (1.4 μg/g), 3,7,7-trimethyl-bicyclo[4.1.0]hept-2-ene (1.4 μg/g), 6,6-dimethyl-bicyclo[3.1.1]hept-2-ene-2-carboxaldehyde (1.4 μg/g), isobornyl acetate (1.4 μg/g),3-cyclopentene-1-acetaldehyde,2,2,3-trimethyl (1.3 μg/g), 1-methyl-3-(1-methylethenyl)-cyclohexene (1.3 μg/g), 1,6,10-dodecatriene,7,11-dimethyl-3-methylene-, [*Z*] (1.1 μg/g), 1α,2,3,5,6,7,7α,7β-octahydro-1,1,7,7α-tetramethyl-1*H*-cyclopropa[α]naphthalene (0.8 μg/g), 1,2,3,4,4α,5,6,8α-octahydro-7-methyl-4-methylene-1-(1-methylethyl)-naphthalene (0.7 μg/g), caryophyllene (0.7 μg/g), decahydro-1,1,7-trimethyl-4-methylene-1*H*-cycloprop[e]azulen-7-ol (0.6 μg/g) and 2,3,6,7,8,8α-hexahydro-1,4,9,9-tetramethyl-1*H*-3α,7-methanoazulene (0.6 μg/g).

Twenty-eight 3-hydroxy triterpenoids of taraxastane-type, ψ-taraxasterol, faradiol, heliantriol C, 22α-methoxyfaradiol, faradiol α-epoxide, arnidiol and taraxasterol; of oleanane type, β-amyrin, maniladiol, erythrodiol, longispinogenin and cofflodiol; of ursane-type α-amyrin, brein and uvaol; of lupine-type, lupeol, 3-epilupeol, calenduladiol and heliantriol B_2; of taraxane-type, taraxerol; of cycloartane-type, cycloartenol, 24-methylenecycloartanol, (24*R*)-cycloartane-3β,24,25-triol, (24*S*)-cycloartane-3β,24,25-triol and (24*S*)-25-ethoxycycloartane-3β,24-diol; of tirucallane-type, helianol, 4,5α-epoxyhelianol and Δ^7-tirucallol; and of dammarane-type, dammaradienol, were isolated from the nonsaponifiable lipid fraction of *C. morifolium* flower extract (Akihisa et al. 2005). One lupane-type 3α-hydroxy triterpenoid (3-epilupeol) was derived from lupeol. Chlorogenic acid; 1,5-dicaffeoylquinic acid; isochlorogenic acid A; isochlorogenic acid C; luteolin-7-*O*-β-d-glucoside; and apigenin-7-*O*-β-D-glucoside were detected in *C. morifolium* flower head (Qin and Wen 2011). The contents of the components in the steam-blanched flower heads were significantly higher than those non-blanched. The contents of chlorogenic acid and isochlorogenic acid A in the steam-blanched semi-opened flower heads were higher than fully opened ones by 53 and 41 %, respectively.

Chrysanthemum morifolium flowers afforded mixtures of the C-3 palmitate and myristate esters (3:2) of mailadiol (1), the C-3 palmitate and myristate esters (3:2) of heliantriol C (2) and fatty acid esters (1:1) of faradiol (3) and arnidol (Ragasa et al. 2005). Two acidic polysaccharides, F4 and F5, were isolated from *C. morifolium* flowers (Zheng et al. 2006). F4 contained arabinose, galactose and galacturonic acid units in a molar ratio of 1.0:2.3:6.8 and F5 contained arabinose, rhamnose galactose and galacturonic acid units in a molar ratio of 1.0:3.2:1.0:4.3. Further, F4 had a homogalacturonan main chain with arabinogalactan side chain linked to three position of (1 → 3,4)-linked galacturonan and F5 had a rhamnogalacturonan main chain with arabinogalactan side chain linked to 3 position of (1 → 3,4)-linked galacturonan or 4 position of (1 → 2,4)-linked rhamnose. Biological tests revealed that F4 and F5, two new acidic polysaccharides from the flowers, could simulate the mitogen-induced T and B lymphocyte proliferation in-vitro.

Lin and Harnley (2010) identified 46 flavonoids and 17 caffeic acid derivatives in the aqueous methanol extract of chrysanthemum (*Chrysanthemum morifolium*) flowers. The following flavonoids were identified: 6,8-C,C-diglucosylapigenin; 6-C-xylosyl-8-C-glucosylapigenin; 6-C-glucosyl-8-C-arabinosylapigenin; 6-C-arabinosyl-8-C-glucosylapigenin; luteolin 7-*O*-dihexoside; isorhamnetin 3-*O*-diglucoside; trihydroxymethoxyflavone 7-*O*-diglucoside; luteolin-*O*-glucuronylhexoside; luteolin 7-*O*-pentosylhexoside; luteolin-7-*O*-rutinoside; quercetin-7-*O*-galactoside; quercetin-3-*O*-*glucoside*; eriodicyol-7-*O*-glucoside; luteolin-7-*O*-glucoside; luteolin-7-*O*-glucuronide; diosmetin 7-*O*-diglucoside; apigenin-7-*O*-rutinoside; diosmetin 7-*O*-rutinoside; apigenin-7-*O*-glucoside; luteolin glucoside; diosmetin 7-*O*-galactoside; diosmetin-7-*O*-glucoside; luteolin-7-*O*-6″-malonylglucoside; quercetin glycoside; diosmetin-7-*O*-glucuronide; trihydroxymethoxyflavone glucoside; acacetin 7-*O*-diglucoside; apigenin-7-*O*-6″-malonylglucoside; luteolin-7-*O*-6″-acetylglucoside; apigenin 7-*O*-6″-acetylglucoside; diosmetin-7-*O*-6″-malonylglucoside; diosmetin-7-*O*-6″-acetylglucoside; acacetin 7-*O*-rutinoside; luteolin; acacetin-7-*O*-galactoside; acacetin 7-*O*-glucuronide;

acacetin-7-*O*-6″-malonylgactoside; apigenin; diosmetin; acacetin-7-*O*-6″-acetylgalactoside; acacetin-7-*O*-acetylgalactoside; acacetin-7-*O*-acetylgalactoside; acacetin-7-*O*-malonylacetylgalactoside; eupatorina or chrysosplenol; chrysosplentin or its isomer; and acacetin. The following hydroxycinnamoylquinic acids were found: 1-caffeyolquinic acid; 3-caffeyolquinic acid; caffeic acid 4-glucoside; chlorogenic acid; 4-caffeoylqunic acid; 5-sinapoylquinic acid; caffeic acid; 1,3-di-caffeoylquinic acid; di-caffeoylquinic acid glucoside; di-caffeoylquinic acid glucoside; 3,4-di-caffeoylquinic acid; 1,4-di-caffeoylquinic acid; 1,5-di-caffeoylquinic acid; 3,5-di-caffeoylquinic acid; 3-methoxyoxaloyl-1,5-di-caffeoylquinic acid; 4,5-di-caffeoylquinic acid; 4-caffeoyl-5-feruloylquinic acid; 4-caffeoyl-5-feruloylquinic acid isomer; and 3,4,5-tricaffeoylquinic acid.

Eight flavonoids vitexin-2-*O*-rhamnoside 0.10 mg/g, quercetin-3-galactoside 2.46 mg/g, luteolin-7-glucoside 50.59 mg/g, quercetin-3-glucoside 1.33 mg/g, quercitrin 21.38 mg/g, myricetin 2.13 mg/g, luteolin 5.22 mg/g, apigenin 0.70 mg/g and kaempferol 0.14 mg/g were identified in *C. morifolium* flowers (Sun et al. 2010). Fifty-eight volatiles were identified in the flowers: β-humulene 96.48 %, ledene oxide-(I) 52.96 %, *cis*-*Z*-α-bisabolene epoxide 36.84 %, 3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran 36.00 %, *trans*-limonene oxide 26.52 %, 2-methyl-5-(1-methylethenyl)-cyclohexanone 22.51 %, 2,6-dimethyl-1,3,6-heptatriene 19.24 %, 1,6-dibromo-hexane 18.79 %, β-elemene 16.64 %, bromo-cyclohexane 15.76 %, 1-(1,5-dimethyl-4-hexenyl)-4-methylbenzene 15.28 %, 3,3,6,6-tetraethyl-ricyclo[3.1.0.0(2,4)]hexane 15.25 %, 3-cyclohexene-1-methanol 13.29 %, 6-isopropenyl-4,8α-dimethyl-1,2,3,5,6,7,8,8α-octahydronaphthalen-2-ol 12.41 %, caryophyllene 11.57 %, 1-tert-butyl-1,5-cyclooctadiene 11.49 %, 6-methyl-5-hepten-2-one 10.53 %, eicosane 9.54 %, caryophyllene oxide 9.45 %, docosane 8.90 %, 5-(1,5-dimethyl-4-hexenyl)-2-methyl-1,3-cyclohexadiene 7.80 %, bicyclo[10.1.0]tridec-1-ene 7.54 %, isoaromadendrene epoxide 7.44 %, 1,5,9,13-tetradecatetraene 7.01 %, eudesma-4(14),11-diene 6.54 %, 1*H*-cyclopropa[α]naphthalene 6.53 %, heneicosane 6.35 %, cedrol 6.29 %, (1,1-dimethylpropyl)-benzene 6.08 %, camphene 5.85 %, longifolenaldehyde 5.81 %, 3-methyl-2-cyclohexen-1-one 5.19 %, 1,7,7-trimethyl-bicyclo[2.2.1]heptan-2-one 5.03 %, *trans*-*Z*-α-bisabolene epoxide 5.01 %, 2,4-bis(1,1-dimethylethyl)phenol 3.03 %, β-sesquiphellandrene 2.96 %, 2,3,3-trimethyl-1-butene 2.92 %, germacrene 2.83 %, 7,11-dimethyl-3-methylene-1,6,10-dodecatriene 2.72 %, 1-methyl-4-(1-methylethylidene)-cyclohexane 2.29 %, 3,5-dimethyl-2-ethyl-1,3-cyclopentadiene 2.21 %, *cis*-α-santalol 2.21 %, 3,4,4-trimethyl-2-cyclohexen-1-one 2.14 %, spathulenol 2.10 %, α-farnesol 2.10 %, borneol 1.88 %, 1,2-benzenedicarboxylic acid, butyl octyl ester 1.75 %, 9,10-dehydro-isolongifolene 1.72 %, 1,3,3-trimethylcyclohex-1-ene-4-carboxaldehyde 1.56 %, α-farnesene 1.48 %, limonene 1.41 %, 1,8-dimethyl-4-(1-methylethyl)-spiro[4.5]dec-8-en-7-one 1.27 %, 5,5-dimethyl-1-ethyl-1,3-cyclopentadiene 1.14 %, α-pinene 1.04 %, 4-bromo-2-methyl-1-butene 0.95 %, 4-methyl-1-(1-methylethyl)-3-cyclohexen-1-ol 0.80 %, 1-(1,4-dimethyl-3-cyclohexen-1-yl)-ethanone 0.64 % and 1,7,7-trimethyl-bicyclo[2.2.1]heptan-2-ol acetate 0.60 %.

The content of flavonoid and chlorogenic acid in *C. morifolium* flowers was the highest at 70 % of full blossom, the anthocyanin at 50 % and polyphenol oxidase (PPO) activity at 30 % (Liang et al. 2007). Differences were found in phenylalanine ammonia-lyase (PAL) and peroxidase (POD) content in the two cultivars; 'huaidabaiju' had 70 and 30 %, and 'huaixiaobaiju' had 50 and 50 %, respectively. From *C. morifolium* cultivars Zaogongju, Wangongju, Huangyaoju, Chuju, Xiaoboju and Daboju, 75, 54, 78, 50, 53 and 43 components were identified, which were composed of 85.67, 82.80, 81.38, 73.22, 71.51 and 72.87 % of the total flower essential oil, respectively (Wang et al. 2008b). Monoterpenoid compounds were more abundant than sesquiterpenoid compounds in the juhua cvs Zaogongju, Wangongju, Huangyaoju, Xiaoboju and Daboju except for Chuju. There was no difference in the constituents of essential oil of Zaogongju and Wangongju; verbenyl acetate was the main chemical constituent and comprised 32.10 and 37.85 % of the total essential oil, respectively.

(1*R*)-camphor and bisabolol oxide A were the predominant constituents in Huangyaoju, comprising 28.70 and 12.58 % of the total essential oil, respectively. β-selinene and borneol were the major constituents in Chuju, comprising 17.85 and 12.84 % of the total essential oil, respectively. Eucalyptol (21.33 %) was the major constituent in Xiaoboju. Verbene oxides and chrysanthenone comprised 25.32 and 8.26 % of the total essential oil, respectively, in the Daboju. The common constituents in the six cultivars of Juhua produced in Anhui province of China were camphene, borneol, bornyl acetate, (1*R*)-camphor, (−)-4-terpineol, α-terpineol, eucalyptol, *cis*-caryophyllene, caryophyllene oxide, juniper camphor, β-sesquiphellandrene, α-curcumene and β-farnesene. Chlorogenic acids, three *p*-coumaroylquinic acids, three feruloylquinic acids, four caffeoylquinic acids, six dicaffeoylquinic acids and two tricaffeoylquinic acids were detected, in herbal chrysanthemum samples (Clifford et al. 2007). Minor components such as five caffeoyl-hexose esters and caffeic acid-4-β-D-glucose, eight caffeoylquinic acid glycosides and 16 dicaffeoylquinic acid glycosides were also present. Succinic acid-containing chlorogenic acids and chlorogenic acids based on epi-quinic acid, previously reported in *Chrysanthemum* spp., were not detected in the samples.

Three unsaturated fatty acid isobutylamides, *N*-isobutyl-2*E*,4*E*,10*E*,12*Z*-tetradecatetraen-8-ynamide(1),*N*-isobutyl-2*E*,4*E*,12*Z*-tetradecatrien-8,10-diynamide (2) and *N*-isobutyl-2*E*,4*E*,12*E*-tetradecatrien-8,10-diynamide (3), were isolated from the leaves and flowers of *C. morifolium* (Tsao et al. 2003). The concentration of compound 1 in chrysanthemum varieties was positively correlated with host-plant resistance against the western flower thrips, *Frankliniella occidentalis*. Chlorogenic acid (5-*O*-caffeoylquinic acid); 2,3,5-*O*-dicaffeoylquinic acid; and "3,3′,4′,5-trihydroxyflavanone-7-*O*-glucuronide (eriodictyol-7-*O*-glucuronide) were isolated from the leaves (Beninger et al. 2004).

Aribaud and Martin-Tanguy (1994a) found that ornithine decarboxylase (ODC) regulated the polyamine putrescine biosynthesis during floral initiation and floral development. Spermidine conjugates were predominant during floral initiation, whereas free amines did not accumulate to any significant extent. Different associations of amides were observed during floral initiation as compared with the reproductive phase. 3,4-Dimethoxyphenethylamine conjugates (water-insoluble compounds) were the predominant amine conjugates observed during flower development. Their results suggested that ODC and polyamine conjugates were involved in regulating floral initiation in *Chrysanthemum morifolium*. They also found that in fertile plants (*C. morifolium* v. Epidote), spermidine conjugates were predominant during floral initiation whereas in male-sterile plants (*C. morifolium* v. Jericho), only putrescine conjugates were detected (Aribaud and Martin-Tanguy 1994b). In both cases, ornithine decarboxylase (ODC) is involved in regulating floral initiation in normal and male-sterile plants. Huh et al. (2005) found that axillary floral bud formation and polyamine contents of nonbranching chrysanthemum were influenced by temperature. They found out that not only low temperature but also the excessively high temperature of 38 °C induced axillary bud formation. Viable axillary buds decreased remarkably at 30 and 34 °C. Exposure to 38 °C increased the putrescine contents and resulted in high putrescine/(spermidine + spermine) ratio as 22 and 26 °C. Temperature of 30 and 34 °C lowered putrescine/(spermidine + spermine) ratio. Results further showed that not polyamine contents but polyamine ratio (putrescine/spermidine + spermine) or transformation of putrescine to spermidine and spermine may be involved in the axillary bud formation in nonbranching *C. morifolium*.

C. morifolium especially the flowers have been reported to contain many phenolic compounds such as flavonoids and hydroxycinnamoylquinic acids, many of which possess a diverse array of biological characteristics such as radical scavenging and antioxidant, antiinflammatory, antivirus, anti-HIV, antimutagenic, anticarcinogenic, anti-hepatotoxic and antiaging activities

that are considered beneficial to human health (Lin and Harnley 2010).

Antioxidant Activity

Chrysanthemum flower extract was found to be rich in flavones which afforded good antioxidative activity in scavenging hydroxyl and oxygen radicals (Zhang et al. 2000). The aqueous chrysanthemum flower extract inhibited the production of free radicals and lipid peroxidation induced by free radicals in the heart and cerebral homogenate of rats (Wang et al. 2001).

Two dicaffeoylquinic acids, 3,5-dicaffeoyl-epi-quinic acid (1) and 1,3-dicaffeoyl-epi-quinic acid, isolated from *C. morifolium* showed potent superoxide anion radical scavenging activity (IC_{50} = 2.9 for 1 and 2.6 μg/ml for 2, respectively) in the xanthine/xanthine oxidase system as compared to quercetin and also showed potent DPPH radical scavenging activity (IC_{50} = 5.6 for 1 and 5.8 μg/ml for 2, respectively) (Kim and Lee 2005). The 60 % methanol flower extracts of *C. morifolium* exhibited high scavenging activities against 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical as well as significant reducing power (Yang et al. 2011). This was attributed to the high total phenolic content (0.37 mg GAE/g). The methanol extract was found to contain 1.34 μg/ml of luteolin. In another study, the methanol extract of *C. morifolium* generally showed higher total antioxidant activity than that of the ethyl acetate extract, and the petroleum ether extract hardly had any antioxidant activity (Liu et al. 2009). The cultivar Mailang exhibited the highest total antioxidant activity, but it showed slightly lower DPPH radical scavenging activity with IC_{50} value of 20.01 mg/l than that of BHT with IC_{50} value of 18.92 mg/l. Its ABTS radical scavenging activity IC_{50} value of 25.93 mg/l was about one third lower than BHT IC_{50} value of 7.72 mg/l.

Studies showed that total flavonoids from *Chrysanthemum morifolium* (TFCM) might improve antioxidant defense system, reverse lipid peroxidation and protect brain, liver and kidney against lead-induced oxidative damage in mice significantly (Xia et al. 2008). The combined treatment of TFCM and DMSA (dimercaptosuccinic acid) could significantly lower the lead levels in blood, brain, liver and kidney and reverse lipid peroxidation and increase antioxidant enzyme levels in lead-poisoned mice dose-dependently, and it had more beneficial effects than treatment with DMSA alone. Radical scavenging activity was found to correlate with the flavonoid components in edible chrysanthemum petals (Sugawara and Igarashi 2009). Radical scavenging activity of polyphenol fractions prepared from each cultivar of *C. x morifolium* was the strongest in cv. Mottenohoka with yellow petals, followed by Kotobuki, Iwakaze and Mottenohoka with pale purple petals. Luteolin 7-*O*-(6″*O*-malonyl)-glucoside, a major flavonoid with the strongest radical scavenging activity, was the most predominant in the yellow petals of the edible chrysanthemum flower Mottenohoka.

Antitubercular Activity

Fifteen 3-hydroxy triterpenoid compounds isolated from the nonsaponifiable lipid fraction of *C. morifolium* flower extract showed a minimum inhibitory concentration (MIC) in the range of 4–64 μg/ml, among which maniladiol (MIC 4 μg/ml), 3-epilupeol (4 μg/ml) and 4,5α-epoxyhelianol (6 μg/ml) exhibited the highest activity against *Mycobacterium tuberculosis* (Akihisa et al. 2005). Cytotoxicity of 3-epilupeol compound against Vero cells gave an IC_{50} value of over 62.5 μg/ml, suggesting some degree of selectivity for *M. tuberculosis*.

Antimutagenic Activity

A methanol extract from *Chrysanthemum morifolium* flower heads exhibited a suppressive effect on umu gene expression of the SOS response in *Salmonella typhimurium* TA1535/pSK1002 against the mutagen 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (furylfuramide) (Miyazawa and Hisama 2003). The ethyl acetate fraction of the flower methanol extract also showed a suppressive effect. The flavonoids

acacetin, apigenin, luteolin and quercetin isolated from the ethyl acetate fraction suppressed the furylfuramide-induced SOS response in the umu test. The ID_{50} (50 % inhibitory dose) values of were 0.62, 0.55, 0.44 and 0.59 μmol/ml, respectively. These compounds had the suppressive effects on umu gene expression of the SOS response against other mutagens, 4-nitroquinolin 1-oxide (4NQO) and *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG), which did not require liver-metabolizing enzymes. These compounds also showed the suppression of SOS-inducing activity against the other mutagens aflatoxin B1 (AfB1) and 3-amino-1,4-dimethyl-5*H*-pyrido [4,3-b]indole (Trp-P-1), which required liver-metabolizing enzymes, and UV irradiation.

Anticancer Activity

Two hundred precancerous patients were treated by the herbal drug Hua-sheng-ping (containing *Chrysanthemum morifolium*, *Glycyrrhiza uralensis*, *Panax notoginseng*) (Yu 1993). The total effective rate was 95.5 % for the drug treatment compared with the control group rate of 57 %. Hydroxy taraxastane-type triterpenes, taraxasterol, heliantriol C and faradiol, isolated from the flowers showed strong inhibitory activity against 12-*O*-tetradecanoyl-phorbol-13-aetate (TPA)-induced inflammation in mice (Yasukawa et al. 1996, 1998). At 0.2 μmol/mouse, these compounds markedly suppressed the tumour promoting effect of TPA (1 μg/mouse) on skin tumour formation following initiation with 7,12-dimethylbenz[a]anthracene (DMBA).

All 15 pentacyclic triterpene diols and triols isolated from the flowers showed inhibitory effects against Epstein–Barr virus early antigen (EBV-EA) activation induced by the tumour promoter, 12-*O*-tetradecanoylphorbol-13-acetate, in Raji cells with potencies either comparable with or stronger than that of glycyrrhetic acid, a known natural anti-tumour promoter (Ukiya et al. 2002). Evaluation of the cytotoxic activity of six compounds, faradiol, heliantriol B0, heliantriol C, arnidiol, faradiol α-epoxide and maniladiol, against 60 human cancer cell lines revealed that arnidiol possessed a wide range of cytotoxicity, with GI_{50} values (concentration that yields 50 % growth) of mostly less than 6 mM. Arnidiol showed cytotoxic activity with GI_{50} values less than 10 mM against all of the human cancer cells tested, namely, leukaemia cell lines, CCFRF-CEM, HL-60 (TB), Molt-4; non-small cell lung cancer cell lines, A549/ATTC, EKVX, HOP-62, NCI-H226, NCI-H23, NCI-H322M, NCI-H522; colon cancer cell lines, COLO 205, HCT-116, HCT-15, HT29, KM12, SW-620; CNS (central nervous system) cancer cell lines, SF-268, SF-295, SF-539, SNB-19, U251; melanoma cell lines, LOX IMVI, MALME-3M, M14, SK-MEL-2, SK-MEL-28, SK-MEL-5, UACC-257, UACC-62; ovarian cancer cell lines, IGROVI, OVCAR-3, OVCAR-4, OVCAR-5, OVAR-8, SK-OV-3; renal cancer cell lines, 786-0, A498, ACHN, CAKI-1, RXF 393, SN12C, TK-10; prostate cancer cell lines, PC-3, Du-145; and breast cancer cell lines, MCF7, NCI/ADR-RES, MDA-MB-231/ATTC, HS 578T, MDA-MB-435, MDA-N, BT-549, T-47D, with two exceptions for leukaemia cells (RPMI-8226 and SR: GI_{50}, 100 mM) which were relatively insensitive to Arnidiol. Arnidiol showed significant cytotoxicity, especially against a leukaemia HL-60 cell with a GI_{50} 0.47 mM. The cytotoxic activities of the other five compounds were not remarkable. Heliantriol C (3) (GI_{50} value, 10.5–23.3 mM) and faradiol α-epoxide (GI_{50}, 13.7–44.0 mM) exhibited some moderate cytotoxicity for all of the cancer cells evaluated. Whereas faradiol showed marked cytotoxicity for leukaemia (CCRFCEM: GI_{50}, 3.2 mM; K-582: GI50, 4.2 mM; SR: GI_{50}, 3.5 mM) and non-small cell lung cancer (EKVX: GI50, 2.2 mM), it showed moderate activity for the other cells (GI50, 10.5–86.9 mM). Heliantriol B0 for renal cancer (RXF 393: GI50, 7.1 mM) and breast cancer (MCF7: GI50, 8.4 mM) and maniladiol for renal cancer (RFX 393: GI50, 7.3 mM) and breast cancer (T-47D: GI50, 9.8 mM) showed some marked activity, but the other cells were relatively insensitive for these compounds (GI50, 11.7–97.4 mM).

Luteolin and diosmetin isolated from the flowers exhibited significant cytotoxicities against

human colon cancer cell colon 205, with their IC_{50} values being 96.9 and 82.9 μM, respectively (Xie et al. 2009).

Antiviral Activity

An active anti-HIV principle, acacetin-7-*O*-β-D-galactopyranoside, was isolated from *C. morifolium* (Hu et al. 1994). They found that flavonoids with hydroxy groups at C-5 and C-7 and with a C-2-C-3 double bond were more potent inhibitors of HIV growth and that the presence of substituents (hydroxyl and halogen) in the B-ring increased toxicity and/or decreased activity. A known flavone, chrysin, was found to be the most promising compound in this series. Acacetin-7-*O*-β-D-galactopyranoside from *Chrysanthemum morifolium* and chrysin, as well as apigenin-7-*O*-β-D-glucopyranoside from *Kummerowia striata*, were found to exhibit anti-HIV activity (Wang et al. 1998). Among compounds isolated from *Chrysanthemum morifolium* flowers, apigenin 7-*O*-β-D-(4″-caffeoyl)glucuronide showed strong HIV-1 integrase inhibitory activity (IC_{50} = 7.2 μg/ml) and anti-HIV activity in a cell culture assay (EC_{50} = 41.86 μg/ml) using HIV-I (IIIB) infected MT-4 cells (Lee et al. 2003).

Antimicrobial Activity

Chrysanthemum morifolium flowers afforded mixtures of the C-3 palmitate and myristate esters (3:2) of mailadiol (1), the C-3 palmitate and myristate esters (3:2) of heliantriol C (2) and fatty acid esters (1:1) of faradiol (3) and arnidol (Ragasa et al. 2005). Compound 1 exhibited moderate activity against *Aspergillus niger* and *Pseudomonas aeruginosa* and low activity against *Trichophyton mentagrophytes*, *Candida albicans* and *Bacillus subtilis*, and was inactive against *Staphylococcus aureus* and *Escherichia coli*. Compound 2 had moderate activity against *A. niger* and low activity against *P. aeruginosa* and *S. aureus* and was inactive against *B. subtillis* and *E. coli.*

Antiinflammatory Activity

The tubular flowers of *Calendula officinalis*, *Carthamus tinctorius*, *Cosmos bipinnatus*, *Chrysanthemum morifolium*, *Helianthus annuus* and *Matricaria matricarioides* showed a characteristic feature by containing helianol as the most predominant component (29–86 %) in the triterpene alcohol fractions (Akihisa et al. 1996). The triterpene alcohols from these flowers showed marked inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate-induced inflammation in mice. Fourteen triterpene diols and triols and 9 fatty acid esters, isolated from the flowers, showed marked antiinflammatory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice with a 50 % inhibitory dose (ID_{50}) of 0.03–1.0 mg/ear, which was more inhibitive than quercetin (ID_{50} = 1.6 mg/ear), a known inhibitor of TPA-induced inflammation in mice (Ukiya et al. 2001).

Hypouricemic Activity

Among 288 extracts, prepared from 96 medicinal plants used in Vietnamese traditional medicine to treat gout and related symptoms, the most active extract was the methanol flower extract of *C. sinense* with an IC_{50} value of 5.1 μg/ml (Nguyen et al. 2004). The active constituents isolated caffeic acid, luteolin, eriodictyol and 1,5-di-*O*-caffeoylquinic acid all showed significant xanthine oxidase inhibitory activity in a concentration-dependent manner, and the activity of luteolin was more potent (IC_{50}1.3 μM) than the clinically used drug, allopurinol (IC_{50} 2.5 μM). Two compounds found in the flowers, acacetin and 4,5-*O*-dicaffeoylquinic acid methyl ester, exhibited hypouricemic activity in rats pretreated with the uricase inhibitor potassium oxonate as an animal model for hyperuricemia (Nguyen et al. 2005). When administered per orally at doses of 20 and 50 mg/kg, acacetin reduced the serum uric acid level by 49.9 and 63.9 %, respectively, and the latter reduced the level by 31.2 and 44.4 %, respectively. When administered intraperitoneally

at the same doses, both of compounds exerted a dose dependent and more marked reduction of the serum uric acid level (% reduction at 20 and 50 mg/kg were 63.0 and 95.1 % in acatin, respectively, and 66.9 and 86.5 % in the dicaffeoylquinic acid methyl ester, respectively). Both compounds inhibited the rat liver xanthine oxidase activity with IC_{50} values of 2.22 and 5.27 μM, respectively, demonstrating that the hypouricemic action of both compounds may be attributable to their xanthine oxidase inhibitory activity. From the methanol flower extract, a flavone glucoside, acacetin 7-*O*-(3-*O*-acetyl-β-D-glucopyranoside), was isolated together with 27 known compounds including flavonoids, caffeoylquinic acid derivatives, phenolics and a monoterpenoid glucoside (Nguyen et al. 2006). Compounds 1–15, 20–24 and 27 displayed significant xanthine oxidase inhibitory activity in a concentration-dependent manner, and compounds 2–11 and 22 showed more potent inhibitory activity, with IC_{50} values ranging from 0.13 to 2.31 μM, than that of a positive control allopurinol (IC_{50} = 2.50 μM). The kinetic study indicated that 1–15 and 20–24 displayed competitive-type inhibition like that of allopurinol, while 27 displayed a mixed-type inhibition. The compounds displayed significant xanthine oxidase inhibitory activity in a concentration-dependent manner and showed potent inhibitory activity.

Aldose Reductase Inhibition Activity

The hot water extract of *Chrysanthemum morifolium* was found to have potent inhibitory activity towards lens aldose reductase (Terashima et al. 1991). Ellagic acid was isolated and found to be a potent inhibitor.

Cardioprotective Activity

Chrysanthemum indicum flower (FCI), *Chrysanthemum morifolium* flower (FCM) and *Salvia miltiorrhiza* root (RSM) extracts were found to be efficient in ameliorating the extent and severity of the lesion in experimental myocardial infarction in the dog (Chen et al. 1983). FCI gave the best results. Experimental coronary insufficiency was also improved both in extent and severity by treating with FCI in moderate dose and with FCM, SMB and FCI in large dose. Studies showed that *Chrysanthemum morifolium* extract exhibited cardioprotective effect during ischemia/anoxia and reperfusion/reoxygenation in the isolated rat heart and the ventricular myocytes (Jiang et al. 2004). The extract (0.25–1.0 g/l) increased left ventricular developed pressure (LVDP), +/− d*p*/d*t*(max), LVDP × HR and coronary flow (CF) and decreased heart rate (HR) in a dose-dependent manner. At 0.5 g/l, it attenuated the reduction of LVDP, +/− d*p*/d*t*(max) and CF caused by ischemia/reperfusion. The extract attenuated the reduction of contraction of isolated rat heart and cardiomyocytes induced by ischemia/reperfusion.

In another study, the ethyl acetate chyranthemum extract significantly decreased the number and duration of ventricular tachycardia (VT) and delayed the occurrence of ventricular premature beats (VPB) and VT induced by aconitine compared with control rat group with experimental arrhythmia induced by aconitine (Zhang et al. 2009). Arrhythmia score of the extract group was lower than that in aconitine-treated group. The extract markedly prolonged the effective refractory period (ERP) and increased the VFT in the isolated perfused rat hearts during ischemia and reperfusion. Results suggested that the extract could reduce myocardial vulnerability and exert its antiarrhythmic effects induced by aconitine or ischemia/reperfusion, which may be related to its prolongation of action potential duration and effective refractory period that enhance the electrophysiological stability of myocardium.

Hot water chrysanthemum flower extract, ethanol flower extract and its flavonoid, apigenin and luteolin dose-dependently inhibited ICAM-1 (intercellular adhesion molecule 1) and E-selectin expression and adhesion of HL-60 (human promyelocytic leukaemia cells) by oxidised LDL

(oxLDL) (Lii et al. 2010). All of them reversed the inhibition of phosphorylation of Akt and cAMP responsive element binding protein (CREB) by oxLDL; however, this reversion was abolished by wortmannin. Their ROS scavenging capability proceeded dose-dependently in the presence of oxLDL. The results indicated that *C. morifolium* to be a plant with cardiovascular-protective potential and its inhibitory effects of on ICAM-1 and E-selectin expression were, at least partially, attributed to its antioxidant activity and modulation of the PI3K/Akt signalling pathway.

Antihypertensive Activity

Research in China reported that using about 60 g daily of *Chrysanthemum morifolium* flowers for lowering vascular pressure gave the following success rates 17.1 % very effective, 51.4 % effective and 31.5 % not effective (Zhou 1987).

Neuroprotective Activity

Chrysanthemum extract effectively inhibited the cytotoxicity induced by 1-methyl-4-phenylpridinium ions (MPP(+)), Parkinsonian toxin and improved cell viability of SH-SY5Y neuroblastoma cells (Kim et al. 2009). The extract also attenuated the elevation of reactive oxygen species (ROS) level, increase in Bax/Bcl-2 ratio, cleavage of caspase-3 and PARP proteolysis. The results demonstrated that *C. morifolium* possessed potent neuroprotective activity and, therefore, might be a potential candidate in neurodegenerative diseases such as Parkinson's disease.

Studies showed that pretreatment of the rat brain with TFCM (total flavones extracted from *Chrysanthemum morifolium*) significantly decreased the neurological deficit scores, percentage of infarction and brain oedema and attenuated the decrease in SOD activity, the elevation of MDA content, and the generation of ROS caused by ischemia/reperfusion (I/R) injury (Lin et al. 2010). In isolated brain mitochondria, Ca(2+)-induced swelling was attenuated by pretreatment with TFCM. The results showed that pretreatment with TFCM provided significant protection against cerebral I/R injury in rats partially by its antioxidant action and consequent inhibition of mitochondrial swelling.

Sleep Enhancement Activity

The ethanol extract of *C. morifolium* flowers was found to prolong sleep time induced by pentobarbital similar to muscimol, a GABA(A) receptor agonist (Kim et al. 2011). The extract also increased sleep rate and sleep time when administrated with pentobarbital at a subhypnotic dosage. Both extract and pentobarbital increased chloride Cl^- influx in primary cultured cerebellar granule cells. The results suggested that chrysanthemum extract augmentation of pentobarbital-induced sleep behaviours may result from Cl^- channel activation. The results supported the traditional use of chrysanthemum flowers in Korea for the treatment of insomnia.

Antidiabetic and Antiaging Activities

All *C. morifolium* flower extracts (aqueous, ethanol, methanol acetone) appeared to have potent inhibitory activity towards α-glucosidase in-vitro (Yang et al. 2011). Among these, the methanol extract (IC_{50} value of 22.0 μg/ml) showed significantly higher inhibitory activity compared to the other extracts. Chrysanthemum was found to contain N^1,N^5,N^{10},N^{14}-tetracoumaroyl spermine, which was reported to increase the production of intracellular glutathione (Nakanishi et al. 2008 cited by Yagi et al. 2012) and inhibit the formation of AGEs (Tsuji-Naito et al. 2009; Kitano et al. 2011; Yagi et al. 2012). Among the various types of edible purple chrysanthemum varieties, the variety 'Enmeiraku' was found to contain high amounts of polyphenol, luteolin and chlorogenic acid (Kitano et al. 2011). In bovine serum albumin (BSA)/glucose (fructose) systems, both

C. morifolium and *C. indicum* strongly inhibited the formation of advanced glycation end products (AGEs) and N^{ε}-(carboxymethyl)lysine (Tsuji-Naito et al. 2009). *C. morifolium*, not *C. indicum*, also inhibited the formation of fluorescent AGEs, including pentosidine. *C. morifolium* was found to have high amounts of chlorogenic acid, flavonoid glucosides (including acetyl glucoside, neohesperiidoside) and apigenin, while *C. indicum* contained large amounts of caffeic acid, luteolin and kaempferol. The results suggested the potential of both *Chrysanthemum* species for the successful treatment of conditions associated with diabetic complications and aging. In a randomized controlled double-blind clinical trial involving 35 women (48.1 ± 6.1 years, BMI 25.7 ± 1.4), the effect of edible purple chrysanthemum (*Chrysanthemum morifolium*) powder on generation of advanced glycation end products (AGEs) and the effect of oral intake of chrysanthemum on skin and serum AGEs were inconclusive (Yagi et al. 2012). However, the in-vitro experiment confirmed that chrysanthemum extracts had an anti-glycation effect. Addition of chrysanthemum powder reduced fluorescence of three F-AGEs (AGEs-derived fluorescence), in-vitro by 50 % (0.039 mg/ml, 3-deoxyglucosone (3DG); pentosidine; *N*ε-(carboxymethyl)lysine (CML): <0.01 mg/ml) to less than or equal to the level produced by AG (F-AGEs: 0.077 mg/ml, pentosidine: >1.0 mg/ml, CML: 0.708 mg/ml).

Vasorelaxant/Vascular Smooth Muscle Activity

Studies by Jiang et al. (2001) found that the ethyl acetate extract of *C. morifolium* induced both endothelium-dependent and endothelium-independent relaxation in the rat thoracic aorta. NO and cGMP were likely involved in the endothelium-dependent relaxation, inhibition of voltage-dependent or receptor-operate Ca^{2+} channel, and activation of ATP-sensitive K^{+} channel contributed in part to the endothelium-independent relaxation by the extract.

Chrysanthemum morifolium extract was found to inhibit apoptosis of vascular smooth muscle cells isolated from thoracic aorta of fetal calf in a concentration-dependent manner (Fang et al. 2002). The level of superoxide dismutase (SOD) was increased and the malondialdehyde (MDA) level decreased.

Antiallergic Activity

Five cultivars of *C. morifolium* flowers were found to have antiallergic activity (Xie et al. 2012) A representative medicinal cultivar, 'hua-iju', showed potential activity on the inhibition of antigen-induced degranulation from RBL-2H3 cells and compound 48/80-induced scratching in mice, whereas the in-vitro and in-vivo antiallergic activities of two edible cultivars were weak.

Anaesthetic Activity

A numbing compound *N*-isobutyl-6-(2-thienyl)-2*E*,4*E*-hexadienamide was isolated from *C. morifolium* (Shahat et al. 2001).

Pharmacokinetic Studies

Studies found that apigenin was absorbed more efficiently than luteolin into the blood plasma after oral administration of *C. morifolium* extract in rats (Chen et al. 2007). The total recovery of the dose was 37.9 % (6.6 % in urine, 31.3 % in feces) for luteolin and 45.2 % (16.6 % in urine, 28.6 % in feces) for apigenin. The cumulative luteolin and apigenin excreted in the bile was 2.05 and 6.34 % of the dose, respectively. Li et al. (2005) found that in dogs after single dose of oral administration of *C. morifolium* extract, the assay recoveries for luteolin and apigenin ranged from 102.7 to 104.5 % and 93.8–101.8 %, respectively. In eight healthy human volunteers, they found that following oral administration of tablet of *C. morifolium* extract, the assay recoveries for luteolin and apigenin were above 85.7 % (Li and Jiang 2006). The limit of quantitation was 39.20 ng/ml ($n = 5$) for luteolin and 31.45 ng/ml ($n = 5$) for apigenin in human urine. In the

pharmacokinetic experiment, *Chrysanthemum morifolium* extract dose-dependently increased plasma concentrations of retinol (vitamin A) after oral administration of retinol to rats treated with *C. morifolium* extract (Wang et al. 2012). Chrysanthemum also stimulated activities and expressions of CYP1A1, CYP1A2 and CYP2B1 in hepatic microsomes of rats.

Toxicity Studies

In the acute toxicity study, a single oral dose of 15 g/kg body weight (bw) *C. morifolium* ethanol extract administered to Sprague–Dawley rats caused no treatment-related death, and the maximal tolerance dose estimated was greater than 15 g/kg body weight (Li et al. 2010). In the long-term toxicity study, daily treatment by gavage at dose levels of 320, 640 and 1,280 mg/kg body weight/day caused no toxicological changes in body weight, food and water consumption, hematologic examination, blood biochemical examination, organ weight and microscopic histopathologic examination. Thus, the extract was considered to be safe in general in rats at the limited dose level.

Allergic Dermatitis Problem

Tests on sensitized guinea pigs with flowers of chrysanthemum as well as with the two sesquiterpene lactones parthenolide and alantolactone, derived from different composite species, gave positive patch test reactions with parthenolide producing stronger reactions than alantolactone (Schulz et al. 1975). Neither parthenolide nor alantolactone or pyrethrosin could be detected in *C. morifolium* extracts, but several other terpenic compounds were present which gave positive colour reactions to certain lactone reagents. Five of them showed strong positive patch test reactions in patients as well as in sensitized guinea pigs. In five patients with allergic contact dermatitis from chrysanthemum, oil of turpentine and its sensitizing compounds gave no patch test responses. A case of occupational chrysanthemum contact dermatitis was reported (Campolmi et al. 1978). Patch tests showed the patient to be sensitized to *Chrysanthemum morifolium* leaves, flowers and stems (alcoholic extracts) and to alantolactone. The 'maximization test' succeeded in sensitizing guinea pigs to alantolactone. Thirty-two patients (24 male, 8 female) with contact dermatitis from *Chrysanthemum morifolium* were reported by Sharma et al. (1989). The common clinical presentations were hand and face dermatitis in 13 (41 %) and airborne contact dermatitis in 10 (31 %) patients. All 32 patients demonstrated positive patch tests to ethanol extracts of the flowers, 30 to the leaves, 28 to the whole plant, and only 6 to the stems, in that order of intensity.

Traditional Medicinal Uses

Chrysanthemum morifolium and *C. indicum* flowers have been used in traditional Chinese medicine since ancient times (Yeung 1985; Duke and Ayensu 1985; Bown 1995; Chevallier 1996). The flowers are regarded as antibacterial, antifungal, antiinflammatory, carminative, depurative, diaphoretic, febrifuge, ophthalmic, refrigerant and sedative. The flowers of *C. indicum* and *C. morifolium* (Kangiku) are listed in Japanese pharmacopeia as treatments of cephalalgia, vertigo and eye inflammation. Flowers have been used as a medication for detoxification, as an antipyretic and antiphlogistic, and for the treatment of some eye problems, such as blurred vision, itching, loss of vision, tired eyes or redness of the eyes (Kitano et al. 2011). The flowers are taken internally as a refreshing tisane to stimulate blood circulation, improve vision, soothe sore eyes, relieve headaches, counter infections and treat hypertension, chronic inflammation, dizziness, cold, coronary heart diseases and angina. Decoction of flowers is used to promote menstruation, as a wash for infected and cancerous sores and carbuncles and as poultice for enlarged glands. Flowers soaked in wine are used to restore vital functions for a variety of digestive, circulatory and nervous problems. Decoction of flowers and leaves is used for stomachache and as an enema. Leaf juice is smeared on wounds.

Other Uses

Garden chrysanthemum or Florist chrysanthemum is commonly grown as ornamental plants for their attractive, decorative and variously coloured flowers. Commercially, chrysanthemums are grown for their cut flowers, in the open or in greenhouses; they are also excellent when grown in pots as garden ornamentals. Potted chrysanthemums can be grown indoors in order to help remove toxins from the atmosphere (Wolverton 1996). It is especially good at removing chemical vapours, especially formaldehyde, benzene and ammonia.

Garden chrysanthemum are classified based on their shape, form and arrangement of the petals in the inflorescences into singles (daisy-like flower, petals radiating from flat central eye), anemones (single mums with rounded crest of deeper coloured petals), pompons (small stiff, globular flower heads), decorative (flowers with closed incurved petals or reflex petals), cushion (azalea mums growing on short bush), quills (petals straight and tubular), spider (long tubular petals with hooked ends), spoons (spoon-shaped flowers) and large-flowered (Ackerson 1957; Kofranek 1980). As a cut flower, chrysanthemum is market as either 'standard' or 'spray' form (Cockshull 1985). The standard form consists of a stem from which all but the terminal flower were removed, whereas in the spray form, the lateral flowers are kept and the terminal flower is removed.

C. moriflium has been reported to have insecticidal properties. *C. morifolium* methanol leaf extract, when incorporated into artificial diet, was found to reduce the growth of cabbage looper (*Trichoplusia ni* Hubner) larvae at concentrations between 500 and 5,000 ppm of diet (Beninger et al. 2004). Fractionation of the methanol extract gave five fractions, three of which reduced the weight of larvae relative to the control. One fraction was found to contain three main constituents, identified as chlorogenic acid (5-*O*-caffeoylquinic acid); 3,5-*O*-dicaffeoylquinic acid; and 3′, 4′,5-trihydroxyflavanone7-*O*-glucuronide (eriodictyol7-*O*-glucuronide). At concentrations between 100 and 1,000 ppm, these compounds reduced both growth and photosynthesis of *Lemna gibba* with the order of efficacy being flavanone>chlorogenic acid>3,5-*O*-dicaffeoylquinic acid. Further, when incorporated separately into artificial diets, these compounds, at 10–1,000 ppm, enhanced or reduced growth of the cabbage looper (*Trichoplusia ni*) and gypsy moth (*Lymantria dispar*).

Comments

Chrysanthemum (Asteraceae–Anthemideae) comprises about 40 species, most of which are distributed in East Asia, with China being the species' diversity centre (Liu et al. 2012). The Chinese *Chrysanthemum* species can be divided into two groups, the *C. zawadskii* group and the *C. indicum* group. The *C. indicum* group is distributed in southern China, mainly represented by *C. indicum* with creeping stems and small capitula with yellow ray florets. In contrast, the *C. zawadskii* group occurs in northern China, predominated by *C. zawadskii* with erect stems and large capitula with white-purple ray florets. At the diploid level, *C. lavandulifolium* and *C. nankingense* belong to the *C. indicum* group and *C. mongolicum* and *C. chanetii* are of the *C. zawadskii* group. *Chrysanthemum morifolium* is a hexaploid cultigen of complex hybrid origin, with an average chromosome number of 54 (Dowrick 1953; Langton 1989), involving probably *C. vestitum* and *C. indicum*, followed by *C. zawadskii*, *C. nankingense*, *C. lavandulifolium*, *C. lavandulifolium* var. *aromaticum* and *C. dichrum* (Chen 2012).

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Chrysanthemum indicum

Scientific Name

***Chrysanthemum indicum* L.**

Synonyms

Achillea bandana Buch.-Ham., *Achillea berdana* Buch.-Ham. ex DC., *Arctotis elegans* Thunb., *Bidens bardanna* Wall., *Bidens marginata* DC., *Chrysanthemum indicum* var. *albescens* Makino, *Chrysanthemum indicum* var. *hiberinumj* Makino, *Chrysanthemum indicum* var. *indicum, Chrysanthemum japonicum* Thunb., *Chrysanthemum japonicum* var. *japonicum, Chrysanthemum koraiense* Nakai, *Chrysanthemum procumbens* Lour., *Chrysanthemum purpureum* Pers., *Chrysanthemum tripartitum* Sweet, *Dendranthema indicum* (L.) Des Moulin, *Matricaria indica* (L.) Ramat., *Pyrethrum indicum* (L.) Cass., *Tanacetum indicum* (L.) Schultz-Bip.

Family

Asteraceae

Common/English Names

Chinese Chrysanthemum, Indian Chrysanthemum, False Camomile, Garden Camomile, Ground Apple, Indian Chrysanthemum, Mother's Daisy, Roman Camomile, Whig Plant, Winter Aster

Vernacular Names

Catalan: Crisantem De L'Índia, Malabars
Chinese: Ye Ju, Ye Ju Hua, You Je
Czech: Listopadka Indická
Danish: Krysantemum
French: Chrysanthème Des Indes, Chrysantheme D'automne
Galician: Crisantemo
German: Winteraster
India: Chandramallika (Hindi), Sevanti (Sanskrit)
Japanese: Abura-Giku,Hama-Kangiku, Shima-Kangiku, Yagikka
Korean: Gamguk
Malaysia: Kekwa
Philippines: Mansanilya-A-Babasit (Iloko), Manzanilla (Spanish), Dolontas, Mansanilya (Tagalog)
Romanian: Floare De Toamnă, Tufănică
Spanish: Crisantelo, Crisantelmo, Crisantemo, Crisantemos, Margarita, Margaritas
Thai: Khek-Huay
Vietnam: Cúc Hoa, Cúc Hoa Vang, Kim Cúc, Hoàng Cúc, Dã Cúc, Cam Cúc, Kh ỏ Ý, Biooc Kim

Origin/Distribution

The plant is indigenous to East Asia—Eastern China and central and southern Japan. It is cultivated as a medicinal plant in India, Vietnam, China and Japan and introduced into many countries as a garden ornamental. In the Philippines, it is cultivated at 1,800 m altitude in Benguet sub-province.

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Agroecology

In its native range, it occurs in grasslands on mountain slopes, thickets, wet places by rivers, fields, roadsides, saline places by seashores and under shrubs from elevation of 100–2,900 m. The plant is hygrophilous and slightly shade tolerant. The plant thrives on fertile alluvial or sandy-loam soil that is well drained but sufficiently moist. It grows well in areas with temperatures of 15–30 °C and with mean annual rainfall between 1,000 and 2,000 mm.

Edible Plant Parts and Uses

In Japan, the flower heads are eaten (marinated in vinegar) (Uphof 1968; Usher 1974; Facciola 1990); in China, they are also used as a vegetable and as an aromatic plant. Dried flowers are used in mixed spices and as food additives for masking flavors, used in making an aromatic herbal tea, and used in beverages after sweetening with sugar or honey and alcoholic beverages in Korea since ancient times (Chang and Kim 2008; Chun et al. 2008). The young leaves are seasoned in combination with *Acorus gramineus*, aff. *Angelica*, *Eupatorium lindleyana*, *Sedum* aff. *sarmentosum*, and *Sedum* aff. *spectabile* and eaten cooked with chicken by the Hmong ethnic group of Vietnam (Corlett et al. 2002).

Botany

Annual or perennial herb, 25–100 cm tall with an erect, sulcate, glabrous, sparingly branched, green stem and short procumbent rhizomes. Leaves alternate, dark green above and pale green below, ovate to elliptic ovate, deeply lobed and irregularly toothed, base cuneate to truncate, apex acute, sparsely hairy to subglabrous on both sides, and on 1–2 cm long petioles (Plate 1 and 2). Inflorescence in axillary or terminal corymb of many small heads, long peduncled, 1–1.5 cm in diameter (Plates 1, 2 and 3). Involucre of many elliptical bracts in 5 rows, flowers yellow, outer ray florets ligulate with 5 mm long, central disc florets tubular; corolla 2.5 mm long, obovoid and glabrous. The achenes are very small, cuneate-oblong, somewhat compressed and grooved.

Plate 1 Flower and foliage

Plate 2 Close up of flowering heads

Plate 3 Flowering heads being dried in the sun

Nutritive/Medicinal Properties

Flower Nutrients/Phytochemicals

Mineral elements found in the flowers were K 37.55 mg/g, P 4.8 mg/g, Ca 9.73 mg/g, Mg 3.01 mg/g, Na 0.77 mg/g, Fe 1426.63 μg/g, Mn 109.22 μg/g, Zn 58.2 μg/g, Cu 19.95 μg/g, and Mo 0.37 μg/g (Cui and Guo 2012).

Chrysanthemum indicum flowers were found to contain a sesquiterpene lactone, arteglasin-A (Hausen et al. 1975; Hausen and Schulz 1976). A sesquiterpene lactone of guaianolide-type, yejuhua lactone, was isolated from the flowers and later confirmed to be handelin (Chen and Xu 1987). The flowers contained chrysanthemaxanthine, chrysanthemin (asterin, kuromamin) luteolin glucoside, n-hexacosane, n-tetracosane, stachydrine, adenine and vitamin A (Le and Nguyen 1999). Three new eudesmane-type sesquiterpenes called kikkanols A, B, and C; flavones, luteolin and eupatilin; three flavone glycosides luteolin 7-*O*-β-D-glucopyranoside, luteolin 7-*O*-β-D-glucopyranosiduronic acid, and acacetin 7-*O*-(60-α-L-rhamnopyranosyl)-β-D-glucopyranoside; two polyacetylenes *cis*-spiroketalnenolether polyyne and *trans*-spiroketalenolether polyyne; three sesquiterpenes clovanediol, caryolane 1,9β-diol, and oplopanone; and chlorogenic acid were isolated from the flowers (Yoshikawa et al. 1999). Five germacrane-type sesquiterpenes kikkanols D, D monoacetate, E, F, and F monoacetate and chrysanthemol (*trans*-eudesmane type sesquiterpene) were isolated from the flowers (Yoshikawa et al. 2000). Two flavanone glycosides, (2*S*)-eriodictyol 7-*O*-β-D-glucopyranosiduronic acid and (2*R*)-eriodictyol 7-*O*-β-D-glucopyranosiduronic acid, and a phenylbutanoid glycoside, (2*S*, 3*S*)-1-phenyl-2,3-butanediol 3-*O*-β-D-glucopyranoside and flavonoids: apigenin 7-*O*-β-D-glucopyranoside (apigetrin); diosmetin 7-*O*-β-D-glucopyranoside; quercetin 3,7-di-*O*-β-D-glucopyranoside; eriodictyol; (2*S*, 3*S*)-1-phenyl-2,3-butanediol, luteolin, luteolin 7-*O*-β-D-glucopyranoside; luteolin 7-*O*-β-D-glucopyranosiduronic acid; acacetin 7-*O*-(60-α-L-rhamnopyranosyl)-β-D-glucopyranoside; and eupatilin were isolated from the flowers (Matsuda et al. 2002). From the methanol flower extract were isolated: two polyacetylenes (*cis*-spiroketalenolether polyyne and *trans*-spiroketalenolether polyyne), eleven sesquiterpenes (kikkanol A, kikkanol B, kikkanol C, kikkanol D, kikkanol D monoacetate, kikkanol E, kikkanol F, kikkanol F monoacetate, clovanediol, caryolane 1,9β-diol, oplopanone), ten aromatic flavonoids ((2*S*)-eriodictyol 7-*O*-β-D-glucopyranosiduronic acid, (2*R*)-eriodictyol 7-*O*-β-D-glucopyranosiduronic acid, eupatilin, luteolin, luteolin 7-*O*-β-D-glucopyranosid, luteolin 7-*O*-β-D-glucopyranosiduronic acid, apigenin 7-*O*-β-D-glucopyranoside, diosmetin 7-*O*-β-D-glucopyranoside, acatin-7-*O*-(6″-α-L-rhamnopyranosyl)-β-D-glucopyranoside, quercetin 3,7-di-*O*-β-D-glucopyranoside), and two other aromatics (a phenylbutanoid glycoside (2*S*,3*S*)-1-phenyl-2,3-butanediol 3-*O*-β-D-glucopyranoside and chlorogenic acid) (Morikawa 2007).

Seven compounds were isolated 80 % ethanol flower extract: acacetin, acacetin-7-*O*-(6″-*O*-acetyl) β-D-glucopyranoside, linarin, apigenin-7-*O*-β-D-glucopyranoside, chlorogenic acid, vanillic acid and sucrose (Gao et al. 2008). Tang et al. (2009) isolated seven compounds from the 80 % ethanol flower extract luteolin, luteolin-7-*O*-β-D-glucopyranoside, luteolin-7-*O*-(6″-*O*-acetyl)-β-D-glucopyranoside, diosmetin, diosmetin-7-*O*-β-D-glucopyranoside, eupatilin and apigenin. Lu et al. (2009) isolated seven compounds from the flowers: acacetin, apigenin, acacetin-7-*O*-β-D-glucopyranoside, apigenin-7-*O*-β-D-glucopyranoside, luteolin, β-sitosterol and daucosterol. Thirteen compounds were isolated from the flowers, and identified as acacetin-7-*O*-β-D-glucopyranoside (1), luteolin (2), luteolin-7-*O*-β-D-glucopyranoside (3), acaciin (4), acacetin 7-*O*-(6″-*O*-α-L-rhamnopyranosyl)-β-sophoroside (5), 3-*O*-caffeoylquinic acid (6), syringaresinol *O*-β-D-glucopyranoside (7), 5,7-dihydroxychromone (8), uracil (9), *p*-hydroxybenzoic acid (10), 4-*O*-β-D-glucopyranosyloxybenzoic acid (11), boscialin (12) and blumenol A (13) (Feng et al. 2010). Four new polyacetylenes, namely,

chrysindins A–D, together with 6 known polyacetylenes, were isolated from the flowers (Liu et al. 2011).

Twelve compounds were isolated and identified as acacetin; tricin; 2′,4′-dihydroxychalcone; 5-hydroxy-4′,7-dimethoxyflavon; 7-hydroxyflavonone; isorhamnetin (6),5,6,7-trihydroxy- 3′,4′, 5′-trimethoxyflanon; quercetin; (3β, 5α, 6β, 7β, 14β)-eudesmen-3,5,6,11-tetrol; syringaresinol; liriodendrin and genkwanin from the flowers (Wang et al. 2010a). Three germacrane-type sesquiterpene stereoisomers 1β,3α,5β-trihydroxyl-7-isopropenyl-germacren-4(15),10(14)-diene; 1β,3β,5α-trihydroxyl-7-isopropenyl-germacren-4(15),10(14)-diene; 1β,3β,5β-trihydroxyl-7-isopropenyl-germacren-4(15),10(14)-diene were isolated from the flowers (Wang et al. 2012). One new disesquiterpenoid and two new sesquiterpenoids were isolated from the dried flowers (Zhou et al. 2012).

The yield of *C. indicum* flower oil was 2.0 % (w/w), and 63 volatile flavour components comprising 89.28 % of the total aroma composition were characterized (Chang and Kim 2008). The essential oil contained 35 hydrocarbons (48.75 %), 12 alcohols (19.92 %), 6 ketones (15.31 %), 3 esters (4.61 %), 5 aldehydes (0.43 %), 1 oxide (0.22 %) and 1 miscellaneous component (0.04 %). α-Pinene (14.63 %), 1,8-cineol (10.71 %) and chrysanthenone (10.01 %) were the predominant volatile components. Chang and Kim (2009) reported the yield of flower oils from Korean and Chinese gamguk were 2.0 and 0.5 % (v/w), respectively. Sixty-three volatile compounds of Korean gamguk representing 89.28 % of the total peak area were tentatively identified, including 35 hydrocarbons, 12 alcohols, 6 ketones, 3 esters, 5 aldehydes, 1 oxide, and 1 miscellaneous component. Thirty-six volatile components of Chinese gamguk constituted 58.15 % of the total volatile composition, consisting of 19 hydrocarbons, 7 alcohols, 2 ketones, 2 esters, 4 aldehydes, 1 oxide, and 1 miscellaneous component. The predominant components of Korean oil were α-pinene, 1,8-cineol, and chrysanthenone. Whereas camphor, α-curcumene, and β-sesquiphellandrene were the main aroma compounds of Chinese gamguk. Thirty-six, 63, and 55 volatiles constituents were detected in the essential oil from fresh and shade-dried and freeze-dried flowers (Choi and Kim 2011). Ketones were predominant in the volatiles of *gamguk* flowers: fresh, 43.8 %; shade dried, 30.3 %; and freeze dried, 36.1 %. Camphor was the most abundant volatile component; borneol was also significant. The content of camphor was higher in fresh sample than those of dried samples, while borneol concentration was significantly increased in the dried samples. Five major components of the flower essential oil are α-pinene, 1,8-cineol, chrysanthenone, germacrene-D, and α-curcumene (Kim and Lee 2009). Germacrene-D decreased by the increase of nitrogen application. However, cumambrin A contents in the flower parts were affected negatively by the increase of nitrogen application, but total yields of cumambrin A in flower parts significantly increased.

Chang et al. (2010) found 63 volatile flavour components which comprised 89.28 % of the total aroma composition of the flower oil. The predominantly abundant volatile chemical components were α-pinene (14.63 %), 1,8-cineol (10.71 %), and chrysanthenone (10.01 %). The other components included germacrene D (5.25 %), β-bisabolene (3.95 %), (−)-sinularene (3.95 %), bornyl acetate (3.64 %), β-elemene (3.18 %), borneol (3.02 %), zingiberene (2.70 %), camphor (2.64 %), terpinene-4-ol (2.41 %), filifolone (2.24 %), γ-terpinolene (2.04 %), (*E*)-β-farnesene (1.87 %), α-curcumene (1.80 %), isopinocarveol (1.55 %), sabinene (1.24 %), β-sesquiphellandrene (1.19 %), pinocarvone (1.19 %), myrcene (1.17 %) and (*E*)-chrysanthenol (1.17 %).

Wu et al. (2010a) detected 63 volatiles in the flower essential oil, and the major volatiles included 2,6,6-trimethyl-bicyclo[3.1.1]hept-2-en-4-ol (21.67 %); 2-(2,4-hexadiynylidene)-1,6-dioxaspiro[4.4]non-3-ene (21.41 %); germacrene D (6.15 %); α-neoclovene (5.10 %); eucalyptol (4.94 %); α-pinene (3.64 %); and 1,4-bis (1-methylethyl)-benzene (3.03 %). Other minor constituents included β-sesquiphellandrene (2.90 %), longipinane (2.89 %), 7, 11-dimethyl-3-methylene-1,6,10-dodecatriene (2.17 %), β-myrcene (1.78 %), caryophyllene (1.77 %),

2,6-dimethyl-6-(4-methyl-3-pentenyl)-bicyclo [3.1.1]hept-2-ene (1.71 %), 1,2,3,6-tetramethyl-bicyclo[2.2.2]octa-2,5-diene (1.64 %), 4-(1,5-dimethylhex-4-enyl)cyclohex-2-enone (1.56 %), caryophyllene oxide (1.25 %), isocyclocitral (1.23 %), cadina-1,6,8-triene (0.99 %), α,α-4-trimethyl-3-cyclohexene-1-methanol (0.84 %), 4-methylene-1-(1-methylethyl)-icyclo[3.1.0] hexane (0.74 %), 3,4-dihydro-1-naphthalene-boronic acid diethyl ester (0.71 %), borneol (0.70 %), (*Z*)-3,7-dimethyl-2,6-octadien-1-ol acetate (0.66 %), *trans*-3-methyl-6-(1-methylethyl)-2-cyclohexen-1-ol (0.64 %), isobornyl acetate (0.63 %), 1,3,3-trimethylcyclohex-1-ene-4-carboxaldehyde (0.60 %), butylated hydroxytoluene (0.59%),4-methyl-1-(1-methylethyl)-3-cyclohexen-1-ol (0.57 %), (*E*)-3(10)-caren-2-ol (0.57 %), 2-isopropyl-5-methyl-9-methylene-bicyclo [4.4.0]dec-1-ene (0.53 %), *cis*-1-methyl-4-(1-methylethyl)-2-cyclohexen-1-ol (0.48 %), iridomyrmecin (0.37 %), benzoic acid, 2-(dimethylamino)-methyl ester (0.37 %), 6,6-dimethyl-2-methylene-icyclo[2.2.1]heptan-3-one (0.35 %), 2-methyl butanoic acid phenylmethyl ester (0.34 %), α-caryophyllene (0.31 %), 5-ethylcyclopent-1-enecarboxaldehyde (0.31 %), camphene (0.30 %), 1,2,5,5-tetramethyl-1,3-cyclopentadiene (0.29 %), 3,7,11-trimethyl-2,6,10-dodecatrien-1-ol (0.29 %), benzyl acetoacetate (0.28 %), 3,7,11-trimethyl-1,3,6,10-dodecatetraene (0.21 %), 6,6-dimethyl-bicyclo[3.1.1]hept-2-ene-2-methanol (0.21 %), 4-dcetyl-3-carene (0.21 %), β-phellandrene (0.19 %), 1-methyl-8-(1-methylethyl)- tricyclo[4.4.0.02,7]dec-3-ene-3-methanol (0.18 %), copaene (0.17 %), 1,5,5-trimethyl-6-methylene-cyclohexene (0.16 %), 3,4-dihydro-2,2-dimethyl-2H-1-benzopyran (0.15 %), (*S*)-2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-one (0.14 %), 4-methylene-2,8,8-trimethyl-2-vinyl-bicyclo[5.2.0]nonane (0.12 %), 2-n-butyl furan (0.10 %), phytol (0.10 %), 4,6,6-trimethyl- bicyclo[3.1.1]hept-3-en-2-ol (0.09 %), 1,2-diethyl-3,4-dimethyl-benzene (0.09 %), isoaromadendrene epoxide(0.08%),2,3-dihydro-2,2,4,6-tetramethyl-benzofuran (0.08 %), alloaromadendrene oxide-(I) (0.08 %), 4,6-dimethyl-2-pyrimidone (0.08 %), 2-methoxy-4-methyl-4-phenyl-2,5-cyclohexadien-1-one (0.07 %), tetracosane (0.07 %), hexatriacontane (0.06 %), and 3,7-dimethyl-1,3,6-octatriene (0.06 %). Further, ten flavonoids (mg/g) were identified, namely, quercitrin 51.88 mg, myricetin 37.81 mg, luteolin-7-glucoside 17.24 mg, quercetin-3-galactoside 12.55 mg, quercetin-3-glucoside 9.88 mg, luteolin 7.29 mg, kaempferol 0.22 mg, vitexin 0.17 mg, rutin 0.16 mg, apigenin 0.09 mg and total flavonoids 137.29 mg (Wu et al. 2010a).

The major constituents of the essential oils from three samples fresh, air-dried and processed flowers of *Chrysanthemum indicum* were 1,8-cineole, camphor, borneol and bornyl acetate (Zhu et al. 2005). The oils also contained α-terpineol, *cis*-sabinol, thujone, terpinen-4-ol, *ρ*-cymene and linalool. Fresh, air-dried and processed flowers of *Chrysanthemum indicum* shared similar qualitative composition of essential oils; the difference was quantitative. The fresh flower oil had a high percentage of 1.8-cineole (30.41 %) and camphor (23.52 %), although air-dried flower oil had a high content of camphor. *Chrysanthemum indicum* essential oil also had chrysanthenone, limonene, β-caryophyllene oxide and α-pinene and β-pinene. The essential oils of dried gamguk flowers were composed of hydrocarbons (shade dried (SD) 20.1, freeze dried (FD) 21.9 %), alcohols (SD 39.7, FD 33.9 %), esters (SD 7.7, FD 7.1 %), ketones (SD 30.3, FD 36.1 %), aldehydes (SD 0.1, FD 0.4 %), oxides (SD 0.7, FD 0.1 %), acids (SD 1, FD 0.4 %), and miscellaneous ones (SD 0.4, FD 0.1 %) (Choi and Kim 2011). The oxygenated compounds were important contributors to aromatic flower flavour. Camphor (SD 28.8, FD 35.2 %) and borneol (SD 28.3, FD 24.3 %) were the most abundant volatile component of shade- and freeze-dried samples, respectively. The newly identified compounds in shade-dried sample in comparison with a fresh sample were (3*E*)-2,5,5-trimethylhepta-1,3,6-triene, isogeraniol, *p*-cymen-8-ol, myrtenol, *cis*-piperitol, *trans*-3(10)-caren-2-ol, 1-methyl-4-(1-methylethyl)-benzene, *trans*-piperitol, verbenene, 4-ethenyl-1,2-dimethyl-benzene, bicyclogermacrene, α-farnesene, α-muurolene, dicyclohexyl-propanedinitrile, 2,3,6-trimethyl-1,4,6-heptatriene, nerolidol, spathulenol, caryophyllene oxide, 5-ethenyl-2-methyl-pyridine, citral,

β-bisabolene, *trans*-α-bisabolene, α-gurjunene, β-eudesmol, *E*-3-phenyl-2-propenyl 3-methylbutanoate, valerenic acid, vulgarone B, aromadendrene epoxide, hexadecanoic acid, *p*-mentha-1(7)2-dien-8-ol, (*Z*,*Z*)-9,12-octadecadienoic acid, tricosane and pentacosane. Shade-dried gamguk flower had the greatest total number of volatile flavour compounds. α-Copaene, isobornyl-3-methylbutanoate and heptacosane were the compounds identified in only the freeze-dried sample.

Sixty-three volatile compounds of Korean gamguk representing 89.28 % of the total composition were identified, including 35 hydrocarbons, 12 alcohols, 6 ketones, 3 esters, 5 aldehydes, 1 oxide and 1 miscellaneous component (Chang and Kim 2009). Thirty-six volatile components of Chinese gamguk that constituted 58.15 % of the total volatile composition were characterized, consisting of 19 hydrocarbons, 7 alcohols, 2 ketones, 2 esters, 4 aldehydes, 1 oxide and 1 miscellaneous component. The predominant components of Korean oil were α-pinene, 1,8-cineol and chrysanthenone, whereas camphor, α-curcumene and β-sesquiphellandrene were the main aroma compounds of Chinese gamguk.

A total of 169 compounds representing 88.79–99.53 % of the oils were identified in the flowerhead essential oil of 8 Chinese *C. indicum* populations (Zhang et al. 2010a). The predominant components were 1,8-cineole (0.62–7.34 %), (+)-(1*R*,4*R*)-camphor (0.17–27.56 %), caryophyllene oxide (0.54–5.8 %), β-phellandrene (0.72–1.87 %), (−)-(1*S*,2*R*,4*S*)-borneol acetate (0.33–8.46 %), 2-methyl-6-(p-tolyl)hept-2-ene (0.3–8.6 %), 4,6,6-trimethylbicyclo[3.1.1]hept-3-en-2-yl acetate (0.17–26.48 %), and hexadecanoic acid (0.72–15.97 %).

Leaf/Aerial Parts Phytochemicals

Mineral elements found in the leaves were K 31.52 mg/g, P 4.28 mg/g, Ca 14.14 mg/g, Mg 2.70 mg/g, Na 0.82 mg/g, Fe 1519.46 μg/g, Mn 186.7 μg/g, Zn 78.04 μg/g, Cu 30.26 μg/g and Mo 0.56 μg/g (Cui and Guo 2012).

Mineral elements found in the stems were K 17.74 mg/g, P 1.45 mg/g, Ca 5.52 mg/g, Mg 1.35 mg/g, Na 0.75 mg/g, Fe 433.36 μg/g, Mn 65.84 μg/g, Zn 76.6 μg/g, Cu 16.34 μg/g and Mo 0.21 μg/g (Cui and Guo 2012).

A flavones glucoside, isolated from *C. indicum*, identified as acacetin-7-rhamnosidoglucoside was found to be identical with buddleoglucoside (Cheng et al. 1962). The sesquiterpenoid valerone was found in *C. indicum* (Uchio et al. 1981). Indicumenone, a bisabolane ketodiol, was isolated from *C. indicum* (Mladenova et al. 1987). Sesquiterpenoids, chrysetunone, chrysetunone monacetate and tunefulin were isolated from aerial parts of *C. indicum* var. *tuneful* (Mladenova et al. 1988). A sesquiterpene compound, named chrysanthetriol, was isolated from the more polar fraction of the plant (Yu et al. 1992). (3β, 5α, 6β, 7β, 14β)-Eudesmen-3, 5, 6, 11-tetrol methanol solvate, systematic name: (3*S*,5*S*,6*R*,7*R*,10*S*)-7-(2-hydroxy-2-propyl)-10-methyl-4-methyleneperhydronaphthalene-3,5,6-triol methanol solvate, $C_{15}H_{26}O_4 \cdot CH_4O$, a new sesquiterpenoid was isolated from *C. indicum* (Wang et al. 2006). Twelve compounds were obtained from *C. indicum* fraction with cardiovascular activity and identified as (2*S*)-eriodictyol-7-*O*-β-D-glucuronide (1), (2*S*)-eriodictyol-7-*O*-β-D-glucoside (2), (2*S*)-esperetin-7-*O*-β-D-glucuronide (3), luteolin-7-*O*-*β*-D-glucoside (4), luteolin-7-*O*-β-D-glucuronide (5), diosmetin-7-*O*-β-D-glucuronide (6), quercetin-7-*O*-β-D-glucoside(7), (2*S*)-eriodict-dicaffeoylquinate (8), 3,5-dicaffeoylquinic acid(9), 3,5-*cis*-dicaffeoylquinic acid (10), 1,5-dicaffeoylquinic acid (11) and 1,3-dicaffeoylquinic acid (12) (Sun et al. 2012). The following compounds were isolated from the methylene chloride fraction of *C. indicum* crude ethanol extract: sudachitin, hesperetin, chrysoeriol and acacetin (Kim et al. 2013).

Seventy-three compounds accounting for 96.65 % of the extracted essential oil of the aerial parts were identified (Jung 2009). The oil comprised 14.88 % monoterpene hydrocarbons (MH), 52.14 % oxygenated monoterpenes (OM), 22.9 % sesquiterpene hydrocarbons (SH), 5.97 % oxygenated sesquiterpenes (OS) and 0.75 % others (O). The main compounds in the oil were α-pinene (4.4 %, MH), 1,8-cineole (10.4 %, OM), α-thujone (6.05 % OM), camphor (10.12 %, OM),

bornyl acetate (6.1 % OM), borneol (3.6 % OM), terpinen-4-ol (3.4 % OM), *cis-chrysanthenol* (3.4 % OM), β-caryophyllene (5.1 %,SH), germacrene D (10.6 %, SH) and α-cadinol (3.0 %, OS). The minor components included monoterpene hydrocarbons (tricyclene, α-thujene, camphene, β-pinene, sabinene, myrcene, α-terpinene, limonene, α-phellandrene, *cis*-β-ocimene, γ-terpinene, *trans*-β-ocimene, *p*-cymene, terpinolene), oxygenated monoterpenes (α-terpinolene, *cis*-3-hexen-1-ol, β-thujone, *trans*-sabinene hydrate, chrysanthenone, linalool, pinocarvone, *cis*-chrysanthenyl acetate, umbellulone, *trans*-chrysanthenyl acetate, *trans*-piperitol, α-terpineol, piperitone, carvone, myrtenol, *trans*-carveol, *p*-cymen-8-ol, *cis*-carveol), sesquiterpene hydrocarbons (α-copaene, α-gurjunene, berkheyaradulen, β-elemene, α-humulene, *trans*-β-farnesene, α-muurolene, γ-cadinene, α-zingiberene, β-selinene, *cis*, *trans*-α-farnesene, δ-cadinene, β-sesquiphellandrene, *ar*-curcumene), oxygenated sesquiterpenes (caryophyllene oxide, *trans*-nerolidol, globulol, guaiol, spathulenol, eugenol, α-cedrol, torreyol, T-muurolol, *cis-trans*-farnesol), and others (1,2,4 trimethylbenzene, *n*-hexanol, 1-octen-3-ol, tricosane, tetracosane). Steam distilled oil from the flowers, leaves and total aerial parts contained borneol, chrysanthenone and bornyl acetate as the major components (Stoianova-Ivanova et al. 1983).

A water-soluble neutral polysaccharide (CIP-C) was obtained from *Chrysanthemum indicum* (Jin et al. 2012). CIP-C was found to be a neutral branched heteropolysaccharide, mainly composed of D-Man, D-Glc and D-Gal, with a small quantity of D-Fuc, L-Ara and D-Xyl. The backbone of CIP-C was linked by β(or α)-D-1,4-Man, β-D-1,6-Glc and β-D-1,4-Gal. In addition,T-Araf,1,5-Araf and T-Gal,1,4-Gal,1,3,6-Gal,1,3,4,6-Gal may be linked as an arabinan branch and an AGI arabinogalactan branch.

Root Phytochemicals

Mineral elements found in the roots were K 15.84 mg/g, P 1.25 mg/g, Ca 10.10 mg/g, Mg 2.54 mg/g, Na 3.16 mg/g, Fe 3219.90 μg/g, Mn 144.33 μg/g, Zn 227.50 μg/g, Cu 64.60 μg/g and Mo 0.22 μg/g (Cui and Guo 2012).

Antioxidant Activity

The water extract of gamguk teas did not differ significantly in yield compared to methanol extracts and showed stronger antioxidant activity (Eom et al. 2008). Catechin contents in gamguk teas were 8–18 % of the extracts. Gamguk teas exhibited faster release of antioxidants, and the antioxidant activity was positively correlated with the thermal treatments. Gukhwacha was the best tea for rapid release (30 seconds) of antioxidants with the 50 °C treatment, whereas antioxidants in other teas were relatively slower.

Anticancer Activity

Chrysanthemum indicum extract inhibited proliferation of human hepatocellular carcinoma (HCC) MHCC97H cells in a time- and dose-dependent manner without cytotoxicity in rat hepatocytes and human endothelial cells (Li et al. 2009). The extract CIE exerted a significant apoptotic effect through a mitochondrial pathway and arrested the cell cycle by regulation of cell cycle-related proteins in MHCC97H cells without an effect on normal cells. Yuan et al. (2009) found that *C. indicum* extract was effective in attenuating the mitogenic effect of isoproterenol on both HepG2 and MHCC97H human hepatocellular carcinoma cells. The inhibitory effect of the extract was mediated by inhibiting the isoproterenol -induced activation of MAPK/ERK1/2 via beta2-AR in tumour cells. In further studies, they found that *C. indicum* ethanol extract reduced MHCC97H cell metastatic capability, in part at least, through decrease of the MMP-2 and MMP-expression with a simultaneous increase of the TIMP-1 and TIMP-2 expression thus restoring their balance in the cancer cells (Wang et al. 2010b). Five Chinese herbs (*Curcuma wenyujin*, *Chrysanthemum indicum*, *Salvia chinensis*, *Ligusticum chuanxiong* and *Cassia tora*) were found to sensitize resistant cancer cells at a nontoxic concentration (10 μg/ml) and markedly increased doxorubicin accumulation in multidrug-resistant human breast cancer MCF-7/ADR cells (Yang et al. 2011b). Fractions from CH_2Cl_2 extracts were more effective than fractions

from ethyl acetate extracts. Fractions from *Curcuma wenyujin* and *C. indicum* exhibited significant effects in sensitization of these resistant MCF-7/ADR cancer cells at nontoxic concentration to doxorubicin and docetaxel (Yang et al. 2011a). All the fractions could enhance the apoptosis induced by doxorubicin in MCF-7/ADR cells and restore the effect of docetaxel on the induction of G2/M arrest in A549/Taxol cells. The fractions also had to induce S-phase arrest.

The methylene chloride fraction of *C. indicum* crude ethanol extract exhibited strong cytotoxic activity as compared with the other fractions and clearly suppressed constitutive STAT3 activation against both human prostate cancer DU145 and U266 cells, but not human breast cancer MDA-MB-231 cells (Kim et al. 2013). It was found that the fraction could induce apoptosis through inhibition of the JAK1/2 and STAT3 signaling pathways. Furthermore, the major components of the fraction were bioactive compounds such as sudachitin, hesperetin, chrysoeriol and acacetin. Sudachitin, chrysoeriol and acacetin also exerted significantly cytotoxicity, clearly suppressed constitutive STAT3 activation, and induced apoptosis, although hesperetin did not show any significant effect in DU145 cells.

Antimicrobial Activity

C. indicum essential oil exhibited antibacterial activities against both *Staphylococcus aureus* and *Escherichia coli* (Aridoğan et al. 2002). The antimicrobial activity of essential oils from air-dried and processed flowers was evaluated against 15 microorganisms including 3 yeasts (Zhu et al. 2005). The results showed that both essential oils possessed significant antimicrobial effect; however, some difference in antimicrobial activity between two oils was observed for several microorganisms, which was attributed to the variation in percentage of the components. Antibacterial activities of the essential oils were exhibited against *Staphylococcus aureus* and *Escherichia coli*. With higher percentage of camphor, the oil of the processed flowers exhibited, in many cases, greater bacteriostatic activity than that of the air-dried ones.

The essential oil of *C. indicum* exhibited moderate activities against most of tested streptococci species (*Streptococcus pyogenes*, *S. mutans*, *S. sanguinis*, *S. sobrinus*, *S. ratii*, *S. creceti*, *S. anginosus*, *S. gordonii)* (MICs, 0.2–0.8 mg/ml; MBCs, 0.4–1.6 mg/ml) (Jung 2009). The oil also showed a strong antimicrobial activity against obligate anaerobic bacteria: *Fusobacterium nucleatum*, *Prevotella intermedia* and *Porphylomonas gingivalis* (MICs, 0.1–0.2 mg/ml; MBCs, 0.2–0.8 mg/ml). The major components of the essential oil from *C. indicum*, terpinon-4-ol, borneol and β-caryophyllene, were indicated as stronger antibacterial activity than α-pinene, camphor and 1,8-cineole. In combination with the essential oil, the MICs/MBCs for ampicillin and gentamicin were reduced by ≥8-fold in tested some of oral bacteria and reference bacteria, suggesting a synergistic effect.

C. indicum leaf volatile oil exerted maximum antibacterial activity against *Pseudomonas aeruginosa* at a concentration of 1 %v/v followed by against *Micrococcus luteus* in comparison with erythromycin as standard antibacterial agent (Pradhan et al. 2011). The volatile oil also exhibited antifungal activity against *Candida albicans* at the same concentration of 1 %v/v, when compared with ketoconazole as standard antifungal agent.

Antiinflammatory Activity

The methanol extract and ethyl acetate-soluble portion from the flowers of *Chrysanthemum indicum* were found to show inhibitory activity against nitric oxide (NO) production in lipopolysaccharide-activated macrophages with potent inhibitory activity shown by the acetylenic compounds and flavonoids from the ethyl acetate-soluble portion (Yoshikawa et al. 2000). Two acetylenic compounds, *cis*-Spiroketalenolether polyyne and *trans*-spiroketalenolether polyyne, and two flavones, luteolin and eupatilin, were found to inhibit nitric oxide production in mouse peritoneal macrophages. Chrysanthemol, a *trans*-eudesmane-type sesquiterpene from *Chrysanthemum indicum*, also possessed antiinflammatory activity (Mou et al. 2001). Studies

showed that the *C. indicum* inflorescence extract (butanol fraction) possessed antiinflammatory, humoral and cellular immunomodulatory and mononuclear phagocytic activities, probably due to the presence of flavonoids (Cheng et al. 2005). At a dose of 150 mg/kg, p.o., the butanol-soluble fraction exhibited significant inhibition of auricle edema in mice. Delayed-type hypersensitivity reaction induced by 2,4-dinitro-fluorobenzene was significantly enhanced by the butanol extract (150 and 300 mg/kg, p.o.) as was antibody generation by splenic cells of mice and IgG and IgM levels in mice sera in response to sheep red blood cells in cyclophosphamide-induced mice. Both these doses potentiated the function of the mononuclear phagocytic system in cyclophosphamide-induced mice.

Separate studies on synoviocytes isolated from the knee joints of rats showed that the total flavonoids of *Chrysanthemum indicum* (TFC) could induce synoviocytes apoptosis and suppress proliferation of synoviocytes in Freund's complete adjuvant-induced arthritis rats (Chen et al. 2008). Further studies in adjuvant arthritis rat model showed that TFC inhibited the proliferation of synovial and induced the apoptosis of synovium and synoviocytes in-vivo in a dose-dependent way and thereby exerted therapeutical effect on rheumatoid arthritis (Xie et al. 2008). Total flavonoids of *C. indicum* extract showed significant therapeutical effect on adjuvant arthritis in adjuvant arthritis rats, and its mechanism was at least in part related to the antioxidant and immunoregulatory effects (Zhang et al. 2010b). The extract decreased the levels of MDA and NO and increased the activity of SOD in serum and supernatant of peritoneal macrophage. Also the suppressed lymphocyte proliferation and IL-2 production of splenic lymphocytes in AA rats were reversed by treatment with the extract.

Studies found 70 % ethanol extract from *Chrysanthemum indicum* to be an effective anti-inflammatory agent in murine phorbol ester-induced dermatitis, suggesting that the extract may have therapeutic potential in a variety of immune-related cutaneous diseases (Lee et al. 2009). The extract caused substantial reductions in skin thickness and tissue weight, inflammatory cytokine production, neutrophil-mediated myeloperoxidase activity and various histopathological indicators. The extract was also effective at reducing inflammatory damage induced by chronic12-*O*-tetradecanoyl-phorbol-13-acetate (TPA). Further studies showed that the antiinflammatory properties of *C. indicum* ethanol flower extract in lipopolysaccharide-induced RAW 264.7 macrophages might result from the inhibition of inflammatory mediators, such as NO, prostaglandin E2 (*PGE2*), TNF-alpha (tumour necrosis factor alpha) and IL-1beta (interleukin-1beta), via suppression of mitogen-activated protein kinases (*MAPKs*) and NF-kappa B (nuclear factor kappa B)-dependent pathways (Cheon et al. 2009). The results indicated that the extract may have therapeutic potential in a variety of immune-related cutaneous diseases.

Studies showed that at 1, 10 and 100 μg *C. indicum* extract inhibited cell loss, decreased the reactive oxygen species production, regulated the Bax/Bcl-2 ratio, and inhibited poly (ADP-ribose) polymerase (PARP) proteolysis in 1-methyl-4-phenylpridinium ion (MPP(+))-induced SH-SY5Y cells (Kim et al. 2011a). Moreover, the extract suppressed the production of prostaglandin E(2,) expression of cyclooxygenase type-2 (COX-2), blocked IκB-α degradation and activation of NF-κB p65 in BV-2 cells in a dose-dependent manner. The activity of the extract might involve its inhibitory actions both on neuronal apoptosis and neuroinflammatory NF-κB/IκB-α signaling pathway. In-vitro studies found that 70 % ethanol extract of *Chrysanthemum indicum* strongly inhibited Epstein–Barr virus (EBV) latent infection membrane protein 1 (LMP1)-induced activation of NF-κB and the viability of EBV-transformed lymphoblastoid cell lines (Kim et al. 2012).

A traditional Chinese medicine (TCM) recipe named CPZ comprising extracts of *Chrysanthemum indicum*, *Pogostemon cablin* and *Curcuma wenyujin* was found to possess potent antiinflammatory activity, which was indicated to be closely associated with its upregulation on interleukin IL-1β and downregulation of prostaglandin E(2) in the edema paw tissue of rats (Su et al. 2012).

Hypouricemic Activity

In a study, a total of 122 traditional Chinese medicinal plants were selected according to the clinical efficacy and prescription frequency for the treatment of gout and other hyperuricemia-related disorders and were evaluated for inhibitory activity of the xanthine oxidase enzyme that catalyses the oxidation of hypoxanthine to xanthine and then to uric acid, which plays a crucial role in gout (Kong et al. 2000). The methanol extract of *C. indicum* exhibited inhibitory effect on xanthine oxidase activity with an IC_{50} of 22 μg/ml and ranked second to *Cinnamomum cassia* twig (IC_{50} 18 μg/ml) thus providing a basis for the use of this medicinal plant for gout treatment.

Hemodynamic/Cardiovascular Activity

An aqueous extract of *Chrysanthemum indicum* flower directly and uniformly produced coronary and systemic vasodilation action and a renal vasoconstricting action in the open-chest dog, and the pharmacological profile of the flower extract was in part similar to that of adenosine (Kato et al. 1986). Intravenous administration of the aqueous extract (5–20 mg/kg) produced a decrease in aortic blood pressure and increases in coronary blood flow, left ventricular d*P*/d*t* (change in pressure/change in time) and heart rate in a dose-dependent manner, while renal blood flow was initially decreased and then increased to the values above the preinjection level. Dipyridamole (0.1 mg/kg i.v.) potentiated an increase in coronary blood flow of the extract and aminophylline (1.0 mg/kg i.v.) attenuated this response. A two-fold increase in coronary blood flow was elicited by the aqueous extract (13.8 mg/kg) and by adenosine (29.5 μg/kg). Intravenous administration of the flower extract (5–20 mg/kg) as well as adenosine (10–50 μg/kg) produced decreases in aortic blood pressure and renal blood flow and increases in aortic blood flow, vertebral blood flow, coronary blood flow and left ventricular d*P*/d*t* (Kato et al. 1987). Calculated coronary, vertebral and total peripheral resistances were decreased by the extract or adenosine in a dose-dependent manner. The results indicated that *C. indicum* extract directly and uniformly produced coronary and systemic vasodilation with renal vasoconstriction and that adenosine directly produced vasoconstriction in renal vasculature and vasodilation which was more potent in coronary vasculature than in systemic ones.

Sun et al. (2012) found that flavonoids, namely, (2*S*)-eriodict-dicaffeoylquinate; 3,5-dicaffeoylquinic acid; 3,5-c*is*-dicaffeoylquinic acid; 1,5-dicaffeoylquinic acid; and 1,3-dicaffeoylquinic acid, were the major components of the active fraction of *C. indicum* that exhibited cardiovascular activity.

Antidiabetic and Antiaging Activities

In bovine serum albumin (BSA)/glucose (fructose) systems, both *C. morifolium* and *C. indicum* strongly inhibited the formation of advanced glycation end products (AGEs) and N^{ε}-(carboxymethyl)lysine (Tsuji-Naito et al. 2009). *C. morifolium*, not *C. indicum*, also inhibited the formation of fluorescent AGEs, including pentosidine. *C. morifolium* was found to have high amounts of chlorogenic acid, flavonoid glucosides (including acetyl glucoside, neohesperiidoside), and apigenin, while *C. indicum* contained large amounts of caffeic acid, luteolin and kaempferol. The results suggested the potential of both *Chrysanthemum* species for the successful treatment of conditions associated with diabetic complications and aging.

Aldose Reductase Inhibitory Activity

Two new flavanone glycosides, (2*S*)-eriodictyol 7-*O*-β-D-glucopyranosiduronic acid (1) and (2*R*)-eriodictyol 7-*O*-β-D-glucopyranosiduronic acids (2), and a new phenylbutanoid glycoside, (2*S*, 3*S*)-1-phenyl-2,3-butanediol 3-*O*-β-D-glucopyranoside, were isolated from *Chrysanthemum indicum* flowers, and (1) and (2) exhibited potent inhibitory activity for rat lens aldose reductase

(Matsuda et al. 2002). However, the inhibitory activities of 1 and 2 were weaker than those of luteolin and luteolin 7-*O*-β-D-glucopyranoside which were also isolated from the flowers of *C. indicum* by Yoshikawa et al. (1999). Aldose reductase is a key enzyme in the polyol pathway that catalyses the reduction of glucose to sorbitol. Accumulation of sorbitol has been implicated in the chronic complications of diabetes such as cataract. The methanol extract of the flower extract exhibited inhibitory activity against rat lens aldose reductase (Yoshikawa et al. 1999). From the methanol flower extract, active components such as flavone and flavone glycosides were isolated by bioassay-guided separation using aldose reductase inhibitory activity together with three new eudesmane-type sesquiterpenes called kikkanols A, B and C. The flavone, luteolin, three flavone glycosides (luteolin 7-*O*-β-D-glucopyranoside, luteolin 7-*O*-β-D-glucopyranosiduronic acid, acacetin 7-*O*-(60-α-L-rhamnopyranosyl)-β-D-glucopyranoside), and chlorogenic acid were potent inhibitors of rat lens aldose reductase, but their activity was weaker than that of a commercial synthetic aldose reductase inhibitor, epalrestat. Another flavone, eupatilin, and two sesquiterpenes (clovanediol, caryolane 1,9β-diol) exhibited less activity than luteolin and the three flavone glycosides. Other sesquiterpenes (kikkanol A, kikkanol C, oplopanone) and two polyacetylenes (*cis*-spiroketalnenolether polyyne, *trans*-spiroketalenolether polyyne) exhibited little activity.

Antidermatitis Activity

Topical application *Chrysanthemum indicum* to mice with atopic dermatitis-like skin lesions in 2,4-dinitrochlorobenzene (DNCB)-treated NC/Nga mice dose dependently reduced severity of clinical symptoms of dorsal skin, ear thickness and the number of mast cells and eosinophils (Park et al. 2012). *C. indicum* (30 %) significantly decreased serum IgE, IgG1, IL-4 and IFN-γ levels and reduced mRNA levels of interferon IFN-γ, interleukins IL-4 and IL-13 in dorsal skin lesion. The results suggested that *C. indicum* may be an effective alternative for the management of atopic dermatitis.

Nephroprotective Activity

Chrysanthemum indicum extract protected human proximal tubular HK-2 cells against cisplatin-induced apoptosis by its antioxidant activity against hydrogen peroxide and hydroxyl radical (Pongjit et al. 2011). In addition, the extract renal cells without significant interfering effect on cisplatin toxicity in lung cancer H460 and melanoma G361 cells.

Neuroprotective Activity

Chrysanthemum indicum was found to possess neuroprotective activity (Chun et al. 2008). It had been recorded as having therapeutic effects for stroke in Korean traditional medicine. Its aqueous extract significantly increased the cell viability of SK-N-SH human neuroblastoma cells exposed to oxygen–glucose deprivation both in-vitro and in-vivo cerebral ischemia models.

Radioprotective Activity

Chrysanthemum indicum flowers were reported being able to absorb ultraviolet and cure sunburn (Huang et al. 2004). It has potential to be a natural additive in health protection cosmetic.

Hepatoprotective Activity

Chrysanthemum indicum was one of the nine Chinese herbal medicine with hepatoprotective and antioxidant activity, inhibiting lipid peroxidation in a dose-dependent manner thereby protecting liver function (Jiang et al. 1997).

Antithrombotic Activity

Studies by Levy and Xie (1988) reported that the aqueous extract of *Chrysanthemum indicum* flowers was 10–12 times more potent on platelet-activating factor (PAF)-induced aggregation of human platelet-rich plasma compared to ADP (adenosine diphosphate) aggregation of rat

platelet-rich plasma providing partial evidence in support of the traditional use of *Chrysanthemum indicum* in the treatment or prevention of thrombosis.

Cardioprotective Activity

Li (1981) reported that *C. indicum* extract protected injured neonatal rat heart cells by reducing the release of lactate dehydrogenase (LDH) from injured heart cells deprived of oxygen and glucose. Further 10^{-5} M propranolol showed similar protective effect, while 10^{-4} M isoprenaline exacerbated heart cell injury.

Chrysanthemum indicum flower (FCI), *Chrysanthemum morifolium* flower (FCM) and *Salvia miltiorrhiza* root (RSM) extracts were found to be efficient in ameliorating the extent and severity of the lesion in experimental myocardial infarction in the dog (Chen et al. 1983). FCI gave the best results. Experimental coronary insufficiency was also improved both in extent and severity by treating with FCI in moderate dose and with FCM, SMB and FCI in large dose. In another study, after 7–9 days of treatment, *C. indicum* significantly reduced the left ventricular weight index and heart weight index in mice and rats with myocardial hypertrophy induced by isoprenaline and L-thyroxine, decreased the content of angiotensin II in ventricular tissue in mice and rats, and reduced the ALD, TNF-alpha concentration in serum, and the hydroxy proline content in ventricular tissue in rats (Wu et al. 2010b).

Antihypertensive Activity

An active fraction from the hot ethanol extract of *C. indicum* was found to lower blood pressure in anaesthetized cats and normotensive dogs (Liu et al. 1962). Four normotensive dogs fed 50, 100, 130 and 150 mg/kg of the fraction, registered diastolic pressure decline of 0, 24, 8 and 36 mmHg, respectively. Weekly tests on EKG (electrocardiogram), serum BSP (bone sialoprotein) retention and blood NPN (nonprotein nitrogen) revealed no serious alterations when three renal hypertensive dogs were fed daily 100 mg/kg in the first 2 weeks and 200 mg/kg for the third week.

Antinociceptive/Analgesic Activity

The petroleum ether fraction from the ethanol extract of flowers and buds administered orally at doses of 188 and 376 mg/kg to mice produced significant inhibitions on chemical nociception induced by intraperitoneal acetic acid, subplantar formalin or capsaicin injections and on thermal nociception in the tail-flick test and the hot plate test (Shi et al. 2011). In the pentobarbital sodium-induced sleep time test and the open-field test, the flower fraction neither enhanced the pentobarbital sodium-induced sleep time nor impaired the motor performance, indicating that the observed antinociception was unrelated to sedation or motor abnormality. The fraction did not affect temperature within 80 minutes. The results suggested that petroleum ether flower fraction-produced antinociception might involved ATP-sensitive K^+ channels and the mAChRs-ATP-sensitive K^+ channels pathway. The aqueous fraction of an ethanol *C. indicum* extract administered orally to mice produced analgesic activity in the chemical nociception induced by intraperitoneal acetic acid, subplantar formalin/capsaicin injections model and in the thermal nociception in the tail-flick test and in the hot plate test (Chen et al. 2011). In the pentobarbital sodium-induced sleeping time test and the open-field test, the aqueous fraction neither significantly enhanced the pentobarbital sodium-induced sleeping time nor impaired the motor performance, indicating that the observed analgesic activity was unlikely due to sedation or motor abnormality. Moreover, the effective dose (600 mg/kg) also showed no toxicity within 7 days. The results suggested the analgesic activity possibly related to the flavonoid glycosides and phenolic glycosides in the fraction.

Otoprotective Activity

Studies found that Chungshinchongyitang (CSCYT), an herbal drug formula containing *Chrysanthemum indicum* and 13 other herbs, prevented the destruction of hair cell arrays induced by cadmium in the rat organ of Corti primary explants (Kim et al. 2011b). CSCYT inhibited cell death, release of cytochrome C, and generation of reactive oxygen species induced by cadmium in HEI-OC1 auditory cell line. Further, it was demonstrated that CSCYT exerted its effect by modulating apoptosis via the caspase-3 activation and extracellular signal-regulated kinase activation. CSCYT is used in Korean medicine for treating auditory diseases.

Antiosteoporotic Activity

Gamuk flower oil was found to increase the collagen, alkaline phosphatase activity and mineralization of osteoblasts (MC3T3-E1 cells) significantly, indicating that 'gamguk' may help in the treatment of osteoporosis (Chang et al. 2010). *Chrysanthemum indicum* extract (100 μg/ml) significantly increased the growth of osteoblastic MC3T3-E1 cells and caused a significant elevation of alkaline phosphatase (ALP) activity and the deposition of collagen and calcium in the cells (Yun et al. 2011). This activity was completely prevented by the presence of 1 μM tamoxifen, suggesting that the extract's effect might be partly involved in estrogen-related activities. The results indicated that the enhancement of osteoblast functionality by *C. indicum* may prevent osteoporosis and inflammatory bone diseases.

Antidiabetic and Antiaging Activities

In bovine serum albumin (BSA)/glucose (fructose) systems, both *C. morifolium* and *C. indicum* strongly inhibited the formation of advanced glycation end products (AGEs) and N^{ε}-(carboxymethyl)lysine (Kentaro et al. 2009). *C. morifolium*, not *C. indicum*, also acted to inhibit the formation of fluorescent AGEs, including pentosidine. *C. morifolium* was found to large amounts of chlorogenic acid, flavonoid glucoside varieties and apigenin, while *C. indicum* contained large amounts of caffeic acid, luteolin and kaempferol. The results suggested the potential of both *Chrysanthemum* species for the successful treatment of pathogenesis in conditions associated with diabetic complications and aging.

Antiplasmodial Activity

The leaf extracts of *Aristolochia indica* (IC_{50} 10 μg/ml), *Cassia auriculata* (IC_{50} 14 μg/ml), *Chrysanthemum indicum* (IC_{50} 20 μg/ml) and *Dolichos biflorus* (IC_{50} 20 μg/ml) showed promising activity against blood stage chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum* (Kamaraj et al. 2012). The high TC_{50} in mammalian cell cytotoxicity assay and the low IC_{50} in antimalarial *P. falciparum* assay indicated selectivity and good resistance indices in the range of 0.9–1.7 for leaf extracts of *A. indica*, *C. auriculata*, *C. indicum* and *D. biflorus*, suggesting that these may serve as antimalarial agents even in their crude form.

Larvicidal Activity

Among three plant extracts (*Annona squamosa*, *Chrysanthemum indicum* and *Tridax procumbens*) tested, the ethyl acetate leaf extract of *C. indicum* exhibited highest toxic effect (LC_{50} = 39.98 mg/l) against larvae of malaria vector, *Anopheles subpictus* and the methanol leaf extract against the larvae of Japanese encephalitis vector, *Culex tritaeniorhynchus* (LC_{50} = 42.29 mg/l) (Kamaraj et al. 2011).

Allergy Problem

Of 12 fractions obtained from *C. indicum* dried flower extract, four fractions gave on epicutaneous application to guinea pigs sensitized with an extract of *C. indicum* (Hausen and Schulz 1976). One of these allergens was identified as a sesquiterpene lactone, Arteglasin-A of the guaianolide-type.

Traditional Medicinal Uses

C. indicum has a long history of use as an Oriental traditional medicine for the treatment of several infectious diseases such as pneumonia, colitis, stomatitis, cancer, fever and sores and used to treat vertigo, pertussis, inflammatory diseases, intoxication, respiratory ailments, hypertension and hypotensive symptoms (Stuart 1979; Duke and Ayensu 1985; Yeung 1985; Yu et al. 1992; Jiang et al. 1997; Corlett et al. 2002; Matsuda et al. 2002; Cheng et al. 2005; Zhu et al. 2005; Morikawa 2007; Chun et al. 2008; Chen et al. 2008; Cheon et al. 2009; Jin et al. 2012). Various parts of the plant have been used in traditional medicine in India and Southeast Asia (CSIR 1950; Burkill 1966; Kirtikar and Basu 1975; Chopra et al. 1986; Le and Nguyen 1999; Stuart 2012). In traditional Chinese medicine, the whole plant is antiphlogistic, blood tonic, aperient, antipyretic, depurative, febrifuge and vulnerary, and the plant is used to treat eye ailments. *Chrysanthemum indicum* is a common traditional herbal medicine used for the treatment of inflammation, hypertension and respiratory diseases due to its strong antagonistic function against inflammatory cytokines (Yun et al. 2011). In India, the plant is used in conjunction with black pepper for treating gonorrhoea and affections of the brain, calculi, as well as antidote for mental depression. The plant is used in ointments used for bruises, sprains and calluses. In Malaya, the plant is used for colds and headaches and as a poultice for sores and infused in spirits as a digestive. The entire plant or flower is used for whooping cough.

The flowers are aperient, bitter, hypotensive, stomachic and vasodilatory. The flowers of *C. indicum* and *C. morifolium* (Kangiku) are listed in Japanese pharmacopeia as treatments of cephalalgia, vertigo and eye inflammation. The flowers of *C. indicum* is prescribed for anti-inflammatory, hypertension, analgesic and antipyretic purposes and the treatment of eye disease in Chinese traditional preparations. In Vietnam, the flowers are employed to treat cold, fever, photopsia, vertigo, headache, ophthalmia, dacryolithiasis, xerophthalmia, amblyopia, hypertension, boils, furunculus and phlegmon. Long-term use is beneficial for qi and blood and rejuvenating. Flowers are externally applied as lotion or poultice to cure furunculosis. The flowers are used in the treatment of furuncle; scrofula; deep-rooted boils; mammary carbuncles; inflammation of the throat, eyes and cervix; eczema; and itchiness of the skin. The flowers are used as general tonic and to alleviate cough as well as externally to reduce bruising by the Hmong group of Vietnam. Emulsion of flowers is used for infections of the cervix; infusion of the flowering heads is used as carminative, and flowers are also burnt as insect repellent. In India, the flowers are employed as a stomachic and laxative. In Malaya, the flowers are used for sore eyes. In Guam, infusion of flowers is used as remedy for intermittent fevers and also used by women as remedy for hysteria and menstrual problems.

The leaves are depurative and used for migraine in Indochina and China.

Other Uses

Indian chrysanthemum is also widely cultivated as an ornamental. In China, it is used as a source of oil and source of nectar for bees.

Comments

Chrysanthemum indicum is one of the main parents of the florists' chrysanthemum (*Chrysanthemum morifolium*).

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Cosmos sulphureus

Scientific Name

***Cosmos sulphureus* Cav.**

Synonyms

Bidens artemisiifolia (Jacq.) Kuntze (illeg.), *Bidens artemisiifolia* f. *grandiflora* Kuntze, *Bidens artemisiifolia* subsp. *intermedia* Kuntze, *Bidens artemisiifolia* f. *parviflora* Kuntze, *Bidens artemisiifolia* f. *rubra* Kuntze, *Bidens artemisiifolia* var. *rubra* Kuntze, *Bidens sulfurea* (Cav.) Sch.Bip., *Bidens sulphurea* (Cav.) Sch.Bip., *Coreopsis artemisifolia* Sessé & Moc. (illeg.), *Coreopsis artemisiifolia* Jacq., *Cosmea sulphurea* Willd., *Cosmos artemisiifolius* (Jacq.) M.R. Almeida, *Cosmos aurantiacus* Klatt, *Cosmos sulphureus* var. *exaristatus*, *Cosmos sulphureus* var. *hirsuticaulis* Sherff.

Family

Asteraceae

Common/English Names

Klondike Cosmos, Orange Cosmos, Sulfur Cosmos, Yellow Cosmos

Vernacular Names

Chinese: Liu Huang Ju
French: Cosmos Soufré
German: Gelbe Kosmee, Gelbes Schmuckkörbchen, Schwefelgelbes
Indonesia: Kembang Goyang, Randa Meedang (Sundanese)
Japanese: Kibana Kosumosu
Mexico: Xochipelli
Philippines: Cosmos (Tagalog)
Portuguese: Cosmos Amarelo
Russian: Kosmos Tscheltys, Kosmos Želtyj
Spanish: Tostón
Swedish: Gullskära
Thai: Dawkajay
Vietnamese: Chuồn Chuồn Hoa Vang, Hoa Chuồn Chuồn

Origin/Distribution

The species is indigenous to Mexico in Central America. The plant has been introduced elsewhere around the world and is cultivated in India, Cambodia and Indonesia.

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Agroecology

The plant thrives in average, medium moisture, moderately fertile, well-drained soils in full sun and tolerates fairly dry soil. Rich fertile soils tend to produce unusually tall, lanky plants that flop over. The plant is not frost hardy.

Edible Plant Parts and Uses

The young shoots and leaves are eaten as vegetables raw or cooked as 'lalab' or 'gudang' (side dish) with rice in Indonesia (Ochse and Bakhuizen van den Brink 1980). The flowers are edible and use in salads in Thailand (Kaisoon et al. 2011, 2012).

Botany

Annual robust, erect herbaceous plant, 30–200 (−100) cm high with terete, slightly compressed, sparsely pubescent to glabrescent and green stem. Leaves opposite, sessile or shortly petiolate, outline broadly ovate-rhomboid, 2–4 pinnately dissected with ultimate segments narrowly linear-lanceolate, 2.5 mm wide, apiculate and glabrous (Plates 1 and 2). Inflorescence terminal or axillary, solitary, 1.5 cm across, peduncle 1–2 cm long, outer involucral bracts narrowly ovate, acuminate, inner involucral bracts with membranous margins. Ray florets obovate, intensely yellow to deep orange, apex denticulate (Plates 1 and 2). Disc florets with narrowly funnel-shaped corolla, yellow, orange-yellow, 6–7 mm. Fruit a 2 cm achene, hispid, blackish, spindle-shaped pappus absent or of 2–3 widely divergent awns.

Nutritive/Medicinal Properties

The anthochlor pigment, named coreopsin, a glycoside of butein, was isolated from the ray florets (Geissman 1942). From the ray florets an anthochlor glycoside, sulphurein, was isolated

Plate 1 Yellowed flowers and leaves

Plate 2 Orange flowers and leaves

and its structure established as the 6-glucoside of sulphuretin (3′,4′,6-trihydroxybenzalcourmaranone) (Shimokoriyama and Hattori 1953). Also isolated from *C. sulphureus* was coreopsin, a glucoside of butein (3,4,2′,4′-tetrahydroxychalcone). The structure of coreopsin was determined to be the 4′-glucoside of butein. *Cosmos sulphureus* flowers were found to contain 2′-hydroxy-4,4′-dimethoxychalcone and the leaves quercetin and stigmasterol-3-*O*-β-D-glucopyranoside (Huỳnh et al. 2005). A chalcone 3-hydroxylase (CH3H) cDNA clone was isolated and characterized from *Cosmos sulphureus* petals accumulating butein (2′,3,4,4′-tetrahydroxychalcone) derivatives as yellow flower pigments (Schlangen et al. 2010).

Phenolic acids were detected in the ethanol extract of *Cosmos sulphureus* flowers (mg/100 g DW): gallic acid 9.25 mg, protocatechuic acid 3.26 mg, *p*-hydroxybenzoic acid 2.74 mg,

chlorogenic acid 6.90 mg, vanillic acid not detected, caffeic acid 13.88 mg, syringic acid 2.91 mg, *p*-coumaric acid 137 mg, ferulic acid 27.85 mg, and sinapic acid 5.88 mg and total 210.27 mg (Kaisoon et al. 2012). Flavonoid compounds found in the lyophilized hydrophilic extracts of *C. sulphureus* flowers (mg/100 g DW): rutin 19.67 mg, myricetin 59.99 mg, quercetin 9.45 mg, apigenin 7 mg, and kaempferol 25.6 mg and total 121.71 mg.

Antioxidant Activity

Soluble phenolic acid content (μg/g DW) of the flowers comprised gallic acid 30 μg, protocatechuic acid 2.2 μg, *p*-hydroxybenzoic acid 10.2 μg, vanillic acid 9.3 μg, chlorogenic acid 72.8 μg, caffeic acid 13.47 μg, syringic acid 81 μg, *p*-coumaric acid 11.6 μg, ferulic acid 76.3 μg, sinapic acid 308.2 μg, and total phenolic acids 615.1 μg (Kaisoon et al. 2011). Bound phenolic acids contents (μg g/g): protocatechuic acid 21.8 μg, syringic acid 5.5 μg, *p*-coumaric acid 54.7 μg, ferulic acid 132.1 μg, sinapic acid 418.5 μg. Soluble flavonoid contents (μg/g DW): rutin 7 μg, myricetin 4.9 μg, quercetin 485.9 μg, apigenin 0.72 μg, kaempferol 3.54 μg, total 502.1 μg. Bound flavonoid contents (μg/g DW): rutin 31.7 μg, myricetin 2.8 μg, quercetin 109.2 μg, apigenin 14.5 μg, total 158.1 μg. The DPPH radical scavenging activity (percentage inhibition) of soluble and bound phenolic fractions were 87.04 and 33.41 %, respectively. The ferric reducing ability power of soluble and bound phenolic fractions expressed as FRAP values (mmol $FeSO_4$/100 g DW) were 53.86 and 21.2 mmol, respectively.

In a subsequent comparative study of four edible flowers, the phenolics (mg GAE (gallic acid equivalent)/g DW) of the flowers were determined as follows: *Tagetes erecta* (212.9) > *Antigonon leptopus* (177.2) > *Bougainvillea glabra* (138.2) > *Cosmos sulphureus* (102.5) (Kaisoon et al. 2012). Total reducing capacity (FRAP) (μmol Fe^{2+}/g DW) was ranked as *Tagetes erecta* (329.4) > *Bougainvillea glabra* (307.1) > *Antigonon leptopus* (281.9) > *Cosmos sulphureus* (99.9). The ORAC (oxygen radical absorbance capacity) (μmol T Eq (trolox equivalent)/g DW) ranks were *Antigonon leptopus* (491.9) > *Tagetes erecta* (394.2) > *Bougainvillea glabra* (276) > *Cosmos sulphureus* (*214.8*). Cellular antioxidant activity (CAA) (μM QE (quercetin equivalent)/g DW) ranks were *Tagetes erecta* (413, most effective) > *Bougainvillea glabra* (859.6) > *Cosmos sulphureus* (966.1) > *Antigonon leptopus* (967.4).

Antidiabetic Activity

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against α-glucosidase enzyme was found as *Tagetes erecta* (98.51 % inhibition, IC_{50} 0.06 mg/ml) > *Antigonon leptopus* (58.24 % inhibition, IC_{50} 3.26 mg/ml) > *Bougainvillea glabra* (37.30 % inhibition, IC_{50} 5.21 mg/ml) > *Cosmos sulphureus* (32.32 % inhibition, IC_{50} 5.62 mg/ml) (Kaisoon et al. 2012).

Hypolipidemic Activity

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against lipase activity was determined as *Cosmos sulphureus* (43.39 % inhibition, IC_{50} 4.60 mg/ml) > *Tagetes erecta* (41.61 % inhibition, IC_{50} 4.82 mg/ml) > *Bougainvillea glabra* (40.05 % inhibition, IC_{50} 5.14 mg/ml) > *Antigonon leptopus* (26.70 % inhibition, IC_{50} 7.87 mg/ml) (Kaisoon et al. 2012).

Antiproliferative Activity

Cosmos sulphureus had lowest antiproliferative activity among four edible flowers tested (Kaisoon et al. 2012). Antiproliferative activity (IC_{50} mg/ml) of polyphenolic extract against HC-29 (colorectal adenocarcinoma) cells was *Tagetes erecta* > (1.5) > *Bougainvillea glabra* (1.7) > *Antigonon leptopus* (2.4) > *Cosmos*

sulphureus (5.2). Antiproliferative activity (IC_{50} mg/ml) of polyphenolic extract against AGS (gastric adenocarcinoma) cells was *Antigonon leptopus* (0.2) > *Bougainvillea glabra* (2.1) > *Tagetes erecta* (2.2) > *Cosmos sulphureus* (44.8). Antiproliferative activity (IC_{50} mg/ml) of polyphenolic extract against Bl-13 (bladder cancer) cells was *Antigonon leptopus* (0.9) > *Bougainvillea glabra* (2.3) > *Tagetes erecta* (3.0) > *Cosmos sulphureus* (56.5).

Antimalarial Activity

In Brazil, the plant is traditionally used for malaria; an ethnobotanical study showed *Cosmos sulphureus* to have activity against *Plasmodium* (Botsaris 2007).

Traditional Medicinal Uses

The leaves are used in native medicine in Indonesia (Ochse and Bakhuizen van den Brink 1980) and in Brazil for malaria (Botsaris 2007).

Other Uses

A popular ornamental plant in cottage gardens and public places, commonly seen in mass planting along roadsides, beds and borders in Korea and Japan.

The flower heads of *Cosmos sulphureus* and other *Cosmos*, *Bidens* and *Coreopsis* species have provided important sources of yellow to orange dyes among the pre-Columbian civilizations of Central and South America (Jansen 2005). In southern Africa, they were adopted as a popular yellow dye by European settlers for domestic textile production and are still used by dyers using natural dyes as a hobby or for textile crafts, to dye wool bright yellow or orange. Wool dyed with *Cosmos* flower dye exhibit excellent to outstanding sunlight fastness irrespective of mordant combination and mordanting method (Kale et al. 2005).

Comments

The flowers of all *Cosmos* including this species attract birds and butterflies.

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Cynara cardunculus

Scientific Name

***Cynara cardunculus* L.**

Synonyms

Carduus cardunculus (L.) Baill., *Carduus cynara* E.H.L. Krause, *Carduus scolymus* Baill., *Cnicus communis* Lam., *Cynara cardunculus* var. *altilis* DC., *Cynara cardunculus* var. *elata* Cavara, *Cynara cardunculus* var. *ferocissima* Lowe, *Cynara cardunculus* var. *inermis* DC., *Cynara cardunculus* var. *scolymus* (L.) Benth., *Cynara cardunculus* var. *sylvestris* (Lam.) Fiori, *Cynara corsica* Viv., *Cynara ferox* Ten. ex Steud., *Cynara horrida* Aiton, *Cynara spinosissima* J. Presl & C. Presl, *Cynara sylvestris* Lam.

Family

Asteraceae

Common/English Names

Garden Artichoke, Globe Artichoke, Artichoke, French Artichoke, Green Artichoke, Bur Artichoke, Artichoke Thistle, Cardoon, Cardoon Artichoke, Ground Thistle, Prickly Cardoon, Scotch Thistle, Scottish Thistle, Spanish Thistle Artichoke, Wild Artichoke, Wild Cardoon, Wood Artichoke, Vegetable Rennet

Vernacular Names

For Globe Artichoke

Albanian: Angjinare
Arabic: Ardi Shauki, El-Kharshűf
Brazil: Alcahofra
Catalan: Carxofa, Carxofera, Escarxofer, Escarxofera
Chinese: Cai Ji, Chao Xian Ji, Chu-Chi, Chui Sin Kai (Cantonese), Ju Ji, Yang Ji
Corsican: Carciofu
Croatian: Artićok, Artičoka, Dragušica, Italijanski Osat, Osat Talijanski, Oset Pitomi, Ratićok
Czech: Artyčok, Artyčok Zeleninový
Danish: Artiskok, Artiskokblad, Artiskokker
Dutch: Artisjok, Artisjokken
Eastonian: Harilik Artišokk
Esperanto: Artiŝoko
Finnish: Artisokka, Latva-Artisokka
French: Artichaut, Artichaut Commun, Artichaut Scolyme
German: Artischocke
Greek: Agginara, Agginares, Agkinara, Agkinares, Κινάρα
Hebrew: Artishok, Kinras Tarbuti
Hungarian: Articsóka, articsóka level, Kerti Articsóka
Icelandic: Ætiþistill, Körfukál
India: Hatichu (Hindi)
Italian: Articiocco, Carciofo, Carciofolo
Japanese: Chousen Azami
Latvian: Artišoka, Artišoka Lapas
Lithuanian: Tikrasis Artišokas

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Maltese: Qaqoċċ, Qaqoċċ Tax-Xewk
Nahuatl: Quahtlahuitzquilitl
Norwegian: Artisjokk
Polish: Karczoch Zwyczajny
Portuguese: Alcachofra, Alcachofra De Comer
Romanian: Anghinară
Russian: Artishok Koliuchii, Artišok Posvenoj
Spanish: Alcachofa, Alcachofera, Alcacil, Alcancil, Alcaucil, Alearrhofa, Capacaballo, Hierba De Cuajo
Slovašcina: Artičoka
Slovencina: Artičoka Zeleninová
Swedish: Kronärtskocka
Turkish: Enginar
Vietnamese: Atisô
Welsh: March-Ysgall

For Cardoon

Chinese: Ci Cai Ji
Croatian: Gardun
Czech: Artyčok Kardový
Danish: Kardon
Dutch: Kardoen
Espernato: Kardono
Finnish: Kardoni
French: Artichaut Carde, Artichaut Épineux, Artichaut Sauvage, Cardon, Cardon D'espagne Chard, Chardonnette, Chardounette
German: Cardoon, Cardy, Cynara, Gemüseartischocke, Karde, Kardone, Spanische Artichjocke, Stachelige Gemüseartischocke, Stachelige Kardone
Greek: Agria Agkinara, Agries Agginares
Hungarian: Bogáncsos Articsóka, Kárdi, Spanyol Articsóka
Italian: Caglio, Cardo, Cardoncelle, Cardone, Cardonnette, Cardoon Artichoke, Cardo Spinoso, Carduccio, Carduni
Maltese: Qaqocc Tax-Xewk
Polish: Kard, Karczoch Hiszpański
Portuguese: Cardo, Cardo Coalhador, Cardo Comestible, Cardo De Espanha, Cardo Hortense, Cardo Manso, Cardo-Da-Gente, Cardo-Do-Coalho, Cardo De Comer, Coalho, Pencas, Pencas De Cardo
Portuguese: Alcachofra Hortense Cardo
Slovašcina: Mala Artičoka
Spanish: Alcachofa, Alcaucil, Alcaucil Silvestre, Capacaballo, Cardo, Cardo De Arrecife, Cardo De Comer
Swedish: Kardon
Turkish: Yabani Enginar

Origin/Distribution

Cynara cardunculus is native to the Mediterranean and Macaronesia. Cladistic studies based on morphological character of a large set of specimens by Wiklund (1992) confirmed the inclusion of cultivated artichoke, leafy cardoon and wild cardoon in a single species: *Cynara cardunculus* L. The wild perennial taxon, *Cynara cardunculus* var. *sylvestris* (Lamk) Fiori, has been recognized as the ancestor of both the globe artichoke [var. *sativa* Moris, var. *scolymus* (L.) Fiori, ssp. *scolymus* (L.) Hegi] and the leafy or cultivated cardoon (var. *altilis* DC) (Rottenberg and Zohary 1996). Recent studies on isozymes and molecular markers such as RAPDs and AFLPs (Rottenberg et al. 1996; Sonnante et al. 2002, 2004; Raccuia et al. 2004a) have confirmed that both crops evolved from the wild cardoon gene pool, which can therefore be considered the progenitor of both of them. *Cynara cardunculus* has been divided into two subspecies: the western morph is subsp. *flavescens* mainly found in Macaronesia, Portugal and the northwest Mediterranean region; the eastern morph is subsp. *cardunculus* found mainly in central to northeast Mediterranean region (Wiklund 1992). The subspecies differ mainly by a yellowish margin on the middle involucral bract (Wiklund 1992). There are also a number of varieties of *C. cardunculus* including the cultivated artichoke var. *scolymus* (L.) Fiori, the wild artichoke var. *sylvestris* (Lam.) Fiori, and the leafy cardoon var. *altilis* DC (Pignone and Sonnante 2004).

Globe artichoke is widely cultivated in the Mediterranean area, chiefly in Spain, Italy and France, also in the southern United States, South America, China, Egypt, Morocco, and elsewhere

including Vietnam, in the Dalat Highlands where it is grown mainly for producing artichoke tea and also as vegetables. In the United States, California provides more than 90 % of the US Crop.

Agroecology

Globe artichoke is a cool-season crop (Basnizki 1985; Bianco 1990; Bratsch 2009), with a wide adaptive range of 7–30 °C. It grows best in areas with day temperatures of 20–22 °C and 12–14 °C in the night, representing the optimal values to obtain compact and tender heads for an extended period. The minimal biological temperature ranges between 7 and 9 °C, while the lethal one is lesser than −10 °C (Bianco 1990). Frosts damage outer portions of the buds; severe or frequent frosts damage or kill the plants. Plants are tolerant to high temperatures (>30 °C) that, however, tend to decrease the quality of edible heads. Perennial plantings are not recommended in areas where warm to hot temperatures are common. In areas with hot, dry summers, shading and mist irrigation may help vegetative growth, but hot growing conditions tend to toughen bud scales, reduce palatability and produce poor yields. New artichoke plants require 'vernalization' or 'chilling' (Bratsch 2009). This occurs just after planting, with seedling exposure to cool temperatures (8–10 days or of 7–10 °C). Globe artichokes are obligated long-day plants with a critical photoperiod of 10.5 hours. In seed-planted individuals, the transition from vegetative to reproductive stage depends on the interaction between the following factors (Basnizki 1985): attainment of a critical plant size (usually a rosette of seven to eight leaves), low temperatures and photoperiod. The globe artichoke are deep-rooted crops; it can be grown on a wide range of soils, but it produces best on deep, fertile, friable, well-drained soils with a pH between 6 and 8. The extremes of heavy clay and light sandy soils should be avoided (Bratsch 2009). It abhors water-logged condition and raised-bed culture is recommended where drainage is suspect.

Edible Plant Parts and Uses

The edible portion of the immature flower head (capitulum) consists primarily of the fleshy lower portions of the involucral bracts (phyllaries) and the fleshy base of the receptacle (Plates 1 and 2), known as the 'heart'; the mass of inedible immature florets in the centre of the bud are called the 'choke'. The lower fleshy parts of the involucral bracts (phyllaries) and the fleshy receptacle are eaten raw boiled, steamed, baked, fried, stuffed, marinated, pickled, made tino artichoke dips or mixed into yoghurt (Grieve 1971; Facciola 1990; Roberts 2000; Anoymous 2013). The young blanched chards (tender leaf stalks) are also eaten and deemed by some to equal that of cardoon chards (Grieve 1971). The bracts are removed after cooking and eaten one at a time, sometimes dipped in butter, hollandaise, mayonnaise, aioli,

Plate 1 Plant habit of globe artichoke

Plate 2 Harvest globe artichokes

Plate 3 Harvested globe artichoke and leaves for sale

Plate 4 Artichoke leaves and petioles sold as vegetables

lemon juice or other sauces. The chards and flowering stems are eaten cooked—blanched, braised or fried, and added to sauces. The bitter young leaves are also eaten cooked (Plates 3 and 4). In France, artichoke receptacles are very popular deep fried or made into artichoke ragout ('artichauts en ragoût'); the dried receptacles are used in soups. In Italy, artichoke hearts in oil are the usual vegetable for spring in the 'Four Seasons' pizza; whole artichoke can be deep fried as in the popular recipe Jewish-style artichokes or used in Italian stuffed artichokes with a stuffing mixture of bread crumbs, garlic, oregano, parsley, grated cheese and prosciutto or sausage. In Greece, a savoury and wholesome stew, 'aginares a la polita', is prepared with artichoke hearts, potatoes and carrots, and flavoured with onion, lemon and dill. In Spain, the more tender, younger and smaller artichokes are sprinkled with olive oil and barbecued or sauteed in olive oil with garlic, with rice as a paella, or sauteed and combined with eggs in a tortilla (frittata).

Plate 5 Artichoke flower-head shavings used for tea

Ground lamb with different spices, raisins, pine nuts and herbs are used as stuffing in artichoke hearts in Turkey, Armenia and throughout North Africa and the Middle East.

The dried flowers are used as rennet substitute for curdling/coagulating milk.

Leaves are often removed and eaten one at a time, sometimes dipped in butter, mayonnaise, aioli or other sauces. Artichokes can also be made into an herbal tea; artichoke tea is produced as a commercial product in the Dalat region of Vietnam (Plate 5). In Mexico, the flower portion is put into water and consumed as a tisane called 'alcachofa'. Artichoke is the primary flavour of the Italian liquor Cynar. It can be served over ice as an aperitif or as a cocktail mixed with orange juice, which is especially popular in Switzerland.

Recent studies found that the incorporation of artichoke leaf and stem meal, as a source of fibre, modified significantly wheat bread textural properties for the formulations of 9 and 12 % (Frutos et al. 2008). Breads with artichoke fibre presented higher fibre content and were considered acceptable by the sensory panel, indicating this ingredient to be adequate for its use as a fibre source in wheat bread.

The blanched leaf stalks of cardoon are eaten boiled, batter fried, sautéed, braised and pickled, or used in stews and soups (Facciola 1990; Hedrick 1972). In Italy, raw strips are dipped in olive oil or bagna cauda, a hot, anchovy and garlic dip. The tender, fleshy root can be cooked like carrot or parsnip and has an agreeable flavour. Flower-head receptacle is eaten like for artichoke.

Flowers of *Cynara cardunculus* (cardoon) have been traditionally used as coagulants in Portugal and Spain for many centuries to produce traditional artisanal cheeses (Cordeiro et al. 1998; Sidrach et al. 2005). Aspartic proteinases from flowers of *Cynara cardunculus* have been extensively studied and long used as coagulants in the manufacture of several traditional Spanish and Portuguese cheeses (Sidrach et al. 2005). Today, the Serpa and Serra cheeses are some examples of typical and highly appreciated products of Portugal.

Plate 6 Artichoke plant with unopened flower head

Plate 7 Close view of fully opened mature flower head

Botany

An erect, spiny, biennial or perennial herb growing to 1–2 m high by 1 m wide (Plate 1) with a fleshy taproot. Young growth is arachnoid tomentose and stems short and striate ribbed. Leaves (Plates 1, 3, 4, and 6) are rosulate on young plants; alternate on stems and on short, rigid petioles; ovate to lanceolate in outline; large, 30–50 cm long by 10–20 cm wide; pinnatifid or parted; silvery glaucous-green; pubescent to glabrescent above greyish-tomentose below; segments lanceolate and spiny; caudate; base sessile; and decurrent into wings on the stem (Plates 1 and 6). Flower purple-blue; all discoid in a loose, large (6–10 cm across the base) ovate capitula (involucre) (Plates 2, 3 and 4); and terminal on a long flowering stem to 1.5 m (Plates 6 and 7). Phyllaries broadly ovate, bases adpressed, spiny apex, green or tinged with purple or wholly purple, base fleshy, 1–5 cm long by 1–2 cm across the base, receptacle flat, and 2–2.5 cm diameter surrounding numerous tubular florets. Corollas blue or purple, 3–5 cm long, membranous, apical appendages rounded, style exerted. Achene, oblong, 4 angled, shiny brown, with plumose, white pappus, and 2–2.5 cm long.

Nutritive/Medicinal Properties

Globe artichoke is largely cultivated for its fleshy head or capitula (immature inflorescence) which accounts for 30–40 % of the fresh weight (Christakia et al. 2012). The edible portion of the head comprised the tender inner bracts and the receptacle commonly referred to as the 'heart', accounting for 33–55 % of the head (Ceccarelli et al. 2010). Analyses carried out in the United States (USDA 2012) reported raw, globe artichoke head to have the following proximate composition (per 100 g edible portion): water 84.94 g, energy 47 kcal (197 kJ), protein 3.27 g, total lipid 0.15 g, ash 1.13 g, carbohydrates 10.51 g, total dietary fibre 5.4 g, total sugars 0.99 g, Ca 44 mg, Fe 1.28 mg, Mg 60 mg, P 90 mg, K 370 mg, Na 94 mg, Zn 0.49 mg, Cu 0.231 mg, Mn 0.256 mg, Se 0.2 µg, vitamin C 11.7 mg, thiamine 0.072 mg, riboflavin 0.066 mg, niacin 1.046 mg, pantothenic acid 0.338 mg, vitamin B-6 0.116 mg, total folate 68 µg, choline 34.4 mg, betaine 0.2 mg, vitamin A 13 IU, vitamin E (α-tocopherol) 0.19 mg, vitamin K (phylloquinone) 14.8 µg, total saturated fatty acids 0.036 g, 12:0 (lauric acid) 0.002 g, 14:0 (myristic acid) 0.002 g, 16:0 (palmitic acid) 0.029 g, 18:0 (stearic acid) 0.003 g,

total monounsaturated fatty acids 0.005 g, 18:1 undifferentiated 0.005 g, total polyunsaturated fatty acids 0.064 g, 18:2 undifferentiated 0.046 g, 18:3 undifferentiated 0.017 g, β-carotene 8 μg and lutein + zeaxanthin 464 μg.

Analyses carried out in the United States (USDA 2012) reported raw, cardoon to have the following proximate composition (per 100 g edible portion): water 94.00 g, energy 17 kcal, protein 0.7 g, total lipid 0.10 g, ash 1.13 g, carbohydrates 4.07 g, total dietary fibre 1.6 g, Ca 70 mg, Fe 0.708 mg, Mg 420 g, P 23 mg, K 400 mg, Na 170 mg, Zn 0.17 mg, vitamin C 2.0 mg, thiamine 0.020 mg, riboflavin 0.06630 mg, niacin 0.30 mg, vitamin B-6 0.116 mg, folate DFE 68 μg, total saturated fatty acids 0.011 g, total monounsaturated fatty acids 0.018 g and total polyunsaturated fatty acids 0.041 g.

Data obtained suggested that the edible parts (receptacles with inner and intermediate bracts) of flower heads of artichoke cultivars could represent a good source of health-promoting polyphenols (chlorogenic acid, coumaric acid, ferulic acid, cynarin, luteolin, apigenin) and therefore should be encouraged as a nutriceutical use, as an alternative to the more traditional phytopharmaceutical applications of leaf extracts of the species (Fratianni et al. 2007). Moreover, it was demonstrated that single polyphenols accumulate preferentially in specific parts of the heads and in specific genotypes.

Phenolic acids (caffeoylquinic acids) and flavonoids (luteolin and apigenin derivatives) were found in the immature inflorescence of globe artichoke, wild cardoon and cultivated cardoon (Pandino et al. 2010). Apigenin derivatives represented the major class in all samples investigated and highest in cardoon forms. Caffeoylquinic acids and luteolin derivatives were observed in globe artichoke only. The outer bracts of the flower head were found to have very low phenolic content (443 mg/kg dry matter (dm)) or zero hydroxycinnamic acid content; in contrast the receptacle (edible part) contained the highest amount, 1,473 mg/kg dm, and the inner bracts contained slightly lower, intermediate content (Pandino et al. 2011b). Globe artichoke is an ancient herbaceous plant native to the Mediterranean Basin. The edible part (flower head) of globe artichoke was found to be particularly rich in polyphenols; 19 phenolic compounds were determined (Lombardo et al. 2010) as follows: 1-*O*-caffeoylquinic acid; 3-*O*-caffeoylquinic acid; 5-*O*-caffeoylquinic acid (or chlorogenic acid); 4-*O*-caffeoylquinic acid; caffeic acid; 1,3-di-*O*-caffeoylquinic acid (or cynarin); luteolin 7-*O*-rutinoside; luteolin 7-*O*-glucoside; luteolin 7-*O*-glucuronide; narirutin; naringenin 7-*O*-glucoside; di-caffeoylquinic acid; 3,4-di-*O*-caffeoylquinic acid; 3,5-di-*O*-caffeoylquinic acid; 1,5-di-*O*-caffeoylquinic acid; apigenin 7-*O*-rutinoside; apigenin 7-*O*-glucoside; apigenin 7-*O*-glucuronide; and 4,5-di-*O*-caffeoylquinic acid. Apigenin 7-*O*-glucuronide was found to be the major flavonoid, with 6,298 mg/kg DM in 'Romanesco clone C3' receptacle, whereas chlorogenic acid represented the main caffeoylquinic acid, reaching 14,841 mg/kg DM in the inner bracts of 'Violetto di Sicilia'.

In fresh marketable artichoke flower heads, only traces of free apigenin and luteolin were identified, while in badly injured heads, measurable amounts of the above flavonoids, as well as of free caffeic acid, were found to occur (Lattanzio and Van Sumere 1987). Also present are vanillic-, syringic-, *p*-coumaric- and ferulic acids, although caffeic acid proved to be the main phenolic component. Additionally, the latter phenolic acid increased considerably during storage of the healthy heads for 2 weeks at 20 °C or for 1 month at 4 °C, the increase at 20 °C being the most pronounced. In injured heads (internal blackening) stored for 2 weeks at 20 °C, a decrease in caffeic acid, as well as in most other phenolics, was recorded, while in badly injured heads, stored for the same period of time, less than half of the total amount of the caffeic acid present in fresh marketable heads was found. However, in injured heads stored for 1 month at 4 °C, the decrease in caffeic acid proceeded less rapidly. The main phenolic compounds in dried artichoke extracts were mono-caffeoylquinic acids (0.48–4.24 %), the most abundant, dicaffeoylquinic acid, and flavonoid contents were smaller, from 0.03 to 0.52 % (Häusler et al. 2002). The compound

identified included pseudochlorogenic acid; neochlorogenic acid; chlorogenic acid; cryptochlorogenic acid; cynarin; 3,4-di-*O*-caffeoylquinic acid; 1,5,-di-*O*-caffeoylquinic acid, 3,5-di-*O*-caffeoylquinic acid; 4,5-di-*O*-caffeoylquinic acid; and cynaroside scolymoside and cynaropikrin. Three di-*O*-caffeoylquinic acid derivatives were isolated from the ethanol extracts of the flower heads of *Cynara scolymus* (Zhu et al. 2009).

Among the 22 major phenolic compounds from artichoke (*Cynara scolymus*) heads, juice and pomace, 11 caffeoylquinic acids and 8 flavonoids were detected (Schütz et al. 2004). Apigenin 7-*O*-glucuronide was found to be the major flavonoid in all samples investigated. 1,5-di-*O*-caffeoylquinic acid represented the major hydroxycinnamic acid, with 3,890 mg/kg in artichoke heads and 3,269 mg/kg in the pomace, whereas in the juice 1,3-di-*O*-caffeoylquinic acid (cynarin) was predominant, due to the isomerization during processing. Total phenolic contents of approximately 12 g/kg on a dry matter basis revealed artichoke pomace to be a promising source of phenolic compounds that might be recovered and used as natural antioxidants or functional food ingredients. Chlorogenic acid represented the major constituent in all artichoke-based dietary supplements investigated with the exception of juice derived from fresh flower heads, which exhibited a higher cynarin content (Schütz et al. 2006a) Furthermore, a distinction between products made from artichoke leaves or flower heads was possible. Caffeoylquinic acid derivatives, including chlorogenic acid, 1,3-di-*O*-caffeoylquinic acid (cynarin) and 1,5-di-*O*-caffeoylquinic acid in artichoke heads and leaves were analyzed and quantified by ultrafast liquid chromatography/tandem mass spectrometry (Shen et al. 2010). Average recoveries ranged from 92.1 to 113.2 %. Seven active polyphenolic compounds including apigenin-7-rutinoside and narirutin were purified from artichoke heads and leaves (Wang et al. 2003).

Both artichoke flower heads and leaves were found to be rich in phenolic compounds: benzoic and cinnamic derivatives, flavonoids and tannins (Lattanzio et al. 2005, 2009). The phenolic aglycons identified as soluble-bound or insoluble bound phenolics were caffeic, *p*-coumaric, ferulic, vanillic and syringic acids, and the flavonoids apigenin and luteolin. In addition, tannins (most abundant), hydrolyzable and condensed tannins or proanthocyanidins were also identified. The content of all identified phenolics decreased with the stages of development of plant tissues. Nevertheless, a high total phenolic content was found in artichoke by-products (about 2–3 % on dry matter basis). The cinnamoyl derivatives comprised four mono-caffeoylquinic acids (1-*O*-caffeoylquinic acid, 3-*O*-caffeoylquinic or neochlorogenic acid, 4-*O*-caffeoylquinic or cryptochlorogenic, and 5-*O*-caffeoylquinic or chlorogenic acid, the most abundant) and six di-caffeoylquinic acids (1,3-*O*-dicaffeoylquinic acid or cynarin; 1,4-*O*-dicaffeoylquinic acid; 1,5-*O*-dicaffeoylquinic acid; 3,4-*O*-dicaffeoylquinic acid; 3,5-*O*-dicaffeoylquinic acid; and 4,5-*O*-dicaffeoylquinic acid). The cynarin content was very low, while 3,5-*O*-dicaffeoylquinic acid and 1,5-*O*-dicaffeoylquinic acid were the most abundant components. Also, two flavonoids, apigenin-7-glycoside and luteolin-7-glycoside, were detected. The nomenclature of the mono-caffeoylquinic and dicaffeoylquinic acids is in accordance with the nomenclatural rules of IUPAC (1976).

Cyanidin 3,5-diglucoside; cyanidin 3-caffeoylsophoroside-5-glucoside; cyanidin 3-sophoroside; cyanidin 3-glucoside; cyanidin 3-caffeoylsophoroside; and cyanidin 3-caffeoylglucoside were identified in artichoke flowers, bracts and leaves (Aubert and Foury 1981). Besides the main anthocyanins found in artichoke heads (cyanidin 3,5-diglucoside; cyanidin 3-glucoside; cyanidin 3,5-malonyldiglucoside; cyanidin 3-(3″-malonyl)glucoside; and cyanidin 3-(6″-malonyl)glucoside), several minor compounds, namely, cyanidin 3-sophoroside; cyanidin malonylglucoside; cyanidin malonyldiglucoside; delphinidin glycoside; cyanidin malonylsophoroside; cyanidin pentoside; cyanidin 3-(6″-malonyl)glucoside; peonidin 3-*O*-β-glucoside; and peonidin 3-(6″-malonyl)glycoside were identified (Schütz et al. 2006c). Total anthocyanin content ranged from 8.4 to 1,705.4 mg/kg dry mass.

Of 32 aroma components of the volatile oil of cooked artichoke, the major components were the sesquiterpenes β-selinene and caryophllene (Buttery et al. 1978). Components deemed most important to the aroma included oct-1-en-3-one, hex-1-en-3-one, decanal, non-*trans*-2-enal, phenylacetaldehyde and eugenol. All the components identified included aliphatic alcohols (2-methylbutanol and 3-methylbutanol (0.9 %), 3-methylbut-2-en-1-ol (2.2 %), hex-*cis*-3-enol (3.5 %), hex-*trans*-2-enol (1.3 %), hexanol (2.7 %), and methyl heptanol (tentative) (2.5 %)), aliphatic aldehydes (non-*trans*-2-enal (0.2 %), pentanal (0.2 %), decanal (0.4 %), hexanal (0.5 %), octanal (0.2 %), nonanal (0.6 %), heptanal (0.2 %), and hex-*trans*-2-enal (1.6 %)), aliphatic ketones (oct-1-en-3-one (0.6 %), hex-1-en-3-one (0.8 %), pentan-2-one (0.1 %), and butan-2,3-dione (90.1 %)), aromatic and heterocylic compounds (phenylacetaldehyde (7 %), eugenol (2–5 %), pyridine (0.2 %), 2-petnylfuran (0.9 %), furfural (2 %), 2-acetythiazole (0.1 %), benzaldehyde (0.8 %), benzyl alcohol (1 %), eugenol), terpene alcohols (linalool (0.4 %), α-terpineol (0.2 %), and linalool oxide C (5-hydroxy-2,6,6-trimethyl-2-vinlytetrahydropyran) (0.5 %), and sesquiterpenes hydrocarbons (β-selinene (40 %), caryophllene (19 %) and humulene (1 %)).

The edible part of artichoke heads was reported to contain a high reducing sugar content and a high percentage of water-soluble polysaccharides (inulin), mainly concentrated in the receptacle; the inulin content may constitute 75 % of the total glucidic content (Lattanzio et al. 2009). Lattanzio et al. (2009) adapting from earlier work (Lattanzio et al. 2002) reported that the glucidic content of the edible portion of artichoke head of cv. Romanesco per fresh weight and dry weight basis were respectively as follows: glucose 0.44 %, 3.18 %; fructose 0.18 %, 1.27 %; sucrose 0.98 %, 6.98 %; and inulin 5.18 %, 37 %. In another study, glucose, fructose, sucrose and individual fructooligosaccharides (kestose, nystose, fructofuranosylnystose) were quantified in the heads of six different artichoke cultivars (Schütz et al. 2006b). The contents ranged from 12.9 to 71.7 g/kg DM for glucose, from 15.8 to 67.2 g/kg DM for fructose, and from 16.8 to 55.2 g/kg DM for sucrose in the artichoke heads. Kestose was the predominant fructooligosaccharide, followed by nystose and fructofuranosylnystose. In four cultivars fructofuranosylnystose was only detectable in traces and reached its maximum value of 3.6 g/kg DM in the cultivar Le Castel.

Two taraxastane-type hydroxy triterpenes, taraxasterol and faradiol, were isolated from the flowers (Yasukawa et al. 1996). A recombinant cyprosin, an aspartic proteinase from cardoon (*Cynara cardunculus*) flowers, was purified and characterized (White et al. 1999). It was found to consist of glycosylated heavy chains (34 or 32 kDa) plus associated light chains with molecular weights in the region of 14,000–18,000. It was also found to be susceptible to inhibitors of human immunodeficiency virus proteinase and particularly of rennin. Polyphenol oxidase (PPO) was purified from hearts of artichoke (Leoni et al. 1990). The best substrates for the enzyme at pH 6.0 were 5-*O*-caffeoylquinic acid (relative activity 100 %) and caffeic acid (relative activity 69 %). Although both ascorbic and citric acids were known to considerably improve the shelf life of artichoke heads, only ascorbic acid proved to be significantly inhibitory towards artichoke polyphenol oxidase. Polyphenol oxidase isolated from artichoke heads exhibited both monophenolase and diphenolase activities (Espin et al. 1997). Monophenolase activity of artichoke PPO was characterized using 4-hydroxyanisole as substrate with 3-methyl-2-benzothiazolinone hydrazone as a coupled nucleophile. The PPO isolated from artichoke head had a 57 kDa molecular mass (Dogan et al. 2005). The enzyme showed activity to 4-methylcatechol, pyrogallol, catechol and L-dopa but not to L-tyrosine, resorsinol and *p*-cresol. The optimum pH values for PPO were 5.0, 8.0 and 7.0 using 4-methylcatechol, pyrogallol and catechol as substrate, respectively. A basic heme peroxidase isoenzyme (AKPC) was purified from artichoke flowers (López-Molina et al. 2003). The enzyme was shown to be a monomeric glycoprotein, $M_r = 42{,}300$. The substrate specificity of AKPC was characteristic of class III (guaiacol-type) peroxidases with

chlorogenic and caffeic acids that are abundant in artichoke flowers, as particularly good substrates at pH 4.5. AKPC, when purified, were found to be a mixture of Ca^{2+}-bound pentacoordinate high-spin (5cHS) and 6-aquo hexacoordinate high-spin (6cHS) ferric heme, and Ca^{2+}-free 5cHS species (Hiner et al. 2003).

Leaf/Aerial Parts Phytochemicals

The amino acid composition of the leaves (g/kg) was determined as aspartic acid 5.21 g, threonine 6.14 g, serine 5.96 g, glutamic acid 9.51 g, glycine 4.17 g, alanine 5.50 g, valine 6.57 g, methionine 10.15 g, isoleucine 4.88 g, leucine 7.71 g, leucine 7.71 g, tyrosine 3.44 g, phenylalanine 6.32 g, histidine 3.19 g, lysine 7.18 g, arginine 4.99 g and total amino acids 80.84 g (Orlovskaya et al. 2007b). They also determined the mineral composition of the leaves (mg %), Na (2070), K (690), Ca (690), Mg (207) and P (207), and 16 were microelements Cu (0.345), Zn (0.414), Ag (0.0007), Mo (0.035), Li (0.207), Pb (0.069), Co (0.007), Ni (0.021), Ti (1.380), V (0.021), Cr (0.041), Fe (20.7), B (2.07), Al (13.8), Si (34.5) and Mn (2.07). The leaves and ethanol leaf extract also contained the following flavonoids (% of total phenolic compounds) (Orlovskaya et al. 2007b): luteolin-7-glucoside 35.19 %, 6.03 %; rutin 0.08 %, 6.33 %; dihydroquercetin 0.91 %, 0; vitexin 5.31 %, 0; orientin 0.46 %, 0; hyperoside 0.01 %, 7.47 %; apigenin 0, 0.89 %; hesperidin 2.33 %, 0; robinin 0, 1.27 %, respectively. The leaves and ethanol leaf extract also contained the following (% of total phenolic compounds): coumarin–4 hydroxycoumarin 0.88 %, 0; phenolic acids–gallic acid 0, 23.48 %; cichoric acid 0, 5.86 %; hydroxycinnamic acids–chlorogenic acid 0.10 %, 23.79 %; neochlorogenic acid 6.88 %, 2.38 %; caffeic acid 38.55 %, 6.30 %; ferulic acid 0, 5.54 %; phenolic glycoside–arbutin 9.31 %, 0, respectively.

From artichoke leaves the following compounds were isolated: flavonoids (apigenin, luteolin, luteolin-4′-glucoside, cynaroside, scolimoside, cosmoside, quercetin, rutin, isorhamnetin and luteolin-7-gentiobioside) (El-Negoumy et al. 1987; Hinou et al. 1989) and phenolic acids (cynarin, chlorogenic acid, caffeic acid, neochlorogenic acid, quinic acid, 4-caffeylquinic acid, 1-caffeylquinic acid (Dranik 1966), and isochlorogenic acid), along with the more uncommon scopoletin, hesperitin, hesperidoside, esculetin-6-*O*-β-glucoside and maritimein (Hinou et al. 1989). Glycosyl flavonoids (cynaroside and scolymoside) were found to be the major constituents, along with cynaropicrin, a sesquiterpene lactone, and the triterpene lupeol and chlorogenic acid in artichoke leaves (Noldin et al. 2003). Cynarin, the main compound described for artichoke, was detected in very low concentration. From the dried leaf powder, the following flavonoids were isolated: luteolin-7-*O*-α-L-rhamnosyl(1 → 6)-β-D-glucopyranoside, luteolin-7-*O*-β-D-glucopyranoside (cynaroside), apigenin-7-*O*-α-L-rhamnosyl(1 → 6)-β-D-glucopyranoside (apigenin-7-rutinoside) and apigenin-7-*O*-β-D-glucopyranoside (Zhu and Zhang 2004). Eight phenolic compounds were isolated from the *n*-butanol-soluble fraction of artichoke leaf extract: four caffeoylquinic acid derivatives, chlorogenic acid (1), cynarin (2), 3,5-di-*O*-caffeoylquinic acid (3) and 4,5-di-*O*-caffeoylquinic acid (4), and the four flavonoids, luteolin-7-rutinoside (5), cynaroside (6), apigenin-7-rutinoside (7) and apigenin-7-*O*-β-D-glucopyranoside (8) (Zhu et al. 2004). The main polyphenols detected in different tissues and developmental stages of 6 artichoke varietal types were chlorogenic acid, cynarin, luteolin 7-*O*-rutinoside and luteolin 7-*O*-glucoside (Negro et al. 2012). 'Violet de Provence' artichoke proved to retain the highest content of total phenols. Single polyphenols accumulated preferentially in specific parts of capitula. In leaves, most polyphenols were detected in the productive stage of the plant. Thirty-nine chlorogenic acids were detected in the leaves of 12 species of the Asteraceae family including *Cynara scolymus* (Jaiswal et al. 2011). Both chlorogenic acids based on *trans*- and *cis*-cinnamic acid substituents were identified. Assignment to the level of individual regioisomers was possible for seven caffeoylquinic acids (1–7), 11 dicaffeoylquinic acids (17–27), six

feruloylquinic acids (9–14), two *p*-coumaroylquinic acids (15–16), two caffeoyl-feruloylquinic acids (28 and 29), four caffeoyl-*p*-coumaroylquinic acids (30–33), three dicaffeoyl-succinoylquinic acids (34–36), two dicaffeoyl-methoxyoxaloylquinic acids (37 and 38) and one tricaffeoylquinic acid (39). In addition, one caffeoylshikimic acid (40), one caffeoyltartaric acid (41), three dicaffeoyltartaric acids (42–44) and three caffeoyl-feruloyltartaric acids (45–47) were detected.

The carbohydrates of the leaves comprised alcohol-soluble sugars 21.34 % with traces of glucose; cold water-soluble polysaccharides 5.1 % made up of rhamnose: xylose: arabinose: mannose: glucose: galactose in the ratio of 1.0:1.4:tr: 24.6:7.3; hot water-soluble polysaccharides 0.78 % made up of rhamnose: xylose: arabinose: mannose: glucose: galactose in the ratio of 1.62:3.2:2.2:1.0:tr:2.4; pectinic substances 2.4 % made up of rhamnose: xylose: arabinose: mannose: glucose: galactose in the ratio of 4.3:1.0:2.5:0:0:1.4; hemicelluloses 2.63 % made up of rhamnose: xylose: arabinose: mannose: glucose: galactose in the ratio of tr:8.76:4.6:1.4:1.0:4.8 (Orlovskaya et al. 2007a).

In the leaves of cultivated and wild *Cynara cardunculus*, the flavones were the major compounds, whereas in the floral stem, caffeoylquinic acids were the most abundant (Pandino et al. 2011a). In particular, 'Sylvestris Creta' (var. *sylvestris*, wild cardoon) and 'Violetto di Sicilia' (var. *scolymus*, globe artichoke) showed the highest content of caffeoylquinic acid ~ 95 % of the total measured polyphenols. The major compounds present in the leaf were luteolin derivatives in globe artichoke and apigenin derivatives in wild and cultivated cardoon.

From the cauline leaves of *C. scolymus*, cyanarin, a substance with stimulatory action on biliary secretion and cholesterinic metabolism, was isolated (Panizzi and Scarpati 1954). From artichoke leaves the following flavonoids were isolated: luteolin 7-β-glycoside and luteolin 7-β-rutinoside (Dranik et al. 1964); a flavonoid glycoside, cynarotriside, having the structure luteolin 7-[*O*-β-D-glucopyranosyl-(6 → 1)-*O*-β-L-rhamnopyranoside]-4′-*O*-β-D-glucopyranoside (Dranik and Chernobai 1966); luteolin, cynaroside (luteolin-7-glucoside) and scolymoside (luteolin-7-β-rutinoside) (Constantinescu et al. 1967); and apigenin, luteolin, apigenin-7-*O*-glucoside, cynaroside (luteolin-7-glucoside) and scolymoside (luteolin-7-β-rutinoside) (Hammouda et al. 1993). From the leaves the following phenolic acids and flavonoids were detected: chlorogenic acid, 1,3-di-*O*-caffeylquinic acid, cryptochlorogenic acid, neochlorogenic acid and 3,5-di-*O*-caffeylquinic acid; flavonoids: luteolin-4′-*O*-glucoside, luteolin 7-*O*-glucoside and luteolin 7-*O*-rhamnoglucoside (Bombardelli et al. 1977). The following organic acids were detected in artichoke: glyceric, malic, citric, glycolic, lactic and succinic acids (Bogaert et al. 1972). Lattanzio and Morone (1979) found that chlorogenic acid content declined from 4.4 to 1.6 % dry matter (dm). As the plant developed to the stage of differentiation of the capitulum and remained stable, a similar tendency was detected for cynaroside (0.4–0.16 % dm) and scolymoside (0.7–0.15 % dm), while the behaviour of cynarin was just the opposite, increasing gradually as the plant grew (0.01–0.05 % dm).

Hydroxymethyl acrylic acid was isolated from artichoke leaves (Bogaert et al. 1974). Two phenolic glucoside gallates, 2-methoxy-4-(2,3-dihydroxy-propionyl)-phenyl-1-*O*-(6′-*O*-galloyl)-β-D-glucopyranoside and 4-hydroxy-3-methoxy-phenyl-1-*O*-(6′-*O*-galloyl)-β-D-glucopyranoside, were isolated from the leaves (Liu et al. 2009b). A sesquiterpenic lactone cynarolide was isolated from artichoke leaves (Drozdz 1968). Two guaiane-type sesquiterpene lactones, cynarinins A and B, together with seven known compounds, cynarascoloside C, cynaropicrin, aguerin B, grosheimin, aguerin A dehydrocynaropicrin and cynaratriol, were isolated from aerial part of *Cynara scolymus* (Li et al. 2005). Guaianolides, cynaropicrin and grosheimin, isolated from artichoke leaves were found to be associated with the leaf bitterness (Cravotto et al. 2005). Bioconversion of the chemicals generated 15 sesquiterpene lactone derivatives which were subjected to a taste sensory panel. Bitterness was markedly abated by either the loss of exomethylenes or the opening of the lactone ring. The bitterness of sesquiterpene lactones cynaropicrin

and grosheimin derivatives was found not to be directly related to molecular polarity (Scotti et al. 2007). Cyanaropicrin, the bitter principle was found only in the green aerial parts in the stem sprouts, leaf stalks and green buds (up to 0.6 %) and in leaf lamina 0.5–4.5 % (in one case to 6.5 %) (Schneider and Thiele 2009). Young leaves contained more bitter principle than old ones. The top of the leaves showed 80 % more bitter substance than the leaf base. No bitter substance was found in the roots, completely developed blossoms and fruits. Three new guaianolides, 11-*H*-13-ethylsulfonylgrosheimin (grosulfeimin); 8-deoxy-11,13-dihydroxygrosheimin; and 8-deoxy-11-hydroxy-13-chlorogrosheimin and 8-epigrosheimin were isolated from the leaves (Barbetti et al. 1993). Other guaianolides, cynaropicrin, 3-deydrocynaropicrin, grosheimin, cynarolide and cynaratriol, had been isolated from artichoke (Barbetti et al. 1992; Jouany et al. 1975; Bernhard et al. 1979; Bernhard 1982). Besides cynaratriol, its derivatives 3,11,13-triacetylcynaratriol and 3,13-dibenzoyl-cynaratriol were also identified from the leaves (Bernhard 1982). A guaiane-type sesquiterpene lactone, 3β, 8α, 11β, 13-tetrahydroxy-10(14)-guaien-1α, 4β, 5α, 6β*H*-6α, 12-olide, and a known sesquiterpene lactone, cynarinin A, were isolated from the leaves (Liu et al. 2009a).

Apigenin 7-*O*-glucoside, cynarin, narirutin, gallic acid and caffeic acid were found as the main flavonoids and phenolic constituents in all parts of artichoke (flowers, leaves, roots, stems, stumps) (Thi and Park 2008). Water extraction gave higher value of total phenolic compounds and flavonoids than that by methanol or methanol:water extractions. Artichoke stem was found to be rich in non-starch polysaccharide (NSP) (∽38 g NSP/kg) and was similar to the receptacle (∽34 g NSP/kg), but bracts were heavily lignified; the stem could prove useful as sources of pectic polysaccharide-rich supplements (Femenia et al. 1998).

In commercially available artichoke leaf extract, the following compounds were identified: 8-deoxy-11-hydroxy-13-chlorogrosheimin, cryptochlorogenic acid, chlorogenic acid, neochlorogenic acid, cynarin, cynaratriol (tentatively), grosheimin, 8-deoxy-11,13-dihydroxygrosheimin, luteolin-7-*O*-rutinoside, luteolin-7-*O*-glucoside and cynaropicrin (Fritsche et al. 2002) The concentration of the compounds, namely, chlorogenic acid, cynarin and luteolin-7-*O*-glucoside, was in the range of 0.35–18.34, n.d.–1.02, 0.04–10.65 mg/g, respectively. Cynar opicrin, the predominant bitter artichoke leaf principle, was present at concentrations between <0.06 and 22.6 mg/g.

Ribulose-1,5-diphosphate carboxylase in artichoke leaves was separated, purified and characterized (Pacoda et al. 1985; Cardinali et al. 1986; Miceli et al. 1986). Cardinali et al. (2012) reported that the cationic peroxidase isoenzyme (CysPrx) isolated from artichoke leaves possessed some interesting properties, suggesting that CysPrx could be a considered as a potential candidate for industrial peroxidase application. In addition, from the CysPrx sequence, two full-length cDNAs, CysPrx1 and CysPrx2, differing for three amino acids, were isolated.

Seed Phytochemicals

Artichoke seeds were found to have crude protein 21.6 %, crude fibre 17.1 %, crude oil 24.05 % and ash 3.8 % (Foti et al. 1999). Artichoke seed oil was found to be an unsaturated semi-drying oil, with a high saponification value and acidic. It thus would require purification before used as edible oil. The fatty acid composition showed a high content of polyunsaturated acids (oleic acid 26.73 %, linoleic acid 58.89 %, linolenic acid 0.25 %) and to contain cholesterol (0.2 %), campesterol (12.8 %), Δ^5-stigmasterol (16.2 %), β-sitosterol (45.6 %), Δ^7-stigmasterol and Δ^7-avenasterol (18.4-6.6 %). The oil had a yield of 20.5 %, free acidity (oleic acid) 11.3 %, acid value 22.4 mg/g, iodine value 108.4 g/100 g, unsaponifiable matter 0.9 %, mean molecular mass 306.2 and refractive index 1.4682 (25 °C) (Miceli and De Leo 1996).

Artichoke seed oil was found to be rich in oleic and linoleic acids (Hassanein et al. 2011). The fatty acid profile of artichoke oil comprised 14:0 (0.1 %), 16:0 (11.3 %), 16:1 (0.1 %), 18:0

(3.2 %), 18:1 *n*–9 (30.2 %), 18:1 *n*–7 (0.70 %), 18:2 (53.5 %), 20:0 (0.40 %), 20:1 (0.20 %) 24:0 (0.30 %). Among the triacylglycerols (TAGs), LLL, LLO LLP LOO and LOP were the major components in artichoke seed oil (L = linoleic, O = oleic, P = palmitic). Artichoke seed oil had a whole sterol content (as silyl derivatives) of 1.2 % of the total lipids and had high content of 5-stigmasterol (22.7 %), β-sitosterol (33.1 %) and 7-stigmasterol (25.7 %) and also possessed campesterol (9.5 %), avenasterol (6.4 %), spinasterol (2.2 %) and isofucosterol (0.4 %). The total content of free sterol (FS) and acylated sterol (AS) as 9-anthroylnitrile derivatives isolated from the oil was 390 mg/100 g oil (0.39 % of total lipid) comprising 280 mg/100 mg of free sterol and 110 mg/100 g acylated sterol. Both FS and AS showed the presence of β-sitosterol, isofucosterol,7-stigmasterol, avenasterol, spinasterol and β-stigmasterol/campesterol (inseparable pair). Artichoke oil also had high content (1,000 ppm) of free sterylglycerols (FSG) (687 ppm) and acylated sterylglycerols (ASG) (313 ppm) as 1-anthroylnitrile derivatives. It was found that β-sitosterol was the major component in both FSG and ASG fractions, followed by campe-/stigma-SG, isofuco-SG, 7-stigma-SG and spina-SG. Artichoke oil was found to have 311 ppm total tocopherols comprising 96.5 % α-tocopherol, 2.5 % γ-tocohpherol and 1.0 % δ-tocopherol.

Seeds and leaves of the artichoke had been reported to contain different constituents such as caffeoylquinic acid derivatives, mono- and di-caffeoylquinic acids, bitter sesquiterpene such as cynaratriol and cynaropicrin and flavonoids glycosides like apigenin, luteolin, cynaroside, scolymoside, quercetin and others (Georgieva et al. 2011). The content of total phenolics, chlorogenic acid and 1.5 dicaffeoyl-quinic-acid (cynarin) in germinating seeds varied considerably between different genetic lines and were higher than that reported in artichoke leaves (Ben-Hod et al. 1992). The authors concluded that compared to the traditional extraction from leaves, germinating seeds offer a richer and more dependable source for cynarin supply.

According to Maccarone et al. (1999), *Cynara* species grain oil especially cardoon had superior alimentary quality with a high content of oleic and linoleic acids in a balanced ratio, a good amount of α-tocopherol and low amounts of free acids, peroxides, saturated and linolenic acids. Triacylglycerols were the dominant constituents together with very little amounts of phospholipids and glycolipids. Curt et al. (2002) reported a range of 20–31.6 % seed oil content for *C. cardunculus*. Cynara seed oil profile was characterized in terms of major fatty acids as 10.7 % palmitic, 3.7 % stearic, 25.0 % oleic and 59.7 % linoleic.

Plant Biomass/Root Phytochemicals

At harvest the total biomass and root production, averaged for all *Cynara cardunculus* genotypes, were 20.4 and 9.8 t DM/ha; they were influenced by genotype (Raccuia and Melilli 2004). On average for all of the genotypes, the roots showed a total sugar content of 367 g DM/kg, with a cv. of 17.1 %; the main compound was inulin (85.0 % of total sugars). The wild cardoon 'SR1' showed the highest total sugar content (470 g/kg DM). On average for all of the genotypes, the total sugar and inulin yields were 3.6 and 3.0 t/ha, respectively. Studies showed that globe artichoke (*Cynara cardunculus* subsp. s*colymus*) crop for heads utilization, at the end of their harvest, gave a remaining above-ground biomass production, on average of all genotypes, of 10.3 t/ha DM with a range of 5.7 to 15.7 t/ha of DM, partitioned between leaves (53.4 %) and stalks (47.6 %) (Raccuia et al. 2004b). The root yield resulted on average of all genotypes 5.7 t/ha of DM. The total extracted sugars from roots resulted on average of all genotypes, 249 g/kg of DM, where inulin accounted for 89.4 % of total sugars. Root total sugars yield resulted on average of all genotypes 1.41 t/ha.

Artichoke By-Products/Waste Phytochemicals

Artichoke by-products such as leaves, external bracts and stems that are produced by the artichoke-processing industry represent a huge amount of

discarded material (about 80–85 % of the total biomass of the plant), which could be used as a source of inulin but also of phenolics especially chlorogenic acid and 1,5-*O*-dicaffeoylquinic, 3,5-*O*-dicaffeoylquinic and 3,4-*O*-dicaffeoylquinic acids and should be considered as a raw material for the production of natural nontoxic food additives and neutraceuticals (Lattanzio et al. 2005, 2009; Ceccarelli et al. 2010).

In Spain, a leading artichoke producer in Europe, the residues proceeding from artichoke industry can form up to 60 % of the harvested plant material. Forty-five phenolic compounds were identified in artichoke waste (Sánchez-Rabaneda et al. 2003): gallic acid; caffeoylquinic acid 1,2, 3; dicaffeoylquinic acid 1, 2,3, 4,5, 6, 7; protocatechuic acid; esculin; chlorogenic acid; *p*-coumaric acid-*O*-glucoside isomers 1 and 2; eriodictyol-glucuronide; rutin (quercetin-3-*O*-rutinoside); dicaffeoylquinic acid derivative; hyperoside (quercetin-3-*O*-galactoside); luteolin-7-*O*-rutinoside; cynaroside (luteolin-7-*O*-glucoside); isoquercitrin (quercetin-3-*O*-glucoside); luteolin-7-*O*-glucuronide; luteolin-7-*O*-galactoside; naringenin-*O*-hexoside; avicularin (quercetin-3-*O*-arabinoside); isorhoifolin (apigenin-7-*O*-rutinoside); quercetin-*O*-pentoside; quercitrin (quercetin-3-*O*-rhamnoside); luteolin-7-*O*-neohesperidoside; apigenin-*O*-glucoside; prunin (naringenin-7-*O*-glucoside); naringin (naringenin-7-*O*-neohesperidoside); scolimoside (luteolin-7-*O*-rhamnoside); apigenin-7-*O*-glucuronide; quercetin-*O*-pentoside; phloridzin (phloretin-2-*O*-glucoside); feruloylquinic acid-*O*-glucoside; luteolin; quercetin; naringenin; and apigenin chrysoeriol. Caffeoylquinic and dicaffeoylquinic acids were the main compounds in the waste residue. A high molecular weight inulin was fabricated from artichoke agroindustrial wastes using environmentally benign aqueous extraction procedures (Lopez-Molina et al. 2005). The main constituent monosaccharide in artichoke inulin was fructose, and its degradation by inulinase indicated that it contained the expected beta-2,1-fructan bonds. Its FT-IR spectrum was identical to that of chicory inulin. The data indicated that artichoke inulin will be suitable for use in a wide range of food applications.

In various molecular, cellular and in-vivo test studies, artichoke (*Cynara scolymus*) leaf extracts showed antioxidative, hepatoprotective, antimicrobial, antiviral, anticancer, urinative, choleretic and anticholestatic effects as well as inhibitory actions on cholesterol biosynthesis and LDL oxidation (Kraft 1997; Lattanzio et al. 2009). The antidyspeptic actions ware mainly based on increased choleresis. Regarding clinical data, lipid-lowering, antiemetic, spasmolytic, choleretic and carminative effects had been described, along with good tolerance and a low incidence of side effects. The results of several clinical investigations showed the efficacy and safety of artichoke extracts (*Cynara scolymus*) in the treatment of hepato-biliary dysfunction and digestive complaints, such as sensation of fullness, loss of appetite, nausea and abdominal pain (Wegener and Fintelmann 1999). Earlier findings on a lipid-lowering and hepatoprotective effects were confirmed, and flavonoids and caffeoylquinic acids were reported to be mainly responsible for the observed actions. These and other pharmacological properties of artichoke are elaborated below.

Antioxidant Activity

In ABTS and DPPH tests, turmeric extract was found to be the most active, followed by artichoke and dandelion (Menghini et al. 2010). A luteolin-rich artichoke extract retarded low-density lipoprotein (LDL) oxidation in a dose-dependent manner as measured by a prolongation of the lag phase to conjugated diene formation, a decrease in the rate of propagation, and a sparing of endogenous LDL α-tocopherol during oxidation (Brown and Rice-Evans 1998). The pure aglycone, luteolin (1 μM), demonstrated an efficacy similar to that of 20 μg/ml artichoke extract in inhibiting lipid peroxidation. Luteolin-7-*O*-glucoside, one of the glycosylated forms in the diet, also demonstrated a dose-dependent reduction of LDL oxidation that was less effective than that of luteolin. Studies of the copper-chelating properties of luteolin-7-*O*-glucoside and luteolin suggested a potential role for chelation in the antioxidative effects of artichoke

extract. The results demonstrated that the antioxidant activity of the artichoke extract was related in part to its constituent flavonoids which acted as hydrogen donors and metal ion chelators, and the effectiveness was further influenced by their partitioning between aqueous and lipophilic phases.

The crude flower head and leaf extracts and different phenolic fractions tested showed good antioxidant activity in the control of the oxidative damage caused by peroxyl radicals (the β-carotene/linoleate assay) (Lattanzio et al. 2005). All phenolics exhibited good antioxidant activity against peroxyl and hydroxyl radicals when assessed using the β-carotene/linoleate assay and the metmyoglobin assay. The same phenolics showed a lower activity when assessed using the deoxyribose assay. Overall, luteolin, caffeoylquinic acids and hydrolyzable tannins, being the most representative artichoke phenolics, may be considered the phenolic constituents responsible for the antioxidant properties of artichoke extracts. In addition other phenolics present in the extracts such as *p*-coumaric, ferulic, vanillic, syringic acids and apigenin-7-glucoside may contribute to the total antioxidant capacity of the extracts.

Artichoke leaf extract exerted a concentration-dependent inhibition of oxidative stress when human leukocytes were stimulated with agents that generated reactive oxygen species (ROS): hydrogen peroxide, phorbol-12-myristate-13-acetate (PMA) and *N*-formyl-methionyl-leucyl-phenylalanine (FMLP) (Perez-Garcia et al. 2000). Cynarin, caffeic acid, chlorogenic acid and luteolin, constituents of artichoke leaf extract, also exhibited a concentration-dependent inhibitory activity in the above models, contributing to the antioxidant activity of the extract in human neutrophils.

The 75 % ethanol artichoke leaf extract exhibited the highest antioxidant activity as evaluated by 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay as well as yielded the largest quantity of polyphenolic compounds (Vamanu et al. 2011). The optimum concentration of 10 mg/ml gave maximum antioxidant activity of 65.15 %. The MIC values obtained using the freeze-dried extract ranged from 5.0 to 15.0 mg/ml. Total phenolic content varied from 2.12 to 30.38 mg/g of the extract. In separate studies, the ethanol extracts prepared from *Cynara scolymus* seeds and leaves were found to have DPPH radical scavenging activities (Georgieva et al. 2011). At any studied concentration of the seeds extract, the percent of the scavenged DPPH radicals was considerably higher than that calculated for the leaves extract. All investigated individual artichoke compounds from commercially artichoke leaf extract—chlorogenic acid, cynarin, luteolin and luteolin-7-*O*-glucoside—showed a remarkable antioxidative effect, chlorogenic acid being the strongest antioxidant compound (Fritsche et al. 2002).

Antioxidant phenolics were extracted from artichoke by-products: raw artichoke (RA), blanched (thermally treated) artichoke (BA) and artichoke blanching waters (ABW) by both methanol and water extractions (Llorach et al. 2002). Phenolic contents (expressed as caffeic acid derivatives) (grams per 100 g of dry extract) were 15.4 and 9.9 for RA when extracted with methanol and water, respectively; 24.3 and 10.3 for BA when extracted with methanol and water, respectively; and finally, 11.3 g of phenolics/100 ml of ABW. The artichoke extracts from industrial by-products showed a high free radical scavenging activity (versus both DPPH* and ABTS*+radicals) as well as capacity to inhibit lipid peroxidation (ferric thiocyanate method). The results suggested the possible use of artichoke extracts from industrial by-products as ingredients to functionalize foodstuffs (to decrease lipid peroxidation and to increase health-promoting properties). In another study one gram (dry matter) of artichoke was found to have a DPPH(*) activity and a FRAP value in-vitro equivalent to those of 29.2 and 62.6 mg of vitamin C and to those of 77.9 and 159 mg of vitamin E, respectively (Jiménez-Escrig et al. 2003). Artichoke extracts showed good efficiency in the inhibition in vitro of low-density lipoprotein oxidation. Neither ferric-reducing ability nor 2,2′-azinobis(3-ethylbenzothiazolin-6-sulfonate) radical scavenging activity was modified in the rat plasma of the artichoke group with respect to the control group. Among different antioxidant enzymes measured (superoxide dismutase, glutathione

peroxidase, glutathione reductase and catalase) in erythrocytes, only glutathione peroxidase activity was elevated in the artichoke group compared to the control group. 2-Aminoadipic semialdehyde, a protein oxidation biomarker, was decreased in plasma proteins and haemoglobin in the artichoke-fed group versus the control group. The results confirmed the in-vitro protective oxidative activity of artichoke in a rat model.

Studies demonstrated that artichoke polyphenolic extract protected cultured rat hepatocytes from the oxidative stress caused by glucose oxidase, comparable to the well-known antioxidant, *N*,*N*′-diphenyl-*p*-phenylenediamine (DPPD) (Miccadei et al. 2008). Further, the extract as well as chlorogenic acid prevented the loss of total glutathione and the accumulation of malondialdehyde. Artichoke leaf aqueous extracts exhibited a dose-dependent free radical scavenging effect of DPPH and an inhibitory effect of xanthine oxidase (Zan et al. 2013). The extract was found to contain phenolic compounds, flavonoids and saponins such as chlorogenic acid, caffeic acid, isoquercetrin and rutin.

The antioxidant capacity of cooked artichokes, measured by three different assays, enormously increased after cooking, particularly after steaming (up to 15-fold) and boiling (up to 8-fold) (Ferracane et al. 2008). Boiling increased the concentration of dicaffeoylquinic acid isomers much more than steaming or frying which showed similar patterns of dicaffeoylquinic concentrations. However, all cooking practices, particularly frying, decreased flavonoid concentration.

In double-blinded study carried out in 22 members of the Polish rowing team who were randomly assigned to a supplemented group ($n = 12$), receiving 1 gelatin capsule containing 400 mg of artichoke leaf extract three times a day for 5 weeks, or a placebo group ($n = 10$), plasma total antioxidant capacity (TAC) was significantly higher in the supplemented group than in the placebo group during restitution (Skarpanska-Stejnborn et al. 2008). Serum total cholesterol levels at the end of the study were significantly lower in the supplemented group than in the placebo group. The authors concluded that consuming artichoke leaf extract, a natural vegetable preparation of high antioxidant potential, resulted in higher plasma TAC than placebo but did not limit oxidative damage to erythrocytes in competitive rowers subjected to strenuous training.

The ethanol extract and fractions (chloroform, ethyl acetate and *n*-butanol) of the ethanol extract of fresh involucral bracts of cardoon, *Cynara cardunculus*, exhibited concentration-dependent antioxidant activity in the FRAP (ferric reducing antioxidant power) assay and scavenging of 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical assays (Kukić et al. 2008).

Antidyspeptic Activity

A significant increase in bile flow was observed in anesthetized Wistar rats after acute treatment with artichoke leaf extract as well as after repeated administration (Sánchez-Rabaneda et al. 2003). The choleretic effects of artichoke extract were similar to those of the reference antidyspeptic compound dehydrocholic acid (DHCA).

In a randomized placebo-controlled double-blind cross-over study of 20 subjects, administration of a standardized, artichoke extract Hepar-SL forte was found to have a choleretic effect (Kirchhoff et al. 1994). At 120 and 150 minutes the volume of bile secreted under the active treatment was also significantly higher than under the placebo. In the placebo group, bile secretion fell below the initial level after 3 hours. An effective period of about 120–150 minutes was regarded as satisfactory to influence enzymatic digestion and the motor function of the intestine when the test substance was given postprandially. No side effects or changes in the laboratory parameters in connection with the experiment were observed. Results indicated that artichoke extract could be recommended for the treatment of dyspepsia, especially when the cause may be attributed to dyskinesia of the bile ducts or disorder in the assimilation of fat.

In postmarketing surveillance (phase IV) studies patients with non-specific gastrointestinal complaints receiving treatment with globe artichoke leaf extract (Hepar-SL forte; up to 1.92 g daily for 6 weeks (Fintelmann and Menssen 1996) or

6 months (Fintelmann and Petrowicz 1998) were monitored. In one study involving 533 patients with non-specific gastrointestinal complaints, including dyspepsia, functional biliary tract complaints, constipation and gastric irritation, seven adverse events (weakness, hunger, flatulence) were reported (1.3 % of participants), but no serious adverse events were reported (Fintelmann and Menssen 1996). In the second postmarketing surveillance study involving 203 patients with symptoms of dyspepsia who received globe artichoke leaf extract up to 1.92 g daily for up to 6 months, no adverse events were recorded (Fintelmann and Petrowicz 1998). The physicians' overall judgement of tolerability was given as 'good' or 'excellent' in 98.5 % of cases. In another postmarketing surveillance study for artichoke leaf extract in a sub-group of patients with irritable bowel syndrome (IBS) symptoms, analysis of data revealed significant reductions in the severity of symptoms and favourable evaluations of overall effectiveness by both physicians and patients (Walker et al. 2001). Additionally, 96 % of patients rated artichoke extract as better than or at least equal to previous therapies administered for their symptoms, and the tolerability of the extract was very good.

Studies by Marakis et al. (2002) found that artichoke leaf extract showed promise in ameliorating upper gastrointestinal symptoms and improving quality of life in otherwise healthy subjects suffering from dyspepsia. Of the 516 participants, 454 completed the study. There was a significant reduction of all dyspeptic symptoms, with an average reduction of 40 % in global dyspepsia score for both dosage groups of 320 or 640 mg daily. There were no differences in the primary outcome measures between the two groups, but relief of state anxiety, a secondary outcome, was greater with the higher dosage. Health-related quality of life was significantly improved in both groups compared with baseline. The efficacy of artichoke leaf extract treatment of patients with functional dyspepsia (129 artichoke treatment, 115 placebo) was assessed in a 6-week, double-blind, randomized controlled trial (Holtmann et al. 2003). The overall symptom improvement over the 6 weeks of treatment was significantly greater with artichoke extract than with the placebo. Similarly, patients treated with artichoke extract showed significantly greater improvement in the global quality-of-life scores (NDI) compared with the placebo-treated patients.

In a subset analysis of a previous dose-ranging, open, postal study in adults (208) suffering dyspepsia, 2 months intervention of artichoke leaf extract was found to ameliorate symptoms of irritable bowel syndrome (IBS) in otherwise healthy volunteers (Bundy et al. 2004). A significant shift in self-reported usual bowel pattern away from 'alternating constipation/diarrhoea' towards 'normal' was observed. Nepean Dyspepsia Index (NDI) total symptom score significantly decreased by 41 % after artichoke treatment. Similarly, there was a significant 20 % improvement in the NDI total quality-of-life (QOL) score in the subset after treatment.

Treatment of a cohort of patients with a clinical diagnosis of functional dyspepsia for 60 days with Cinarepa, a commercial mixture of dry extracts of artichoke leaf (*Cynara scolymus*) 15 % of chlorogenic acid (150 mg per capsule), dandelion radix (*Taraxacum officinalis*) 2 % of inulin, turmeric rhizome (*Curcuma longa*) 95 % of curcumin and rosemary bud essential oil microencapsulated (*Rosmarinus officinalis*), was found to ameliorate severity of dyspepsia symptoms (Sannia 2010). Global clinical response, defined as a 50 % reduction in the total scores of all symptoms, was recorded in 38 % of patients at 30 days and in 79 % at 60 days. At 60 days, total cholesterol, LDL and triglyceride levels had decreased by 6–8 % over baseline values; transaminase (AST, ALT) and gamma GT concentrations had diminished by 13–20 U/l in patients with relatively elevated baseline values.

Hepatoprotective Activity

In rats receiving ethanol and 1,5-dicaffeylquinic acid (cynarin) simultaneously, a distinct reduction of the serum and hepatic cholesterol levels was observed (Wójcicki 1978). In contrast, rats treated with ethanol alone, the serum and hepatic cholesterol showed a significant rise of 44 and

75 %, respectively. Of the polyphenolic compounds of artichoke, only cynarin and, to a lesser extent, caffeic acid showed hepatoprotective activity against CCl_4 toxicity in isolated rat hepatocytes (Adzet et al. 1987).

The results of in-vitro studies indicated artichoke extracts had a marked antioxidative and protective potential (Gebhardt 1997). Addition of artichoke extracts to primary rat hepatocyte cultures exposed to *tert*-butylhydroperoxide (*t*-BHP) or cumene hydroperoxide did not affect basal malondialdehyde (MDA) production but prevented the hydroperoxide-induced increase of MDA formation in a concentration-dependent manner when presented simultaneously or prior to the peroxides. The artichoke extracts did not affect the cellular level of glutathione (GSH) but diminished the loss of total GSH and the cellular leakage of GSSG resulting from exposure to *t-BHP*. Chlorogenic acid and cynarin accounted for only part of the antioxidative principle of the extracts which was resistant against tryptic digestion, boiling, acidification and other treatments but was slightly sensitive to alkalinization. In another study, aqueous artichoke extracts added prior or simultaneously with *tert*-butylhydroperoxide (*t*-BHP) to primary cultures of rat hepatocytes reduced both lipid peroxidation and cytotoxicity with EC_{50} values of about 95 and 12 µg artichoke powder/ml, respectively (Gebhardt and Fausel 1997). Further, the extract prevented the loss of intracellular glutathione caused by *t*-BHP. Several polyphenolic and flavonoid constituents of AE were found to reduce malonaldehyde (MDA) production. EC_{50} values were 8.1, 12.5, 15.2 and 28 µg/ml for caffeic acid, chlorogenic acid, cynarin and cynarosid, respectively. A similar ranking for the extract and constituents was found when using the chemiluminescent xanthine oxidase assay for determination of the antioxidative potency, but EC_{50} values were consistently lower. Regarding the hepatoprotective effect, that is, prevention of LDH (lactate dehydrogenase) leakage, all constituents were almost equipotent and EC_{50} values were lower than for MDA production. Other studies showed artichoke leaf extracts exerted a potent anticholestatic action in primary cultured rat hepatocytes at least in the case of taurolithocholate-induced cholestasis (Gebhardt 2001, 2002b). Taurolithocholate-induced bizarre bile canalicular membrane distortions could be prevented by artichoke leaf extracts in a dose-dependent manner when added simultaneously with the bile acid. Flavonoids and their metabolites flavonol luteolin and, to a lesser extent, by luteolin-7-*O*-glucoside, may contribute significantly to this effect. Chlorogenic acid and 1.5-dicaffeoyl quinic acid were almost ineffective.

Speroni et al. (2003) showed that the *Cynara scolymus* leaf extract with the highest content in phenolic derivatives (GAE) exerted the major effect on bile flow and liver protection. Also the results of the antioxidant capacity (BR) of the different preparations were in good agreement with the results obtained in-vivo. On the contrary, administering rats with doses of chlorogenic acid, equivalent to those present in this extract, did not elicit any choleretic or protective action. They suggested that caffeoyl derivatives had a role in the therapeutic properties of *C. scolymus* extracts, as reported in literature for 'in-vitro' studies, but when administered alone, they were not so effective in exerting this effect. Separate studies showed that in rats pretreated with artichoke leaf extract, significant decreases in plasma transaminase activities and amelioration in histopathological changes in the liver were observed following carbon tetrachloride (CCl_4) treatment as compared to CCl_4-treated rats (Mehmetçik et al. 2008). In addition, hepatic malondialdehyde and diene conjugate levels decreased, but glutathione levels and glutathione peroxidase activities increased without any change in other antioxidant parameters following CCl_4 treatment in artichoke-pretreated rats. Their findings indicated that in-vivo artichoke extract administration may be useful for the prevention of oxidative stress-induced hepatotoxicity.

Antihypercholesterolemic Antihyperlipidemic Activity

Cynara scolymus was one of seven plant species that had preclinical data that indicated a potential

role in the control of certain conditions which are associated with obesity, such as hyperlipidaemia (Dickel et al. 2007).

In-Vitro Studies

High-dose aqueous extracts from artichoke leaves were found to inhibit cholesterol biosynthesis from 14C-acetate in primary cultured rat hepatocytes in a concentration-dependent biphasic manner with moderate inhibition (approximately 20 %) between 0.007 and 0.1 mg/ml and more strong inhibition at 1 mg/ml (Gebhardt 1998). It was found that an indirect modulation of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA)-reductase activity was the most likely inhibitory mechanism of the artichoke extracts. Screening of several known constituents of artichoke extracts revealed that cynaroside and particularly its aglycone luteolin were mainly responsible for inhibition, whereas chlorogenic acid was much less effective and caffeic acid, cynarin and other dicaffeoylquinic acids were without significant influence. Also, luteolin also efficiently blocked the insulin effect on cholesterol biosynthesis. The results demonstrated that artichoke extracts may inhibit hepatic cholesterol biosynthesis in an indirect but efficient manner and, thus, may contribute via this action to its hypolipidemic influence in man. In a subsequent paper, high-dose aqueous artichoke leaf extracts were found to inhibit cholesterol biosynthesis from (14) C-acetate rather moderately in HepG2 cells in contrast to primary cultured rat hepatocytes in which the inhibition was stronger (Gebhardt 2002a). Preincubation of the extracts with beta-glucosidase considerably reinforced the inhibition. At extract concentration of 0.2 mg/ml, almost 60 % inhibition was observed. Cytotoxic effects detected by the MTT-assay were restricted to higher concentrations of the extracts with and without beta-glucosidase pretreatment. It was demonstrated that cynaroside was one of the targets of beta-glucosidase and that the liberated luteolin was responsible for the inhibitory effect. Direct measurements of beta-glucosidase activity in rat hepatocytes and HepG2 cells revealed that endogenous enzyme activity in hepatocytes may be sufficient to convert cynaroside to its aglycone, while in HepG2 cells this may not be the case.

Of all individual artichoke compounds from commercially artichoke leaf extract, chlorogenic acid showed a strong, dose-dependent linear 3HMG-CoA reductase inhibitory effect at concentrations between 5 and 50 mg/ml (Fritsche et al. 2002). Luteolin and luteolin-7-*O*-glucoside showed an even stronger inhibitory effect at 10 mg/ml (relative HMG-CoA reductase activity: 2.4 and 6.5 %, respectively, compared to 26.5 % activity after chlorogenic acid treatment). All studied commercially available artichoke leaf extracts showed a moderate inhibitory effect at 10 mg/ml.

Animal Studies

Results of several earlier animal studies suggested that artichoke and cardoon extracts exerted a marked reduction in serum cholesterol and triglyceride levels after experimentally induced hypercholesterolaemia (Samochowiec 1962a, b; Lietti 1977).

The methanol artichoke leaf extract was found to suppress serum triglyceride elevation in olive oil-loaded mice (Shimoda et al. 2003). The sesquiterpenes cynaropicrin, aguerin B and grosheimin were isolated as the active components together with new sesquiterpene glycosides (cynarascolosides A, B and C). Further, inhibition of gastric emptying was shown to be partly involved in antihyperlipidemic activity. Studies on the effect of the artichoke extract on oxidation of palmitic-1-14C acid administered intravenously to rats at a dose 25 and 50 mg/kg body weight demonstrated marked dose-dependent enhancement of both $14CO_2$ expiration rate and $14CO_2$ recovery in the expired air (Juzyszyn et al. 2008a). The extract suppressed accumulation of palmitic-1-14C acid in serum lipids and epididymal fat pad tissue in a dose-dependent manner. The results demonstrated that artichoke extract possessed stimulatory properties with respect to oxidation of palmitic acid administered to rats and provided new information on the mechanism of antilipidemic activity of the extract associated with activation of lipid oxidation in rats.

Significant decreases in serum malondialdehyde (MDA) and diene conjugate levels and

increases in plasma antioxidant activity were detected in serum in artichoke-treated hypercholesterolemic rats (Küskü-Kiraz et al. 2010). Endogenous diene conjugate and copper-induced MDA levels were also lower in LDL+VLDL fraction due to artichoke-treatment in hypercholesterolemic rats. Their results indicated that artichoke leaf extract may be useful for the prevention of hypercholesterolaemia-induced pro-oxidant state in LDL+VLDL fraction and the reduction of increased serum cholesterol and triglyceride levels. Küçükgergin et al. (2010) found that serum cholesterol and triglyceride levels and ratio of cholesterol to high-density lipoprotein (HDL)-cholesterol decreased in hypercholesterolemic rats treated with artichoke leaf extract, but liver cholesterol and triglyceride levels remained unchanged. Significant decreases in hepatic and cardiac malondialdehyde (MDA) and diene conjugate levels and increases in hepatic vitamin E and glutathione peroxidase activities were observed in artichoke-treated hypercholesterolemic rats. Their results indicated that artichoke leaf extract decreased serum lipids and hypercholesterolaemia-induced pro-oxidant state in both hepatic and cardiac tissues. In another study, treatment with artichoke flowering head extract (500–1,500 mg/kg by gavage) resulted in a significant decrease of postprandial glycaemia in both nonselected Wistar and genetically obese Zucker rats (Fantini et al. 2011). The lack of any fibre content in this *Cynara scolymus* flowering head extract excluded the involvement of dietary fibres in glycaemia reduction. The results obtained suggested a hypoglycaemic effect of an artichoke preparation in laboratory rodents and confirmed previous observations made in humans.

Studies showed that after 42 days of feeding, artichoke leaf extract (ALE)-fed male Golden Syrian hamsters had significantly lower total cholesterol (15 %), non-HDL-cholesterol (30 %) and triglycerides (22 %) and female hamsters fed ALE showed reductions of 15 % for total cholesterol, 29 % for non-HDL-cholesterol and 29 % for triglycerides compared with controls (Qiang et al. 2012). Total neutral sterol and bile acids concentrations increased significantly by 50 and 53 % in faecal samples of ALE fed males, and 82.4 and 25 % in ALE fed females compared with controls. The ALE lowered hamster plasma cholesterol levels by a mechanism involving the greater excretion of faecal bile acids and neutral sterols. Studies in hyperlipidemic animal models (10 days and 7 weeks) showed that a treatment combination of artichoke leaf extract, turmeric extract, prickly pear dried leaves and garlic extract prevented dyslipidaemia, decreasing significantly serum LDL levels and LDL/HDL ratio (Qinna et al. 2012). This was mediated partially by the inhibition of HMG-CoA reductase activity by artichoke and prickly pear leaves.

Clinical Studies

Studies demonstrated that the serum level of the lipids decreased after cynarin administration to patients affected with diabetes (Wojcicki and Kadykow 1974). The data obtained in one patient affected with remarkable hyperlipidaemia appeared to confirm the abovementioned action. Studies involving seventeen ambulant outpatients with familial Type IIa or Type IIb hyperlipoproteinaemia found that oral administration with cynarin, the 1,5-dicaffeyl ester of quinic acid, the constituent of the artichoke at doses of 250 mg, and 750 mg daily for 3 months exerted no hypolipidaemic effect in familial Type II hyperlipoproteinaemia (Heckers et al. 1977). The mean serum cholesterol and triglyceride concentrations were not significantly changed within 3 months.

In a randomized, double-blind, placebo-controlled trial of a globe artichoke leaf extract (Hepar-SL forte; 640 mg three times daily for 12 weeks) involving 44 healthy volunteers, subgroup analysis suggested lipid-lowering effects (cholesterol and triglycerides) with globe artichoke extract for participants with baseline total cholesterol concentrations >210 mg/dl (Petrowicz et al. 1997). Another double-blind, randomized, placebo-controlled, multicenter clinical trial involving 143 adult patients found dry artichoke extract as tablets to be efficacious in treating hyperlipoproteinaemia over 6 weeks (Englisch et al. 2000). The decrease of total cholesterol in the artichoke-treated group was 18.5 % compared to 8.6 % in the placebo group. LDL-cholesterol

decrease in the artichoke-treated group was 22.9 and 6.3 % for placebo. LDL/HDL ratio showed a decrease of 20.2 % in the artichoke-treated 0 group and 7.2 % in the placebo group. There were no drug-related adverse events during this study indicating an excellent tolerability of artichoke dry extract. In a study of 18 moderately hyperlipidemic patients (LDL-cholesterol >130 <200 mg/dl and/or triglycerides >150 <250 mg/dl), supplementation of artichoke juice to an isocaloric hypolipidic diet appeared to positively modulate endothelial function in hypercholesterolaemia (Lupattelli et al. 2004). After artichoke treatment there was an increase of triglycerides and a reduction of total cholesterol, LDL-cholesterol and humoral markers such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), and an increase in brachial flow-mediated vasodilation (FVM). Univariate analysis showed that in artichoke patients, changes of VCAM-1 and ICAM-1 were significantly related to changes in brachial FMV.

Studies involving healthy adults with mild to moderate hypercholesterolaemia showed that consumption of artichoke leaf extract resulted in a modest but favourable statistically significant difference in total cholesterol after 12 weeks (Bundy et al. 2008). Plasma total cholesterol decreased in the treatment group by an average of 4.2 % (from 7.16 to 6.86 mmol/l) and increased in the control group by an average of 1.9 %. No significant differences between groups were observed for LDL-cholesterol, HDL-cholesterol or triglyceride levels. In a double-blind, randomized, placebo-controlled trial of 92 overweight subjects with primary mild hypercholesterolaemia, dietary supplementation of artichoke leaf extract for 8 weeks was associated with a significant increase in mean high-density lipoprotein (HDL)-cholesterol and in mean change in HDL-cholesterol (HDL-C) (Rondanelli et al. 2013a). A significantly decreased difference was also found for the mean change in total, low-density lipoprotein (LDL)-cholesterol, total cholesterol/HDL ratio, and LDL/HDL ratio, compared to placebo. The data suggested that artichoke leaf extract could play a relevant role in the management of mild hypercholesterolaemia.

In a double-blind, randomized, parallel-controlled study of 39 subjects from 21 to 55 years with moderate hypercholesterolaemia, daily consumption of a dietary supplementation containing red yeast rice, sugar cane-derived policosanols and artichoke leaf extracts, for 16 weeks, decreased LDL-cholesterol and total cholesterol, providing an interesting, convenient aid in managing mild to moderate hypercholesterolaemia (Ogier et al. 2013).

Review Studies

Wider et al. (2009, 2013) found that data from three randomized controlled trials (262 participants) assessing monopreprations of artichoke leaf extract for treating hypercholesterolaemia met all inclusion criteria. There was an indication that artichoke leaf extract had potential in lowering cholesterol levels; the evidence was, however, as yet not convincing. The limited data on safety suggested only mild, transient, and infrequent adverse events with the short-term use of artichoke leaf extract.

Antihyperglycaemic/Antidiabetic Activity

Studies found that diabetic individuals (15) of both sexes and of age 35–45 years supplemented with wheat biscuits with 4 globe artichoke incorporated wheat biscuits (containing 6 g of processed globe artichoke powder) for the period of 90 days had a significant reduction at one percent level in fasting and postprandial blood glucose compared to the control group (Nazni et al. 2006). Results of the serum lipid profile showed a significant reduction at one percent level in total cholesterol, serum triglyceride, low-density lipoprotein (LDL) and significant increase in high-density lipoprotein (HDL) levels of the artichoke/wheat group compared to the control group. The results recommended that the type 2 diabetic subjects should use globe artichoke vegetable in their food preparation on regular basis which showed good hypoglycaemic and hypolipidemic activities. Studies in rats showed that a mixture of *Phaseolus vulgaris* and *C. scolymus* extracts additively contributed to the reducing effect of

the combination on glycemic rise as it combines the anorectic effect of the *P. vulgaris* extract with the hypoglycaemic effect of both extracts (Loi et al. 2013). The data supported the recent clinical use of the combination of *P. vulgaris* and *C. scolymus* extracts in the control of appetite, food intake and postprandial glycaemia.

In a randomized, double-blind, placebo-controlled clinical trial of 39 overweight subjects (20 supplemented group, 19 placebo group) diet supplementation with a combination of *Phaseolus vulgaris* and *Cynara scolymus*, for 2 months, was found to be useful in the management of overweight and dysglycaemia (Rondanelli et al. 2011). At the end of treatment, the net change of the Haber's mean score on satiation increased significantly in the intervention group. The net change of glycaemia and of the dietary restriction score of the three factor eating questionnaire (TFEQ) were reduced significantly only in the intervention group. Also in the homeostasis model assessment, the body mass index and the susceptibility-to-hunger score of the TFEQ decreased significantly after intervention; these parameters did not change in the controls. In another double-blind, placebo-controlled, randomized clinical trial of 55 overweight subjects with naive impaired fasting glycaemia (fasting blood glucose [FBG]: 6.11 mmol/l), dietary supplementation with artichoke extract for 8 weeks resulted in significant decreases of FBG (−9.6 %), HOMA (homeostatic metabolic assessment) (−11.7 %), glycosylated haemoglobin (−2.3 %), ADAG (A1c-derived average glucose) (−3.1 %), and lipidic pattern compared to placebo (Rondanelli et al. 2013b). The data demonstrated the efficacy of artichoke extract on the reduction of glycometabolic parameters in overweight subjects with impaired fasting glycaemia.

Anticancer Activity

Hexanoic artichoke leaf fraction exhibited considerable cytotoxicity in the brine shrimp *Artemia salina* assay (Noldin et al. 2003). Artichoke extract exhibited antiproliferative activity in a dose-dependent manner against HepG2 cells. In the same cell line, pre-treatment with the extract was efficient in reducing the release of prostaglandin E2 induced by hydrogen peroxide oxidative stimulus (Menghini et al. 2010).

Two hydroxy taraxastane-type triterpenes, taraxasterol and faradiol, isolated from the flowers showed strong inhibitory activity against 12-*O*-tetradecanoyl-phorbol-13-aetate (TPA)-induced inflammation in mice (Yasukawa et al. 1996). At 0.2 μmol/mouse, these compounds markedly suppressed the tumour-promoting effect of TPA (1 μg/mouse) on skin tumour formation following initiation with 7,12-dimethylbenz[a] anthracene (DMBA). The methanol flower extract of artichoke exhibited marked antitumor activity in an in-vivo two-stage carcinogenesis test in mice, induced by 7,12-dimethylbenz[a]anthracene as an initiator and 12-*O*-tetradecanoylphorbol-13-acetate (TPA) as a promoter (Yasukawa et al. 2010). From the active fraction of the methanol extract, four triterpene alcohols and their corresponding acetates were isolated and identified. These compounds showed marked antiinflammatory effects against TPA-induced inflammation, with a 50 % inhibitory dose of 0.50–0.91 μmol/ear. Studies demonstrated that 10 % fish oil and 1 g% artichoke head or leaves administered to rats for 25 days before diethylnitrosamine (DEN) injection led to significant amelioration of DEN-induced changes in the biochemical parameters (Metwally et al. 2011). The administration of DEN affected the liver cell through occurrence of hepatic cellular degeneration and necrosis. An almost normal histological architecture of the liver, in treated groups, was shown as compared to the controls. The results pointed that 10 % fish oil and 1 g% artichoke succeeded to protect from hepatocellular carcinoma to a certain degree.

Studies showed that the polyphenolic extracts from the edible part of artichokes (AEs) reduced cell viability, inhibited cell growth, triggered apoptotic mechanisms, and showed inhibitory properties against the invasive behaviour of the human breast cancer, oestrogen receptor negative, and MDA-MB231 cancer cell line (Mileo et al. 2012). Importantly, the extract did not have any effect on normal breast epithelial cell line, MCF10A. Chlorogenic acid, the most

representative component of the polyphenolic fraction of artichoke, had no prominent effects on the cell death rate of MDA-MB231 cells. The addition of the extract to the cells rather than chlorogenic acid triggered apoptosis via a mitochondrial and a death-receptor pathway, as shown by the activation of caspase-9 and caspase-8, respectively. Similarly, treatment of human hepatoma HepG2 cells for 24 hours with artichoke polyphenolic extract reduced cell viability in a dose-dependent manner; however, chlorogenic had no prominent effects on the cell death rate (Miccadei et al. 2008). Similarly, the extract rather than chlorogenic acid induced apoptosis in HepG2 cells. In separate studies, cynaropicrin and grosheimin isolated from artichoke aerial parts showed weak cytotoxicity against MCF-7 cancer cell line, and other compounds had no obvious activity against the same cell line (Li et al. 2005).

Antiviral Activity

The use of cycloferon and phytopreparations of *Cynara scolymus* in the medical rehabilitation period was found to normalize the elevated proinflammatory cytokines concentration in the blood serum of the patients with chronic viral hepatitis C (Frolov et al. 2012). A pilot study involving 17 patients with chronic hepatitis C found that artichoke leaf extract appeared not effective in mitigating elevated amino transferase levels or viral load compared to baseline levels (Huber et al. 2009). Fatigue and joint problems significantly improved after 4 weeks of treatment; however, after 12 weeks, there was no significant difference to baseline. Tolerability of the extract was rated as good to excellent. Severe side effects did not occur.

Antimicrobial Activity

The dichloromethane extract of artichoke at the MIC concentration of 5 mg/ml completely inhibited the growth with a bactericidal effect on *Staphylococcus aureus*, *Bacillus cereus* and *B. subtilisis* (Mossi and Echeverrigaray 1999). Five different unidentified components with antimicrobial activity were found. A preliminary antimicrobial disk assay of chloroform, ethyl acetate and *n*-butanol fractions of artichoke leaf extracts showed that the *n*-butanol fraction exhibited the most significant antimicrobial activities against seven bacteria species, four yeasts and four moulds (Zhu et al. 2004). Eight phenolic compounds were isolated from the *n*-butanol-soluble fraction of artichoke leaf extract: four caffeoylquinic acid derivatives, chlorogenic acid (1), cynarin (2), 3,5-di-*O*-caffeoylquinic acid (3) and 4,5-di-*O*-caffeoylquinic acid (4), and the four flavonoids, luteolin-7-rutinoside (5), cynaroside (6), apigenin-7-rutinoside (7) and apigenin-7-*O*-β-D-glucopyranoside (8). Among them, chlorogenic acid, cynarin, luteolin-7-rutinoside and cynaroside exhibited a relatively higher activity than other compounds; in addition, they were more effective against fungi than bacteria. The minimum inhibitory concentrations of these compounds were between 50 and 200 μg/ml. In subsequent studies, artichoke leaf extract was found to be most effective in vitro against all of the tested organisms: 7 foodborne bacterial pathogens, *Bacillus subtilis*, *Staphylococcus aureus*, *Agrobacterium tumefaciens*, *Micrococcus luteus*, *Escherichia coli*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*, 4 yeasts, *Candida albicans*, *Candida lusitaniae*, *Saccharomyces cerevisiae* and *Saccharomyces carlsbergensis*, and 4 molds, *Aspergillus niger*, *Penicillium oxalicum*, *Mucor mucedo* and *Cladosporium cucumerinum* (Zhu et al. 2005a, b). It was followed by the head and stem extracts, and the ethanol fraction showed the most significant antimicrobial activity against all of the tests among 3 soluble fractions of extract, followed by the chloroform and ethyl acetate fractions. The minimum inhibitory concentrations (MICs) of extracts determined by the agar and broth dilution method ranged from 1.25 to 10.0 mg/ml. The MIC of the ethanol fraction of leaf extracts was the lowest compared to the other two extracts. The MIC for fungi was at or below 2.5 mg/ml and for bacteria was at or above 2.5 mg/ml.

C. cardunculus fresh involucral bracts extracts showed antimicrobial activity in vitro against

Salmonella typhimurium, *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, as well as micromycetes: *Aspergillus niger*, *Aspergillus ochraceus*, *Aspergillus flavus*, *Penicillium ochrochloron*, *Penicillium funiculosum*, *Trichoderma viride*, *Fusarium tricinctum* and *Alternaria alternata* comparable with standard antibiotics (Kukić et al. 2008). The ethanol artichoke leaf extract showed significant inhibitory activity against the tested strains of *Listeria innocua*, *Staphylococcus aureus* and *Bacillus cereus* with MICs of 5 mg/ml and lower inhibitory activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans* and another *Candida* sp. with MICs of 15 mg/ml (Vamanu et al. 2011).

The extracts of *Acacia farnesiana*, *Artemisia ludoviciana*, *Opuntia ficus-indica*, and *Cynara scolymus* were the most effective in-vitro against *Campylobacter jejuni* and *Campylobacter coli* at minimal bactericidal concentrations (MBCs) of 0.3, 0.5, 0.4 and 2.0 mg/ml, respectively (Castillo et al. 2011). No effect on growth was detected with lower concentrations of extract (25 %, 50 % or 75 % of the MBC). Adherence of *Campylobacter* to Vero cells was significantly affected by all the extracts. Campylobacter contamination in foods can cause campylobacteriosis, which can range from asymptomatic to dysentery-type illnesses with severe complications, such as Guillain–Barre syndrome.

Prebiotic/Probiotic Activity

The health-promoting prebiotic effects of artichoke inulin were demonstrated in an extensive microbiological study showing a long-lasting bifidogenic effect on *Bifidobacterium bifidum* cultures and also in mixed cultures of colonic bacteria (Lopez-Molina et al. 2005). Valerio et al. (2006) found that probiotic strains of *Lactobacillus plantarum* and *Lactobacillus paracasei* were able to survive on artichokes for at least 90 days in simulated gastrointestinal digestion. Further, when *L. paracasei* IMPC2.1 was used in an artichoke human feeding study involving four volunteers, the organism could be recovered from stools. *Cynara scolymus* was found to accumulate about 50–70 g/kg of its fresh weight as inulin-type fructan (Leroy et al. 2010). Inulin fermentation increases gas production and thereby provokes intestinal discomfort in some people. The scientists found that eating stored artichoke led to consumption of an inulin quantity that did not provoke unwanted symptoms related to gas production but sufficient to have a prebiotic effect. Storage time caused a decrease in inulin content and an average degree of polymerization, accompanied by an increase of free fructose and sucrose due to depolymerization of inulin. In a double-blind, placebo-controlled, cross-over study of 32 healthy adults, daily consumption for 10 days of a very-long-chain inulin (VLCI), derived from globe artichoke, was found to significantly increased numbers of faecal bifidobacteria and lactobacilli compared to placebo (Costabile et al. 2010). Additionally, levels of *Atopobium* group significantly increased, while *Bacteroides–Prevotella* numbers were significantly reduced. No significant changes in faecal SCFA concentrations were observed. There were no adverse gastrointestinal symptoms apart from a significant increase in mild and moderate bloating upon VLCI ingestion. The results showed that daily consumption of VLCI extracted from globe artichoke exerted a pronounced prebiotic effect on the human faecal microbiota composition and was well tolerated by all volunteers.

In a study of 8 volunteers suffering from constipation, daily consumption for 15 days of a normal diet supplemented with artichokes (180 g) enriched with 20 billions of *Lactobacillus paracasei* resulted in marked reduction in abdominal distension and feeling of incomplete evacuation (Valerio et al. 2010). The gut of all volunteers was found to be colonized by the probiotic strain after 15 days feeding. No significant differences in the microbiological counts throughout the experimental period were registered, whereas a significant increase of butyric and valeric acids with a concomitant decrease of lactic acid was registered. At the same time, the faecal beta-glucuronidase activity was significantly reduced.

In a randomized, double-blind, controlled, crossover study of 20 constipated patients, eighty

percent of patients preferred probiotic (*Lactobacillus paracasei*)-enriched artichokes which generated a positive effect compared to ordinary ones (Riezzo et al. 2012). Satisfactory relief of symptoms was significantly higher during the probiotic-enriched artichoke period. The Gastrointestinal Symptom Rating Scale (GSRS) constipation score was significantly lower in the probiotic group compared with the baseline. As for short-chain fatty acid (SCFA) production in faecal samples, propionic acid was significantly higher in the probiotic group compared with baseline.

Antiinflammatory Activity

Oral administration of a 10 % infusion (dry plant) or 20 % (fresh plant) corresponding to 1 or 2 g/kg of *Cynara scolymus* was found to have analgesic and/or antiinflammatory activities in mice (Ruppelt et al. 1991). Aqueous and ethanol artichoke extracts were found to inhibit basal and inflammatory mediators (TNFalpha and LPS) and ox-LDL stimulated reactive oxygen species (ROS) production in endothelial cells and monocytes in dose-dependent manner (Zapolska-Downar et al. 2002). In endothelial cells, the ethanol extract (50 µg/ml) reduced ox-LDL-induced intracellular ROS production by 60 % while aqueous extract (50 µg/ml) by 43 %. The ethanol extract (50 µg/ml) reduced ox-LDL-induced intracellular ROS production in monocytes by 76 %. Effective concentrations (25–100 µg/ml) were well below the cytotoxic levels of the extracts which started at 1 mg/ml as assessed by LDH leakage and trypan blue exclusion. The results demonstrated artichoke extracts to have marked protective properties against oxidative stress induced by inflammatory mediators and ox-LDL in cultured endothelial cells and monocytes. Flavonoids apigenin, luteolin, apigenin-7-glucoside, luteolin-7-glucoside, apigenin-7-rutinoside, luteolin-7-ritonoside and cynarin from *C. cardunculus* inhibited 12-lipoxygenase activity particularly at pH 9. The highest inhibitory activity was observed for apigenin and luteolin. Lipoxygenase inhibition activity was positively correlated with antioxidant activity ($R^2 = 0.81$).

Antispasmodic Activity

Of six Brazilian medicinal plants evaluated, only the methanol extracts of *Calophyllum brasiliense* and *Cynara scolymus* showed probable antispasmodic activity (Emendörfer et al. 2005b). Both plant extracts exhibited significant inhibitory activity for the contractile response elicited by acetylcholine on guinea pig ileum and on rat duodenum in a noncompetitive and concentration-dependent manner. The results confirmed and justified their use in folk medicine for the treatment of intestinal disorders. The dichloromethane fraction of *C. scolymus* exhibited antispasmodic effect against acetylcholine-induced contractions of guinea pig ileum (Emendörfer et al. 2005a). It showed the most promising biological effects, with an IC_{50} of 0.93 (0.49–1.77) mg/ml. Its main active component, the sesquiterpene lactone cynaropicrin, exhibited potent activity, with IC_{50} of 0.065 (0.049–0.086) mg/ml, being about 14-fold more active than dichloromethane fraction and having similar potency to that of papaverine, a well-known antispasmodic agent. The results confirmed the popular use of artichoke for the treatment of gastrointestinal disturbances.

Antiulcerogenic Activity

Oral administration of artichoke leaf extract dose dependently prevented absolute ethanol-induced gastric mucosal injury at 125–500 mg/kg or restraint plus water immersion stress-induced gastric mucosal injury at 1,000–2,000 mg/kg in rats (Ishida et al. 2010). Cynaropicrin, a component of artichoke, prevented ethanol-induced gastric mucosal injury at 5 mg/kg, p.o. and stress-induced mucosal injury at 20 mg/kg, p.o. However, dextrin and chlorogenic acid at doses contained in the leaf extract were ineffective in both models. When artichoke leaf extract (500–2,000 mg/kg) was given orally to normal rats, it dose dependently increased gastric mucus

content. Further, it (125–500 mg/kg, p.o.) dose dependently prevented the decrease in gastric mucus content by absolute ethanol. On basal gastric acid secretion in rats, artichoke leaf extract (500–2,000 mg/kg, p.o.) dose dependently increased the volume of gastric juice in normal rats. However, it was ineffective in decreasing basal gastric acid secretion in normal rats. These results indicated that artichoke leaf extract was effective against acute gastritis and its beneficial effect was due to that of cynaropicrin. The artichoke flower-head scale extracts (200 and 400 mg/kg) significantly reduced the ulcer index (55.33 % and 72.14 % inhibition, respectively) (Nassar et al. 2013). Histopathological examination of the rat stomach found that artichoke induced an increase in gastric mucus production, reduction of the depth and severity of mucosal lesions. Artichoke dose dependently reduced the elevated ethanol gastric MDA, GSH levels and CAT activity. The results suggested that artichoke flower-head scales possessed potential antiulcer activity.

Antiphotoaging Activity

Studies showed cynaropicrin, a sesquiterpene lactone from artichoke, to be an effective antiphotoaging agent that acted by inhibiting nuclear factor kappa (NF-κB)-mediated transactivation of basic fibroblast growth factor (bFGF) and matrix metalloprotease-1 (MMP-1) (Tanaka et al. 2013). NF-κB is activated by stimulation such as ultraviolet rays and inflammatory cytokines and induces the expression of various genes such as those of bFGF and MMP-1. Further, it was confirmed that in an in-vivo mouse model, cynaropicrin prevented skin photoaging processes leading to the hyperproliferation of keratinocytes and melanocytes.

Studies by Moglia et al. (2008) found that exposure of artichoke plants of different genotypes to UV-C radiation consistently increased the levels of dicaffeoylquinic acids in all genotypes, whereas the effect on compounds from the same biosynthetic pathway, for example, chlorogenic acid and luteolin-7-glucoside, was much less pronounced. The major phenolic compounds identified in globe artichoke leaves were four isomers of dicaffeoylquinic acid, three isomers of caffeoylquinic acid, and the flavone luteolin 7-glucoside. On the basis of these results, a role of dicaffeoylquinic acids in UV protection in globe artichoke was hypothesized.

Cardiovascular Activities

In EA.hy 926 cells, a cell line derived from human umbilical vein endothelial cells (HUVECs), an artichoke leaf extract (ALE) increased the activity of the human endothelial nitric-oxide synthase (eNOS) promoter (determined by luciferase reporter gene assay) (Li et al. 2004). An organic subfraction from the leaf extract was more potent in this respect than the crude extract, whereas an aqueous subfraction of the extract was without effect. In organ chamber experiments, ex-vivo incubation (18 hours) of rat aortic rings with the organic subfraction enhanced the NO-mediated vasodilator response to acetylcholine, indicating that the upregulated eNOS remained functional. Caffeoylquinic acids and flavonoids were identified as the two major groups of constituents of the extract. The flavonoids luteolin and cynaroside increased eNOS promoter activity and eNOS mRNA expression, whereas the caffeoylquinic acids cynarin and chlorogenic acid were without effect. The results suggested that in addition to the lipid-lowering and antioxidant properties of artichoke, an increase in eNOS gene transcription may also contribute to its beneficial cardiovascular (antithrombotic and anti-atherosclerotic) profile. Studies by Juzyszyn et al. (2008b) suggested that artichoke extracts could act as endothelium protecting agents. Preincubation of cultured human umbilical endothelial cells (HUVECs) with the artichoke extract at concentrations of 25–100 μg/ml for 24 hours abolished ROS (reactive oxygen species) generation induced by LPS and oxyLDL. Also potent, concentration-dependent reductive properties of the artichoke extract were demonstrated by the reduction kinetics of cytochrome c in reference to ascorbate.

Hypotensive Activity

In a randomized, placebo-controlled trial of patients with mild hypertension (systolic blood pressure [SBP]/diastolic blood pressure [DBP], 140–159/90–99 mmHg), 12 weeks consumption of concentrated artichoke leaf juice significantly reduced SPB compared with the baseline data, and DBP was significantly lower from the baseline as compared with the placebo group (Roghani-Dehkordi and Kamkhah 2009). It was concluded that the use of artichoke juice concentrate may have a blood pressure-lowering effect in mild hypertension.

Genotoxicity/Antigenotoxicty Activities

In the evaluation for genotoxicity, all doses of artichoke leaf extract (0.62, 1.25, 2.5 and 5.0 mg/ml) used led to a significant increase in the frequency of DNA damage, after exposure for 1 and 24 hours (Jacociunas et al. 2012a). In the antigenotoxicity experiments, the leaf extract reduced the frequency of DNA damage induced by the alkylating agent ethyl methanesulfonate in the simultaneous treatment only. However, the lowest dose was more protective than higher concentrations. Flavonoids and phenolic compounds in *C. scolymus* were suggested to be probably responsible for its genotoxic and antigenotoxic effects. Results of a study employing the cytokinesis-block micronucleus cytome assay in Chinese hamster ovary cells suggested that high concentrations of artichoke leaf extract could pose a risk associated to its consumption (Jacociunas et al. 2012b). All concentrations of the extract produced increments in micronuclei frequencies in both exposure times, when compared to the negative control. No significant differences were observed in the nuclear division cytotoxicity index (NDCI), reflecting the absence of cytotoxic effects attributable to the leaf extract.

Genotoxic and mutagenic studies in mice showed that artichoke leaf aqueous extracts did not increase micronuclei in peripheral blood cells in the micronuclei test (Zan et al. 2013). Compared to the control group, a significant increase in comet assay values was observed only in bone marrow of group treated with 2,000 mg/kg, the highest dose tested, indicating that artichoke tea should be consumed with moderation. The results indicated that artichoke lack of mutagenicity in vivo and had low genotoxicity.

Chemoprotective Activity

The study by Gurel et al. (2007) found that artichoke extract supplementation exerted a protective effect on gonads of cadmium-treated rats; in particular it exhibited a clear protective effect against cadmium-induced testicular damage and lowered nitric oxide production to the same level of that in the control groups.

Hypouricemic Activity

Studies showed that an aqueous artichoke leaf extract and some of its components, caffeic acid derivatives and flavones, exerted xanthine oxidase inhibitory effects in vitro but a hypouricemic activity could not be confirmed after acute oral treatment in potassium oxonate-treated rats (Sarawek et al. 2008). After intraperitoneal injection of luteolin a decrease in uric acid levels was detected suggesting that the hypouricemic effects of luteolin were due to its original form rather than its metabolites produced by the gut flora.

Mitochondrial Respiratory Chain (MRC) Activity

In-vitro studies showed that artichoke extract in the range of 0.68–2.72 μg/ml demonstrated potent and concentration-dependent mitochondrial respiratory chain (MRC) inhibitory activity in isolated rat liver mitochondria (Juzyszyn et al. 2010). Concentrations > or =5.4 μg/ml entirely inhibited MRC activity. The succinate oxidase system (MRC complexes II–IV) was the most potently inhibited. Inhibition of the succinate oxidase system was competitive (K(i)=0.23 μg/ml),

whereas isolated cytochrome oxidase was inhibited noncompetitively ($K(i) = 126$ µg/ml). The results suggested that the health-beneficial effects of artichoke extracts may partly rely on the effects of their active compounds on the activity of the mitochondrial respiratory chain system.

Urinary Excretion of Nicotine Activity

Studies showed that co-administration of nanozeolites and artichoke leaf extract had a synergetic effect on increasing the urinary excretion of nicotine in rats (Malekshah et al. 2012). Artichoke leaf extract caused increase in urinary excretion of nicotine in longer post-administration times.

Alcohol Hangover Ameriolation

In a randomized double-blind, placebo-controlled, crossover trial of 15 healthy adult volunteers between 18 and 65 years, administration of 3 capsules of commercially available standardized artichoke extract immediately before and after alcohol exposure was found not effective in preventing the signs and symptoms of alcohol-induced hangover (Pittler et al. 2003). None of the outcome measures differed significantly between interventions. Adverse events were rare and were mild and transient.

Pharmacokinetics Studies

Six metabolites derived from artichoke leaf extract, namely, hydroxycinnamates—caffeic acid, dihydrocaffeic acid, ferulic (FA), dihydroferulic acid, and isoferulic acid and the flavonoid luteolin were detected in human plasma by high-performance liquid chromatography-coulometric-array detection (Wittemer and Veit 2003). After oral administration of Artichoke leaf extracts to 14 healthy human volunteers, none of the genuine target extract constituents could be detected in the plasma or urine (Wittemer et al. 2005). However, caffeic acid (CA), its methylated derivates ferulic acid (FA) and isoferulic acid (IFA), and the hydrogenation products dihydrocaffeic acid (DHCA) and dihydroferulic acid (DHFA) were identified as metabolites derived from caffeoylquinic acids. Except for DHFA, all of these compounds were present as sulfates or glucuronides. Peak plasma concentrations of total CA, FA and IFA were reached within 1 hour and declined over 24 hours showing almost biphasic profiles. In contrast maximum concentrations for total DHCA and DHFA were observed only after 6–7 hours, indicating two different metabolic pathways for caffeoylquinic acids. Luteolin administered as glucoside was recovered from plasma and urine only as sulfate or glucuronide but neither in form of genuine glucosides nor as free luteolin. Peak plasma concentrations were reached rapidly within 0.5 hour. Studies by Azzini et al. (2007) confirmed the bioavailability of metabolites of hydroxycinnamic acids after ingestion of cooked edible *Cynara scolymus* (cultivar Violetto di Provenza). They found a plasma maximum concentration of 6.4 ng/ml for chlorogenic acid after 1 hour and its disappearance within 2 hours. Peak plasma concentrations of 19.5 ng/ml for total caffeic acid were reached within 1 hour, while ferulic acid plasma concentrations showed a biphasic profile with 6.4 and 8.4 ng/ml within 1 hour and after 8 hours respectively. A significant increase of dihydrocaffeic acid and dihydroferulic acid total levels after 8 hours was observed. No circulating plasma levels of luteolin and apigenin were detected. In another study, the limits of detection in rat plasma for cynarin and luteolin were 0.75 and 0.1 µg/cm^3 and the limits of quantification were 2.25 and 0.2 µg/cm^3, respectively (Kulza et al. 2012b). Recovery was 67 % for cynarin and 96 % for luteolin.

Milk Clotting Activity

Aspartic proteinases from flowers of *Cynara cardunculus* have been extensively studied and long used as coagulants in the manufacture of several traditional Spanish and Portuguese cheeses (Sidrach et al. 2005) and as an alternative to calf stomach rennet (Chazarra et al. 2007). Two aspartic proteinases were isolated from stigmas

of the cardoon *Cynara cardunculus* and named cardosin A and cardosin B (Veríssimo et al. 1996). Cardosin A showed two bands with apparent molecular masses of 31,000 and 15,000 Da, whereas the chains of cardosin B showed bands of 34,000 and 14,000 Da. The partial amino acid sequences of the two cardosin revealed that they were similar but not identical and that they differed from the previously reported cardoon proteinases named cynarases, which were assumed to be derived from a common precursor. Both cardosins were active at low pH and were inhibited by pepstatin. A heterodimeric milk-clotting proteinase consisting of 30- and 15-kDa subunits was isolated from artichoke flowers (Llorente et al. 2004). The amino terminal sequence of the 30-kDa chain proved to be identical to the larger cardosin A subunit (an endopeptidase). Maximum proteolytic activity was recorded at pH 5.0 and was inhibited by pepstatin. The crude protease extract was found to be potentially useful for cheese production. According to Sidrach et al. (2005) cardosins and cynarases are similar and are called differently by various authors. Three endopeptidases, cynarases A, B and C, with milk-clotting properties were purified from the stigma of globe artichoke (Sidrach et al. 2005). All three proteinases were found to be glycoproteins and to compose of one large and one small subunits. Cynarase A was found to be an aspartic proteinase and expressed maximum activity at pH 5 and 70 °C. The results indicated artichoke extract could also be used in the milk industry in the same way as the extract obtained from the flower of cardoon *C. cardunculus*. Milk coagulation activity of artichoke flower extract was highly dependent upon milk pH and temperature (Chazarra et al. 2007). The rennet strength (RS) of this extract was found to increase hyperbolically with increasing calcium concentrations. The crude extract was found to contain cynarases A, B and C. Purification led to a decrease in the specific coagulant activity relative to that of the crude extract in the case of cynarases A and C, whereas cynarase B increased its specific clotting activity. Also cynarases A and C showed a slight increase in specific peptidase activity relative to the initial extract; the specific peptidase activity of cynarase B was much higher. Crude water extracts of dried and fresh cardoon flowers had high yield of rennet-like proteases but low protein content and proteolytic activity, whereas citric acid extracts had low yield but high protein content and proteolytic activity (Chen et al. 2003). Fresh flower extracts gave higher yield and proteolytic activity but lower protein content in comparison with dried flower extracts. Irrespective of extraction method, all extracts had higher proteolytic activity against ovine whole and kappa-caseins compared to their bovine counterparts, showing optimal activity at 37 °C and pH 6.0. Separation of purified extracts yielded three active fractions, each with two subunits with molecular masses of 15.5 and 33.1 kDa, respectively.

Toxicity Studies

Studies in Bulgaria found that 75 day administration of artichoke preparation at doses 35.70 and 150 mg/kg to sexually mature male white Wistar rats caused no significant changes in the structure of the semen of white rats, established at both cellular and subcellular level (Ilieva et al. 1994). There was no evidence that the artichoke preparation was injurious or stimulating to the male gonads.

Allergic Problems

Some individuals handling artichoke have been reported to develop contact hand dermatitis (Meding 1983) and contact urticaria syndrome on exposure to globe artichoke, a type-1 allergen (Quirce et al. 1996). Case studies of 2 vegetable warehouse workers who developed occupational rhinitis and bronchial asthma by sensitization to artichoke were presented (Miralles et al. 2003). In both patients, results of skin prick tests to artichoke were positive. Levels of specific IgE for artichoke were 0.68 kU/l in patient 1 and 2.14 kU/l in patient 2. Nasal challenge with artichoke extract triggered a peak nasal inspiratory flow decrease of 81 and 85 % in patient 1 and patient 2, respectively.

A woman with a past history of allergy to artichoke presented with two episodes of immediate allergic reactions, one of which was a severe anaphylactic shock after eating two types of health foods containing inulin (Franck et al. 2005). Specific IgEs to artichoke, to yoghurt F, and to a heated BSA + inulin product were identified. Dot-blot inhibition techniques confirmed the anti-inulin specificity of specific IgE.

Traditional Medicinal Uses

Artichoke has a long history of traditional use in herbal medicine dating back to the sixteenth century. The leaves are anticholesterolemic, antirheumatic, cholagogue, digestive, diuretic, hypoglycaemic and lithontripic (Lust; Chiej 1984; Bown 1995; Chevallier 1996). They are used in cases of jaundice, oedema (fluid retention), hepatitis, arteriosclerosis, urinary gallstones, and early stages of late-onset diabetes. Artichoke is also used to stimulate digestive juices and lower cholesterol (Grammelis et al. 2008). Globe artichoke leaves extracts have long been used in folk medicine for their choleretic and hepatoprotective activities (Speroni et al. 2003), for treatment of hepatitis, obesity, hyperlipidaemia and dyspeptic disorders (Nassar et al. 2013). Artichoke tinctures containing caffeoylquinic acids and flavones are largely used in hepatic disorders (Bilia et al. 2002). In Poland, artichoke with multiple therapeutic properties and practically no side effects is recommended as herbal medicine not only in disorders of the liver but also in the prevention of atherosclerosis and hyperlipidaemia or dyspeptic disorders (Horoszkiewicz et al. 2012; Kulza et al. 2012a).

Other Uses

Globe artichoke/cardoon is also an attractive plant, valued as an ornamental for its bright floral display, and sometimes grown in herbaceous borders and beds for its bold foliage and large purple/blue flower heads. The flowers are used as cut flowers for flower arrangements. The flowers attract bees, the principal pollinators. The plant also improves soil characteristics and prevents erosion.

C. cardunculus (cardoon) also known as cynara in the field of energy crops can be cultivated as an energy crop producing biomass and be used for biodiesel production and other industrial purposes (Fernández and Curt 2004; Fernández et al. 2006). Studies have reported on the feasibility of cynara, for biomass production as an energy crop in several Mediterranean countries (Encinar et al. 1999; Fernández and Curt 2004; Fernández et al. 2006; Grammelis et al. 2008; Ierna and Mauromicale 2010; Gominho et al. 2011). Studies showed that on average for the 14 genotypes of *C. cardunculus* L., five cultivated cardoons and nine wild cardoons grown in a Mediterranean environment, a 3-year cumulative above-ground biomass of 47.4 t/ha DM, the 6.3 % of which was grain (Raccuia and Melilli 2007). Two types of products can be harvested: lignocellulosic biomass and oil seeds (Fernández et al. 2006). Cynara lignocellulosic biomass is a solid biofuel that can be used directly for heating or for electric power generation. The cynara oil exhibits a similar fatty acid profile to the common sunflower oil and has been successfully experimented for the production of biodiesel by a process of transesterification (Encinar et al. 1999). The biodiesel from cynara has similar properties to those of biodiesel 2.

Cynara oil was reported to have the following properties: refractive index 1.47, iodine index 125, saponification index 186.6, peroxide value 4.77 meq O_2/kg, unsaponifiable matter 10.7 %, fatty acids—palmitic acid 10.7 %, stearic acid 3.7 %, oleic acid 25 %, linoleic acid 59.7 %, fuel properties—density 0.924, HCV 32.00 MJ/kg, viscosity 40° 31.3 mm/s, cetane number 51.4, flash point 350 °C (Fernández and Curt 2004). Studies by Grammelis et al. (2008) found that *Cynara cardunculus* (cardoon), under certain circumstances, can be used as a solid biofuel of acceptable quality. It is now considered the most important and promising sources for solid biofuel production in Greece. Thermogravimetric analysis showed that the decomposition process of cardoon followed the degradation of other

lignocellulosic fuels, meeting high burnout rates. Considering its high adaptability to the xerothermic conditions of southern Europe and its high biomass productivity on most soils with modest or without any inputs of irrigation and agrochemicals, *C. cardunculus* may produce the cheapest biofuel compared to all other bioenergy crops known.

In addition to the energy applications of the crop, other alternative applications include green forage for ruminants, paper pulp production, cheese production and pharmacological active compounds extraction. Artichoke seed oil may be used for making soap, hair shampoo, alkyd resin and shoe polish (Miceli and De Leo 1996). *C. cardunculus* seed presscake has potential to be used as fertilizer or animal feed (Curt et al. 2002; Fernández et al. 2006).

A study showed that lambs fed a diet supplemented with artichoke bracts (550 g/day for 133 days), produced lambs with a lower content in monounsaturated fatty acids in the meats and a higher one in saturated fatty acids in the subcutaneous fat. Also fat deposits had a higher percentage of w3-series fatty acids (Marsico et al. 1999). Studies showed that the silage by-product after industrial processing of artichoke (*Cynara scolymus*) could be used as ruminant feed after 12 days of ensilage (Meneses et al. 2007). Cajarville et al. (2000) found that *C. cardunculus* (cardoon) seed inclusion in the ruminant diets up to a 25 % had no effect on rumen fermentation patterns or on ruminal fibrolytic activity, in spite of the high content of fat rich in unsaturated fatty acids (85.5 % of total fatty acids) of the seed. Crude protein (CP), ether extract (EE) and neutral detergent fibre (NDF) contents of whole cardoon seed were 225, 250 and 338 g/kg DM, respectively. Rumen dry matter degradability of whole seed was 56.8 %, while CP degradability was 82.9 %. Digestibility coefficients (%) were 83.8 for CP, 82.8 for EE, 20.3 for NDF, 56.1 for organic matter, and 59.2 for energy.

Studies reported that *Cynara cardunculus* has potential as a new fibre crop for pulp and paper production (Gominho et al. 2001). The plant stalks were found to have 7.7 % ash, 14.6 % extractives, 17.0 % lignin and 53.0 % polysaccharides, mainly cellulose and xylans. The pith had more lignin than the depithed stalk. Depithing of the stalks had a positive impact on pulp yield, chemical consumption and on the pulp strength properties. Studies found the hairs and pappi from *Cynara cardunculus* capitula to be suitable material for paper pulp production (Gominho et al. 2009). Pulps could be produced using a conventional kraft process with high yields and low residual lignin. Hairs and pappi are filamentous structures made up of longitudinally aligned fibre cells, without intercellular voids or pitting, and were found to have low content of ash (1.9 and 1.1 %, respectively), extractives (5.4 and 6.0 %) and lignin (10.6 and 17.8 %), and high content of holocellulose (77.5 and 72.8 %) and α-cellulose (55.2 and 46.8 %). The utilization of hairs and pappi may strengthen the differentiated use of biomass fractions of the *Cynara* plant and its potential as a bioenergy crop.

A statistically significant protective effect of 5 % total water extract of artichoke on humoral immune response (increase of haemagglutination-inhibition antibody titer), on relative organ weight, as well as on pathomorphological, haematological and biochemical changes induced by ochratoxin A in broiler chicks was established (Stoev et al. 2000). Subsequent studies found a protective effect of artichoke aqueous extract as a feed additive against the suppressive effect of ochratoxin A on egg production of laying hens (Stoev 2010). A significant protection was found against the decrease of the weight or the quantity of eggs as well as against the delay of the beginning of the laying period of chicks, both of which were provoked by ochratoxin A.

Comments

Leading producers of artichokes in the world are Italy 474, 550 t; Egypt 202,458 t; Spain 182,111 t; Peru 150,417 t; Argentina 100,891 t; China 75,000 t; France 52,032 t; Morocco 44,187 t; United States 43,640 t; and Chile 41,694 t (FAO 2012).

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Dahlia coccinea

Scientific Name

***Dahlia coccinea* Cav.**

Family

Asteraceae

Synonyms

Bidens cervantesii (Lag.) Baill. ex B.D. Jacks. (Illeg.), *Bidens coccinea* (Cav.) Baill., *Dahlia acutiflora* Moc. & Sessé ex DC. (inval.), *Dahlia bidentifolia* Salisb., *Dahlia cervantesii* (Sweet) Lag., *Dahlia cervantesii* (Lag. ex Sweet) Lag. ex DC., *Dahlia chisholmi* Rose, *Dahlia coccinea* var. *gentryii* (Sherff) Sherff, *Dahlia coccinea* var. *palmeri* Sherff, *Dahlia coccinea* var. *steyermarkii* Sherff, *Dahlia coronata* Hort. ex Sprague, *Dahlia crocata* Sessé ex Lag., *Dahlia crocea* (Willd.) Poir., *Dahlia crocea* var. *coccinea* Poir., *Dahlia crocea* var. *flava* (Willd.) Poir., *Dahlia frustranea* (DC.), *Dahlia gentryi* Sherff, *Dahlia gracilis* Ortgies, *Dahlia jaurezii* Van der Berg, *Dahlia lutea* Van der Berg, *Dahlia pinnata* var. *cervantesii* (Lag. ex Sweet) Voss, *Dahlia pinnata* var. *coccinea* (Cav.) Voss, *Dahlia pinnata* var. *gracilis* (Ortgies) Voss, *Dahlia popenovii* Saff., *Georgina cervantesii* Lag. ex Sweet, *Georgina coccinea* Cav., *Georgina coccinea* (Cav.) Willd., *Georgina coccinea* var. *crocea* Willd., *Georgina coccinea* var. *flava* Willd., *Georgina crocata* Sweet, *Georgina frustranea* DC., *Georgina frustranea* var. *coccinea* DC., *Georgina frustranea* var. *crocea* (Willd.) DC., *Georgina frustranea* var. *flava* (Willd.) DC.

Common/English Name

Red Dahlia

Vernacular Names

Indonesia: Bunga Kana
Mexico: Cohuanenepilli (Aztec), Cohuanenepilli (Nahuatl), Kachana
Polish: Dalia Szkarłatna
Swedish: Scharlakansdahlia

Origin/Distribution

The species is native to central Mexico and has been introduced and grown in other subtropical and tropical areas.

Agroecology

The plant thrives in a sunny position in well-drained, moderately moist, fertile, deep, loamy soils soil. The plant needs protection from cold winds and is sensitive to frosts.

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Edible Plant Parts and Uses

Flowers can be used in salads, cream, cheese and dip; some recipes include a dahlia dip, sundried tomato and dahlia bread (Hedrick 1972; Roberts 2000). In Mexico, boiled tubers of kachana were eaten (Laferriere et al. 1991). Tubers of *Dahlia* spp. were widely used in pre-Spanish Mexico and are very high in inulin and fructose (Whitley 1985).

Botany

A deciduous, branched, perennial herb, to 2 m high with large underground tuberous roots. Leaves opposite or alternate, simple to pinnate with 3–5 elliptic, serrate-dentate leaflets, glabrous (Plates 1 and 2). Inflorescence of solitary, long-pedunculate, involucrate, radiate, stellate capitulum. Involucral bracts in 2 series, the outer series rather fleshy and foliaceous, inner series membranous. The central portion of the capitulum is comprised of florets with tubular bisexual, tubular, short 5-lobed, yellow corollas. The outer, more showy portion of the capitulum is comprised of a single row of ray florets with a single, flat ligulate corolla, yellow, red, orange, orange-red or bicoloured in some cultivars (Plates 1 and 2). Achenes dorsally compressed, pappus absent.

Nutritive/Medicinal Properties

Proximate composition of *D. coccinea* tuber (% moisture free basis) was reported as energy 258 kcal, protein 16.39 %, carbohydrate 47.81 %, lipids 0.15 %, fibre 31.28 % and ash 4.37 %, Fe 41 ppm, Cu 9 ppm, Ca3756 ppm and Mg 1,513 ppm (Laferriere et al. 1991).

Dahlia flower colour appeared to be exclusively based on the accumulation of flavonoids and biochemically related anthochlors (chalcones, aurones) (Harborne 1967; Giannasi 1975; Halbwirth et al. 2008). Malonic acid also occurred bound to non-anthocyanic glycosides; butein (2′4′,3,4-tetrahydroxyxhalcone) 4′-*O*-glucoside and 4′-*O*-sophoroside existed as their respective malonate esters in both *D. coccinea* and *D. variabilis* (Harborne et al. 1990).

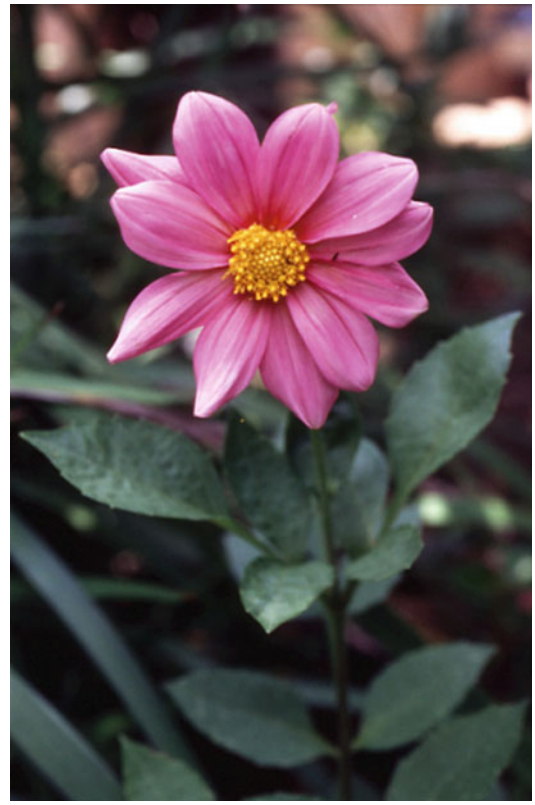

Plate 1 *Dahlia coccinea* flower

Plate 2 Leaves and bicoloured dahlia flowers

Polyacetylene compounds were found in the tubers and aerial plant parts of *D. coccinea* (Lam et al. 1968). Polyacetylene compounds with an ene-diynediene chromophore were found abundantly in *D. pinnata*, whereas at most traces of compounds with this chromophore were detected in *D. coccinea* (Bendixen et al.1969). Three *Dahlia pinnata* varieties were found to contain 1-phenylhept-5-ene-1,3-diyne and 1-phenyl-hepta-1,3,5-triyne and derivatives which had previously been found in one *Dahlia coccinea* variety and in a horticultural form (Lam 1973). Nineteen polyacetylenes were detected in *Dahlia coccinea* Cav. var. *coccinea* comprising eight C_{13}, eight C_{14} and three C_{17} compounds (Chin et al. 1970). Five of them were previously unknown, including C14-tetrahydropyranyl compounds. Twenty-six polyacetylenes of known structures 1-phenylhept-5-ene-1,3-diyne and 1-phenyl-hepta-1,3,5-triyne and derivatives together with cosmene and eugenol were isolated and characterized from roots, leaves and flowers of *Dahlia australis*, one *D. coccinea* variety, and two varieties of *D. sherffii* (Lam et al. 1991).

According to Christensen (2010) polyacetylenes appear to be an important group of nutraceuticals in vegetable foods that are obvious targets for the development of healthier foods and food products. The beneficial effects of most bioactive polyacetylenes from higher plants occur at nontoxic concentrations. However, some polyacetylenes are known to be potent skin sensitizers, and to be neurotoxic in high concentrations, but are also highly bioactive compounds with potential health-promoting properties.

Tubers of *D. coccinea* were reported to have antibiotic and antiatherogenic properties and to act as central nervous system depressants (Whitley 1985; Jiu 1966). The Aztecs used the petals of the dahlia, as well as its tuber in skin treatments for rashes, infected grazes and cracks in the skin. The roots of the plant were found to contain antibiotic compounds which were most plentiful in the skin of the tuber. In the past, the petals were crushed, mashed up and used to soothe insect bites or stings.

Other Uses

The dahlia flower was a solar symbol worn by Montezuma and nobles (Whitley 1985). Dahlia is widely planted as border plants or in pots. The flowers are used as cut flowers.

Comments

Most commonly grown dahlias are hybrids of *D. pinnata* and *D. coccinea*. Dahlias are propagated from seeds, division of tubers or cuttings.

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Dahlia pinnata

Scientific Name

***Dahlia pinnata* Cav.**

Family

Asteraceae

Synonyms

Bidens variabilis (Desf.) Baill., *Coreopsis crassifolia* Sessé & Moc. (Illeg.), *Coreopsis georgina* Cass., *Dahlia astrantiaeflora* (Sweet) G. Don, *Dahlia* × *hortensis* Guillaumin, *Dahlia hybrid*, *Dahlia nana* Andrews, *Dahlia pinnata* var. *nana* B.D. Jacks., *Dahlia pinnata* var. *variabilis* (Willd.) Voss, *Dahlia purpurea* (Willd.) Poir., *Dahlia purpurea* var. *flavescens* (DC.) Poir., *Dahlia purpurea* var. *lilacina* (Willd.) Poir., *Dahlia purpurea* var. *pallida* (Willd.) Poir., *Dahlia purpurea* var. *rubra* (DC.) Poir., *Dahlia pusilla* Zucc. ex DC., *Dahlia rosea* Cav., *Dahlia royleana* Knowles & Westc., *Dahlia sambucifolia* Salisb., *Dahlia sphondyliifolia* Salisb. (Illeg.), *Dahlia superflua* (DC.) W.T. Aiton, *Dahlia variabilis* (Willd.) Desf., *Georgia superflua* DC., *Georgia superflua* var. *flavescens* DC., *Georgia superflua* var. *lilacina* (Willd.) DC., *Georgia superflua* var. *pallida* (Willd.) DC., *Georgia superflua* var. *purpurea* DC., *Georgia superflua* var. *rubra* DC., *Georgia variabilis* (Willd.) Spreng., *Georgina astrantiaeflota* Sweet, *Georgina purpurea* Willd., *Georgina rosea* (Cav.) Willd., *Georgina variabilis* Willd.

Common/English Names

Aztec Dahlia, Dahlia, Garden Dahlia, Pinnate Dahlia

Vernacular Names

Catalan: Dàlia, Daliera
Chinese: Da Li Hua
Czech: Jiřina Zahradní
French: Dahlia
German: Dahlie, Georgine
Italian: Dalia, Georgina
Japanese: Tenjikubotan
Korean: Dalria
Malay: Bunga Dalia
Mexico: Acocotli, Cocoxochitl (Nahuatl), Dalia (Spanish)
Nepal: Lajure Phool
Polish: Dalia Ogrodowa, Dalia Zmienna, Georginia
Portuguese: Dahlia, Dália-Vulgar
Spanish: Dalia
Turkish: Dalya, Yildiz Çiçegi, Yıldız Çiçeği
Vietnamese: Thược Dược, Thổ Thược Dược, Đại Lệ Cúc

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Origin/Distribution

The species is native to Mexico and Central America to Columbia.

Agroecology

Dahlia grows best in full sun in friable, moderately moist, well-drained, fertile soils with pH 6–6.5. It thrives best in volcanic soils as found in its natural habitat in Mexico. It is frost tender and drought intolerant.

Edible Plant Parts and Uses

The flower petals are eaten in salads; the tubers are eaten as vegetables in some parts of Mexico (Uphof 1968; Hedrick 1972; Facciola 1990; Roberts 2000). A sweet extract of the tuber, called 'dacopa', is used as a beverage or as a flavouring, mixed with hot or cold water or milk or sprinkled on ice cream. Its naturally sweet mellow taste is said to combine the characteristics of coffee, tea and chocolate. Some culinary recipes of Dahlia flowers include Mexican mealie and chili dish, cream cheese and Dahlia dip and sun-dried tomato and Dahlia bread (Roberts 2000).

The tubers are rich in reserve carbohydrate, inulin, a fructan, which is composed of β(2 → 1) linked D-fructose residues and provides a good natural source for the production of fructose syrups that are widely used in the food industry (Mino et al. 1985; Mangunwidjaja et al. 2002). Fructose is an interesting sweetener because of its high sweetening power. Fructose is claimed to be less cariogenic than other sugars and to be more suitable for diabetics since it is insulin nondependent (Barker and Petch 1985). Purified inulin from Dahlia tubers was partially hydrolyzed to form fructooligosaccharides by using citric or phosphoric acids (pH, 2.0–2.5) as mild acid catalysts (Fontana et al. 2011). These whole hydrolysates can be advantageously added as nutraceuticals to carbonated beverages and acidic foods, such as soft drinks and yogurts.

The common garden variety Dahlia was once an important root crop and medicinal plant among the pre-Columbian Indians of Central Mexico, Yucatan and Guatemala. Its roots were valued both for the nutritious inulin stored inside them and for the antibiotic compounds concentrated in the skin of the tubers (Whitley 1985).

Botany

A deciduous, branched, perennial herb, to 1.8 m high with large subterraneous tuberous roots. Internode of stems hollow, leaves opposite or whorled, simple to 2-pinnatisect with 3–5 elliptic, serrated leaflets, glabrous and glaucous beneath (Plates 2 and 3). Inflorescence of solitary or few, long-pedunculate, involucrate, radiate capitulum, 10–20 cm across. Involucral bracts in 2 series, the outer series rather fleshy and foliaceous, inner series membranous and shortly united at the base, receptacle scaly. Disc florets bisexual, actinomorphic, tubular, 5-lobed sometimes mostly or all replaced by ray florets as in cultivated hybrid progeny. Ray florets, several marginal rows, zygomorphic, female and fertile, or neuter, the ligules patent with incurved or recurved margins, purple in wild plants and white, yellow, pink, red or purple in horticultural improved plants (Plates 1, 2 and 3). Achenes dorsally compressed, pappus absent or shortly bidentate.

Plate 1 Red-flowered pinnate Dahlia

Plate 2 Pale lilac-flowered pinnate Dahlia and leaves

Plate 3 Yellow-flowered pinnate Dahlia

Nutritive/Medicinal Properties

Pigments responsible for the diverse range of floret colours ivory, yellow, pink, red, purple and red-black in Dahlias had been reported to include flavonoids, mainly anthocyanins, butein, and flavones and their derivatives (Bate-Smith and Swain 1953; Nordstrom and Swain 1953, 1956, 1958; Bate-Smith et al. 1955; Harborne et al. 1990; Yamaguchi et al. 1999). Pigments were first studied in Dahlia in the early 1950s when the presence of anthocyanins, flavones, flavonols, chalcones and aurones were elaborately described in Dahlia species (Bate-Smith and Swain 1953; Nordstrom and Swain 1953, 1956, 1958; Bate-Smith et al. 1955). Bate-Smith and Swain (1953) isolated 2,4,4′-trihydroxychalcone from yellow varieties of *Dahlia variabilis.* Apart from anthocyanins and 6′-deoxychalcones, flavones and flavonols could accumulate in Dahlia flowers (Nordstrom and Swain 1953, 1956, 1958). Blue-coloured flower of *D. variabilis* var. Dandy was found to contain apigenin, its 4- and 7-monoglucosides and 7-rhamnoglucoside, luteolin 5-mono-glucoside and 7-diglucoside, cyanidin arabinoglucoside, and a few minor compounds (Nordstrom and Swain 1953). Flavonoid glycosides extracted from the yellow petals of two yellow Dahlias included 3′,4′,6-trihydroxyaurone in var. ‘Pius IX’. The 6-mono- and diglucosides of this compound were found in var. ‘Coton’ together with the 7-mono- and diglucosides of liquiritigenin, the 4-monoglucosides of both butein and 2,4,4′-trihydroxychalcone, and the 4-diglucoside of the last named compound (Nordström and Swain 1956). The ivory Dahlia ‘Helly Boudewyn’ contained the same flavone glycosides as those which had previously been found in the blue Dahlia ‘Dandy’, and naringenin and eriodictyol were found in a white Dahlia ‘Clare White’ (Nordström and Swain 1958). Polyacetylene compounds with an ene-diynediene chromophore were found abundantly in *D. pinnata*, whereas most traces of compounds with this chromophore were detected in *D. coccinea* (Bendixen et al. 1969). Three *Dahlia pinnata* varieties were found to contain 1-phenylhept-5-ene-1,3-diyne and 1-phenyl-hepta-1,3,5-triyne and derivatives which had previously been found in one *Dahlia coccinea* variety and in a horticultural form (Lam 1973).

Kaufmann and El Baya (1970) and Harborne et al. (1990) found 6′-deoxychalcones (derivatives of butein and isoliquiritigenin) and the corresponding 4-deoxyaurones (derivatives of sulfuretin) to be the chemical base of yellow flower colour in *D. variabilis*; these were mixed with anthocyanins (derivatives of pelargonidin

and cyanidin) in orange and red forms. The yellow pigments, the 4′-malonylsophoroside and 4′-malonylglucoside of butein, were found in the petals of *Dahlia variabilis* and *D. coccinea*, co-occurring with malonylated anthocyanins in these flowers (Harborne et al. 1990). A screening of more than 200 Dahlia cultivars revealed that the different red tones were based on the same set of anthocyanins and that variation in the anthocyanin concentration, the modification pattern of the core structures, and probably also pH were responsible for the formation of different hues (Halbwirth et al. 2008). Orange, rose and lilac cultivars frequently showed lower anthocyanin contents than red and magenta cultivars. Rose and lilac cultivars appeared to be primarily based on a lower chalcone synthase activity (Halbwirth et al. 2008). Thus, Dahlia flower colour appeared to be exclusively based on the accumulation of flavonoids and biochemically related anthochlors (chalcones, aurones) (Harborne 1967; Giannasi 1975; Halbwirth et al. 2008). Recently, Thill et al. (2012) reported that Dahlia resulted from the accumulation of red anthocyanins, yellow anthochlors (6′-deoxychalcones and 4-deoxyaurones) and colourless flavones and flavonols, acting as copigments.

Garden Dahlias (*Dahlia variabilis*) are autoallooctoploids with redundant genes producing wide colour variations in flowers (Ohno et al. 2011b). Genetically, four elements were believed to explain the inheritance of ray floret colours in Dahlia: A (pale anthocyanin), B (deep anthocyanin), I (flavone), and Y (yellow) (Lawrence 1931; Lawrence and Scott-Honcrieff 1935; Bate-Smith et al. 1955; Broertjes and Ballego 1967). Yellow and white cultivars appeared not to accumulate anthocyanins due to a bottleneck or blockage of the anthocyanin pathway. For yellow cultivars, this was most frequently observed at the levels of both flavanone 3-hydroxylase (FHT, synonym F3H) and dihydroflavonol 4-reductase (DFR) (Halbwirth et al. 2008). Fischer et al. (1988) purified and characterized (+) dihydroflavonol (3-hydroxyflavanone) 4-reductase from flowers of *Dahlia variabilis*. Cyanic flowers of *Dahlia variabilis* were found to contain monomalonylated anthocyanins, 3-(6″-malonylglucoside)-5-glucosides of pelargonidin and cyanidin, and dimalonylated anthocyanins, 3,5-di(malonylglucoside)s of pelargonidin and cyanidin, in addition to nonmalonylated 3,5-diglucosides of these anthocyanidins (Yamaguchi et al. 1999). Enzyme extracts from this plant catalyzed the malonylation of anthocyanidin 3-glucoside to anthocyanidin 3-(6″-malonylglucoside), but not the 3,5-diglucoside to 3-(6″-malonylglucoside)-5-glucoside or 3,5-di(malonylglucoside). The anthocyanin 5-*O*-glucosyltransferase (5GT) was shown to catalyze glucosyl group transfer from UDP-glucose to the 5 position of anthocyanidin 3-*O*-glucoside and 3-*O*-malonylglucoside; it was purified from cyanic flowers of *Dahlia variabilis* (Ogata et al. 2001). The apparent Km values for cyanidin 3-*O*-glucoside, cyanidin 3-*O*-(6″-*O*-malonyl)glucoside, and UDP-glucose were 120, 75, and 250 μmol/l, respectively. Pelargonidin 3-*O*-glucoside and malonylglucoside were also considerable substrates, but low relative activity was observed for delphinidin 3-*O*-glucoside which has yet not been found in *Dahlia* flowers. Suzuki et al. (2002) identified a cDNA coding for the 3-glucoside-specific malonyltransferase for anthocyanins, that is, malonyl-coenzyme A/anthocyanidin 3-*O*-glucoside-6″-*O*-malonyltransferase, from Dahlia (*Dahlia variabilis*) flowers. Schlangen et al. (2010) found that the enzyme flavonoid 3′-hydroxylase (F3′H) could catalyzed chalcone 3-hydroxylation during flavonoid synthesis in the petals of *D. variabilis*. Other enzymes involved in the regulation of anthocyanin synthesis in Dahlia included chalcone synthase 1 (DvCHS1), flavanone 3-hydroxylase (DvF3H), dihydroflavonol 4-reductase (DvDFR), anthocyanidin synthase (DvANS), chalcone isomerase (DvCHI) and DvCHS2 (Ohno et al. 2011a, b). A bHLH transcription factor, DvIVS, is involved in regulation of anthocyanin synthesis in Dahlia (*Dahlia variabilis*) (Ohno et al. 2011a).

Noguchi and Yamamoto (2006) found Dahlia tubers to be a good source of inulin, a soluble dietary fibre. Dahlia inulin was extracted and purified free from atropine, and the average purities of inulin before and after refining were 83.2 % ($n=16$) and 97.9 % ($n=8$). Inulin with a content of 95.72 % and bound glucose 4.38 % were extracted from Dahlia tubers (Anan'ina

et al. 2009). Inulin from Dahlia tubers (50 g% yield, dry basis; 12.5 g% yield, wet basis) can be processed to yield fructose and by-products hydroxymethylfurfural (HMF), (di)fructose anhydrides (DFA), and oligosaccharides (Hauly et al. 1992). Pure nonhydrolyzed inulin was directly converted to ethanol in a simultaneous saccharification and fermentation process using *Aspergillus niger* and *Saccharomyces cerevisiae* (Ohta et al. 1993) The maximum volumetric productivities of ethanol were 6.2 and 6.0 g/l/h for chicory and Dahlia inulins, respectively. The conversion efficiency of inulin to ethanol was 83–84 % of the theoretical ethanol yield.

Inulin was reported to contain 1/3 to 1/4 of the food energy of sugar and 1/6 to 1/9 food energy from fat, which serves as the carbohydrate reserves (Franck and Leenheer 2002). Inulin is useful to replace fat and sugar; it also improves mineral absorption and is reported to possess immunomodulatory properties and to have a preventive effect against colon cancer (Franck and Leenheer 2002).

The chloroform dried leaf extract showed highest antibacterial activity against *Enterobacter aerogenes* (Bissa et al. 2011). Fresh root extract inhibited the growth of *Escherichia coli* and *E. aerogenes*; the fresh stem extracts were effective against *E. aerogenes*, while the fresh leaf and fresh flower extracts were inhibitory to *Agrobacterium tumefaciens*. The dried flower extracts exhibited antimicrobial activity against *E. coli* and *A. tumefaciens.* Rai and Acharya (1999) reported the antimycotic property of *D. pinnata* against *Fusarium oxysporum*. They found, however, that the essential oil of *Dahlia pinnata* had minimum fungitoxic activity against *F. oxysporum* and *Trichophyton mentagrophytes* (Rai and Acharya 2000).

Traditional Medicinal Uses

Tubers of *Dahlia* spp. were widely used in pre-Spanish Mexico and were found to be very high in inulin and fructose (Whitley 1985). The Aztecs used the petals of the Dahlia as well as its tuber in skin treatments for rashes, infected grazes and cracks in the skin. The skin of the tubers was found to be rich in antibiotic compounds. In the past, the petals were crushed, mashed up, and used to relieve insect bites or stings.

Other Uses

Dahlias are attractive and popularly planted as a garden ornamental in the ground or in containers. The flowers also provide good cut flowers as Dahlia blooms profusely over a long season, may have particularly stunning form or colour, and has long, strong stems and good bloom substance. Dahlias can be used in many ways in the garden. Individual plants or small clusters within existing landscaping provide summer-long colour and highlight. Long straight rows look impressive and are easily managed and accessed for cutting blooms. Dahlias can also be planted as hedges. Large Dahlias can be situated as to provide background colour for other landscape plants. Small Dahlias can be intermixed with other plants or used as borders.

The Dahlia is also the official flower of the city of Seattle and the national flower of Mexico.

Comments

Older Dahlia varieties are propagated by dividing the large tuberous roots. New varieties are propagated from seeds, and rare varieties are propagated by grafting onto rootstocks. Generally propagation by cuttings is deemed best.

Most commonly grown Dahlias are hybrids of *D. pinnata* and *D. coccinea*.

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Echinacea purpurea

Scientific Name

***Echinacea purpurea* (L.) Moench**

Synonyms

Brauneria purpurea (L.) Britton, *Echinacea intermedia* Lindl. ex Paxton, *Echinacea purpurea* var. *arkansana* Steyerm., *Echinacea purpurea* f. *liggettii* Steyerm., *Echinacea purpurea* var. *serotina* (Nutt.) L.H. Bailey, *Echinacea serotina* (Sweet) D. Don ex G. Don f., *Echinacea speciosa* (Wender.) Paxton, *Helichroa purpurea* (L.) Raf. *Rudbeckia purpurea* L.

Family

Asteraceae

Common/English Names

Black Sampson, Comb Flower, Coneflower, Eastern Purple Coneflower, Echinacea, Indian Head, Missouri Snakeroot, Purple Coneflower, Red Sunflower.

Vernacular Names

Brazil: Equinácea, Equinocea, Flor De Cone (Portuguese)
Chinese: Zi Hua Song Guo Ju, Zi Zhui Ju
Czech: Třapatka Nachová
Danish: Have-Purpursolhat, Purpur Solhat, Solhat
Dutch: Kogelbloemsoort, Purperen Rudbeckia, Rode Zonnehoed
Eastonian: Purpur-Siilkübar
Finnish: Auringonhattu, Kaunopunahattu, Punahattu
French: Echinacée, Echinacée Pourpre, Rudbeckie Pourpre
German: Echinacea, Echinacin, Echter Sonnenhut, Kegelblume, Purpurroter Sonnenhut, roter Scheinsonnenhut, Roter Sonnenhut, Rudbeckie, Sonnenhut
Hungarian: Bíbor Kasvirág, Bíbor Kúpvirág, Lángvörös Kasvirág, Piros Kasvirág
Icelandic: Echinacea, Sólhattur
Italian: Echinacea Purpurea
Norwegian: Echinacea, Purpursolhatt, Rød Solhatt
Polish: Jeżówka Purpurowa, Jeżogłówka Purpurowa, Rudbekia Purpurowa
Portuguese: Equinácea Purpúrea
Russian: Echinacija purpurovaja
Slovaščina: Ameriški Slamnik, Purpurni Ameriški Slamnik, Škrlatni Ameriški Slamnik

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Spanish: Echinacea
Swedish: Purpurrudbeckia, Röd Rudbeckia, Röd Solhatt
Turkish: Ekinazya, Güneş Çiçeği, Kipriciceği, Kipriotu

Origin/Distribution

Eastern Purple Coneflower is native to eastern North America. It is present to some extent in the wild in much of the eastern, southeastern and midwest United States.

Agroecology

In its native temperate range, it occurs in open woodlands, thickets, prairies, near waterways and roadsides. It is extensively grown as ornamentals in gardens and parks and is also cultivated commercially as an herbal remedy.

E. purpurea thrives best in full sun and is shade intolerant. It is not fastidious of soil pH but plant prefers loamy or sandy, well-drained soils. It is also quite drought tolerant.

Edible Plant Parts and Uses

The petals are edible. Some dishes include echinacea Pane bagno (bathed bread) decorated with fresh echinacea petals and a wedge of lemon, American Indian savoury echinacea spread, echinacea and melon fruit salad (Roberts 2000). Petals are fried with watercress, onion and mustard leaves and spread over sweet potatoes.

Botany

A herbaceous perennial 5–120 cm high with erect, branched brownish-green glabrous or hairy stems (Plate 1) and fibrous roots. Leaves alternate, simple and lower leaves broader ovate (Plate 2) and petiolate with weakly winged petioles, lengths decreasing in upper leaves, lamina ovate lanceolate to narrolyl lanceolate, 5–30 by 5–12 cm, margins serrate, apex acute, base rounded to acute. Flowering heads solitary on stout terminal peduncle, 8–25 cm (Plates 1, 3 and 4). Involucral bracts linear to lanceolate. Receptacle with 9–15 mm palea, red orange tipped, slightly curve and pointed. Discs conic to subglobose 1.4–45.5 by 2–4 cm, disc florets corolla greenish to pink or purple, 1.5–4.5×2–4 cm. Ray florets corolla pink to purple pink to purple, laminae spreading to recurved,

Plate 1 Echinacea in flowers and lanceolate upper leaves

Plate 2 Broadly ovate juvenile leaves

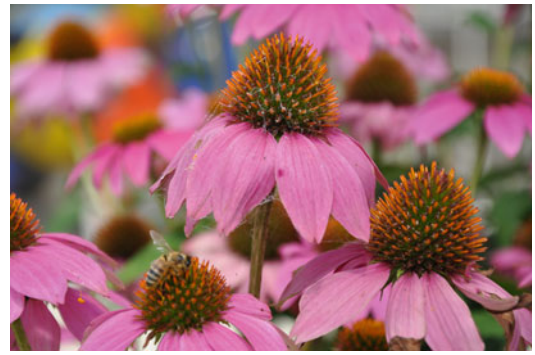

Plate 3 Close view of flowers with conic discs

Plate 4 Flowers with subglobose and flattish round discs

3–8 cm × 0.8–2 cm, two-toothed at apex, sparsely hairy abaxially (Plates 1, 3 and 4). Cypselae, 3–4 angled, glabrous, tan or bicoloured with a dark brown distal band, pappi persistent, 1.2 mm with 0–4 prominent teeth.

Nutritive/Medicinal Properties

Plant/Cell Culture Phytochemicals

Traces of pyrrolizidine alkaloids (0.006 %) tussilagine and isotussilagine were found in dried materials of *Echinacea angustifolia* and *E. purpurea* (Roder et al. 1984).

A 35-kDa water-soluble, acidic polysaccharide, 4-*O*-methyl-glucuronoarabinoxylan, was isolated from hemicellulosic fraction of *E. purpurea* and characterized by Wagner et al. (1984, 1985) and Proksch and Wagner (1987). The polysaccharide contained a (1 → 4)-linked β-D-xylan backbone with branching points at C-2 and C-3. Three homogeneous polysaccharides, two neutral fucogalactoxyloglucans with mean molecular weight of 10,000 and 25,000 and an acidic arabinogalactan with a mean molecular weight of 75,000 were isolated from the medium of *Echinacea purpurea* cell cultures (Wagner et al. 1988). An arabinogalactan protein (AGP) with molecular weight 1.2×10^6 Da, from pressed juice of *Echinacea purpurea*, was isolated from a high molecular weight fraction by precipitation with the β-glucosyl Yariv reagent (Classen et al. 2000). It comprised a high amount of polysaccharide (83 %) with a ratio of galactose to arabinose of 1.8:1, some uronic acids (4–5 %) and a low-protein content (7 %) with high levels of serine, alanine and hydroxyproline. The amino acid profile in the arabinogalactan protein comprised serine 16 %, alanine 12.5 %, hydroxyproline 11.5 %, asparagine/aspartic acid 10.6 %, threonine 10.5 %, glutamine/glutamic acid 9.4 %, arginine 7.5 %, glycine 4.6 %, valine 4.1 %, histidine 3.7 %, lysine 3.3 %, leucine 2.5 %, isoleucine 2.2 % and phenylalanine 1,6 %. The monosaccharide profile in the arabinogalactan protein comprised galactose 59.1, arabinose 33.2, glucosamine 4.0 %, mannose 2.6 % and rhamnose 1.1 %. The molecular weight arabinogalactan protein (AGP) from the pressed juice of *Echinacea purpurea* was found to have hydroxyproline (42.9 % w/w) as the dominant amino acid and the major amino acid responsible for the binding between the protein and the arabinogalactan subunits via an *O*-glycosidic linkage (Volk et al. 2007). Large amounts of glutamine/glutamic acid (24.5 % w/w) and asparagine/aspartic acid (17.3 % w/w) were also found. Another arabinogalactan protein was purified from *E. purpurea* suspension culture (Classen 2007). It comprised high amount of polysaccharide (90 % w/w) with the dominating monosaccharides galactose and arabinose and some glucuronic acid and a small protein moiety (10 % w/w) with the main amino acids alanine, hydroxyproline, serine, glutamine/glutamic acid, asparagines/aspartic acid and threonine. The polysaccharide part was composed of a branched core-polysaccharide of 3-, 6- and 3,6-linked Galp residues with terminal Araf, Arap, Galp and GlcAp residues. Compared to an arabinogalactan protein from pressed juice of the aerial parts of *Echinacea purpurea*, differences particularly in terminal arabinose mono- and oligosaccharides in arabinogalactan (AG) side branches could be detected.

Two groups of minerals (I, Fe, Cu, Mn, Li and, II, Ca, Mg, Zn, Ni) were identified in the aerial parts and roots of *E. purpurea* in Serbia (Razić et al. 2003). The trace element profiles in the roots, stem, leaves and flowers were found to differ significantly.

The aerial parts of *Echinacea purpurea* afforded, in addition to known compounds, five highly unsaturated acetylenic amides and a derivative of linolen (Bohlmann and Hoffmann 1983). The aerial parts of *E. purpurea* were found to contain different structural types of alkamides; the roots yielded similar alkamide pattern (Bauer and Reminger 1989). Alkamide levels differed significantly among roots, rhizomes, stems, leaves and flowers of *E. purpurea* (Perry et al. 1997). Roots were distinguished from other plant parts by higher levels of the C12 diene-diyne alkamides, whereas levels of the C12 tetraene alkamides and C11 diene-diynes were highest in vegetative stems. The ratio of the 2 stereoisomeric C12 tetraene alkamides differed between flowers and all other *E. purpurea* parts. The alkylamides and cichoric acid in dried roots and aerial parts of *E. purpurea* grown in eastern Australia were determined as follows: total alkylamide concentration in root samples was 6.2 mg/g (range 1.2–12.1 mg/g) and in aerial samples was 1.0 mg/g (range 0.2–3.9 mg/g) (Wills and Stuart 1999). The cichoric acid concentration in root samples was 13.2 mg/g (range 1.4–20.5 mg/g) and in aerial samples was 12.9 mg/g (range 4.9–21.4 mg/g). Stuart and Wills (2000) found that total alkamide concentration in *E. purpurea* root, stem and leaf decreased throughout the first growing season while the concentration in flowers increased. In mature plants, the root contained about 70 % of the total plant alkamides with approximately 20 % in flower, 10 % in stem and 1 % in leaf tissue. The relative proportion of individual alkamides in the root did not change during plant growth, but cichoric acid concentration in plant tissues did decrease during plant senescence. Similar concentrations of cichoric acid were measured in root, flower and leaf tissues, but stem levels were lower. In mature plants, the flower and leaf each contained about 35 % of the total plant cichoric acid, while the root and stem contained approximately 20 and 10 %, respectively. Cichoric acid was the main phenolic in *E. purpurea* roots (mean 2.27 % summer, 1.68 % autumn) and tops (2.02 % summer, 0.52 % autumn) followed by caftaric acid was the other main phenolic compound in the roots (0.40 % summer, 0.35 % autumn) and tops (0.82 % summer, 0.18 % autumn) (Perry et al. 2001). Autumn-grown *Echinacea purpurea* plants in Taiwan produced more caffeoyl phenols, particularly cichoric acid and caftaric acid, in leaf and flower tissues than spring-grown plants (Chen et al. 2008). Iranian cultivated *E. purpurea* tops was found to have a high content of cichoric acid (3.5–5.7 %), followed by caftaric acid (3.1–4.5 %) and caffeic acid (0.6–1.1 %) with total polyphenol content of 7.9–10.9 %, (Iranshahi and Amanzadeh 2008). After 2 hours of boiling water extraction, the content of cichoric acid was 5.7 %, whereas the content of this acid in 60:40 ethanol–water extraction did not exceed 3.9 %.

For total alkamides, concentrations (mg/g dry weight basis) among individual *E. purpurea* plants varied from 5.02 to 27.67 (mean = 14.4 %) in roots, from 0.62 to 3.42 (mean = 1.54) in nearly matured seed heads, and from 0.22 to 5.25 (mean = 0.77) in young tops (about ½ flower heads, ¼ leaves, and ¼ stems) (Qu et al. 2005). For cichoric acid, concentrations among individual plants varied from 2.65 to 37.52 (mean = 8.95), from 2.03 to 31.58 (mean = 10.9) and from 4.79 to 38.55 (mean = 18.88) in the roots, the seed heads and the tops, respectively. Dodeca-2*E*, 4*E*, 8*Z*, 10*E*-tetraenoic acid isobutylamide and dodeca-2*E*, 4*E*, 8*Z*, 10*Z*-tetraenoic acid isobutylamide (alkamides 8/9) accounted for only 9.5 % of the total alkamides in roots but comprised 87.9 % in the seed heads and 76.6 % in the young tops. Two cinnamic acids, 2-*O*-caffeoyl-3-*O*-isoferuloyltartaric (3) and 2, 3-di-*O*-isoferuloyltartaric acid (5), along with three known caffeic acids, cichoric acid (1), 2-*O*-caffeoyl-3-*O*-feruloyltartaric acid (2) and 2-*O*-caffeoyl-3-*O*-*p*-coumaroyltartaric acid (4), were isolated and purified from *Echinacea purpurea* (Lu et al. 2012). From 250 mg of crude extracts, 65.1 mg of 1, 8.3 mg of 2, 4.0 mg of 3, 4.5 mg of 4 and 4.3 mg of 5 were isolated, with purities of 98.5, 97.7, 94.6, 94.3 and 98.6 %, respectively.

Nineteen phenolics were identified in the medium of *E. purpurea* cell cultures after elicitation with biotic elicitors (Li and Barz 2005, 2006) . The medium contained lignan, neolignan and acetophenone derivatives as the main elicitor-enhanced products. *E. purpurea* cells mainly contained phenolic glycosides including a new compound α-*O*-β-D-glucopyranosyl-acetovanillone.

Constitutive compounds identified in the cell culture medium of *E. purpurea* included α-hydroxyacetovanillone (1), coniferyl alcohol (4), methyl (*E*)-*p*-coumarate (7), and 1-hydroxypinoresinol (8). After elicitation of *E. purpurea* cell culture with yeast, the compounds found in the medium included α-hydroxyacetosyringone (2); 4-hydroxyacetophenone (3); 4,7,9,8′-tetrahydroxy-3,3′-5′-trimethoxy-8,4′-oxy-9′-norneolignan-7′-one (5); 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxy-4-[1-(*E*)-propen-3-ol]-phenoxy]-propane-1,3-diol (6a,b); 4,7,9-trihydroxy-3,3′,5′-trimethoxy-8,4′-oxy-9′-norneolignan-7′-one (9); and buddlenol B (10). Phenolics found in *E. purpurea* cells were 4-hydroxyacetophenone (3); scopoletin (11); 4-hydroxybenzoic acid glucose ester (12); 4-*O*-β-glucopyranosylacetophenone (13); α-*O*-β-D-glucopyranosyl-acetovanillone (14); 4-*O*-β-glucopyranosylconferyl alcohol (15); scopoline (16); 1-(4-*O*-B-glucopyranosyl-3-methoxyphenyl)-2-(2-methoxy-4[1-(*E*)-propen-3-ol]-phenoxy]-propane-1,3-diol (17a,b); 4(*O*-β-D-glucopyranosyl)-7,9-dihydroxy-3,3′,5′-trimethoxy-8,4′-oxy-9′-norneolignan-7′-one (18); 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxy-4-[1-(*E*)-propen-3-ol]-phenoxy]-propane-1,3-diol (6a,b); and longiloroside (19). The optima accumulation of *Echinacea purpurea* suspension culture biomass (73.6 g/l FW and 10.03 g/l DW), phenolics (61.14 mg/g DW) and flavonoids (38.30 mg/g DW) was achieved in 0.5 MS (Murashige and Skoog) medium (Wu et al. 2007b). High adventitious root biomasses (83.1 g/l FW and 15.30 g/l DW) were achieved with feeding of the 0.5 MS medium at the end of 2nd week. This led to slight decreases in the total production of phenolics and flavonoids; however, this feeding was responsible for increases in the accumulation of caftaric acid (5.76 mg/g DW) and cichoric acid (26.12 mg/g DW).

Beside the above, many other studies had isolated and identified alkamides and caffeic acid derivatives in *E. pur*purea plant, various plant parts and products (Bergeron et al. 2000; Laasonen et al. 2002; Mølgaard et al. 2003). Ultrasonic extraction of dried samples of *E. purpurea* roots and aerial parts with methanol–water (7:3) or ethanol–water (7:3) gave good yields of cichoric acid, echinacoside and the alkamides, undeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide and a mixture of dodeca-2*E*,4*E*,8*Z*,10*E/Z-tetraenoic* acid isobutylamides (recoveries of 89, 85, 80 and 90 %, respectively) (Bergeron et al. 2000). The HPLC separation of the phenolic compounds cichoric acid, chlorogenic acid and echinacoside was also improved by careful attention to the pH of the mobile phase. The profile of phenolic compounds (mean concentration μg/ml) in *E. purpurea* herb was determined as 0–767 μg caftaric acid, 0–45 μg chlorogenic acid, 0–220 μg caffeic acid, 0 μg cynarin, 0–2,879 μg cichoric acid, 0 μg echinacoside and 0–25 μg tet 8/9 (dodeca-2*E*,4*E*,8*Z*,10*E/Z*-tetraenoic acid isobutylamide) (Vimalanathan et al. 2005).

Studies showed that the content of caffeic acid derivatives in *E. purpurea* aerial parts and roots reached its highest in the middle stage of full blossoming (Liu et al. 2007). The content of caffeic acid derivatives in fresh raw material was generally higher than that in dried raw material. The developmental pattern of total phenolics in *E. purpurea* was the same as that of caffeic acid derivatives. The stage of mid-bloom was the optimal harvesting period for both caffeic acid derivatives and total phenolics. There was no significant difference in the content of caffeic acid derivatives among three Chinese geographical populations of *E. purpurea*.

E. purpurea extracts stored for 18 months were found to contain caftaric acid, cichoric acid and undeca-2*Z*,4*E*-diene-8,10-diynoic acid isobutylamide at concentrations of 0.7, 0.71 and 2.0 mg/ml, respectively (Cech et al. 2006). Using HPLC/electrospray ionization mass spectrometry, isomeric isobutylamides and 2-methylbutylamides could be distinguished. The cichoric acid was the main phenolic compound detected in dried *E. purpurea* materials (flowers, leaves, stems and roots), followed by caftaric acid (Lin et al. 2011). The bioactive constituent contents in different plant parts were in the descending order: flowers > leaves > stems > roots. Both caffeic acid derivatives and total phenolics contents were affected by drying method and storage/packing condition. Cool wind-dried materials retained more bioactive constituents content (>85 %) compared to vacuum freeze-dried materials.

The storability results indicated that the freeze-dried *E. purpurea* materials sealed in polyethylene terephthalate/aluminium foil/polyethylene or nylon/polyethylene bags and stored under 10–20 °C and 40–60 % relative humidity without light conditions retained the highest content of bioactive compounds.

Flower Phytochemicals

Volatiles in the headspace of *E. purpurea* flowers were acetaldehyde, dimethyl sulphide, 2-methylpropanal and acetone, 2-butanone, 2-methylbutanal, 3-methylbutanal, unknown, α-pinene, camphene, hexanal, β-pinene, sabinene/β-thujene, unknown, 2-methyl-4-pentenal, β-myrcene, α-terpinene, limonene, 2-hexenal (*trans*), ocimene, γ-terpinene, *trans-ocimene*, *p*-cymene, α-terpinolene, unknown, 1-hexanol, *allo*-ocimene, 3-hexen-1-ol (*cis*), 2-hexen-1-ol (*trans*) and α-cubebene/α-copaene (Mazza and Cottrell 1999). Major volatiles in headspace of flower tissues were myrcene 43 %, β-pinene 7.4 %, α-pinene 22.6 % and dimethyl sulphide 1.0 %.

The essential oil of *E. purpurea* flower heads was found to contain 89 components of which 63 (monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpenes, oxygenated sesquiterpenes) were identified comprising 92.8 % of the total oil yield (Diraz et al. 2012). The major components were germacrene D (11.3 %), caryophyllene oxide (8.7 %), β-caryophyllene (7.2 %) and α-cadinol (6.2 %). The other components higher than 1 % included β-pinene (1.3 %), α-phellandrene (2.9 %), *p*-cymene (2.65), β-elemene (2.1 %), a-cadinene (1.0 %), naphthalene, 1,2,3,5,6,8a-hexahydro-4,7-dimethyl-1-(1-ethylethyl)-,(1*S-cis*)- (3.3 %), α-farnesene (1.0 %), 1,5 epoxysalvia-4(14)ene (3.3 %), naphthalene, 1,2,3,4,4a,7-hexahydro-1,6-dimethyl-4-1(1-methylethyl) – (1.6 %), α-bisabolene (2.3 %), bicylo[4.4.0]dec-1-ene,2-isopropyl-5-methyl-9-methylene- (1.8 %), α-cadinene (2.0 %), decatone (1.5 %), ethyl oleate (1.6 %0, vulgarol B (1.9), aromadendrene oxide (1.1 %), 3,4,-difloro-4-methoxybiphenyl (2.7 %), isoaromadendiene epoxide (1.9 %), *trans* (*Z*)-α-bisabolene epoxide (2.3 %), benzenepropanoic acid, octadecyl ester (1.2 %) and diepi-α-cedrene epoxide (1.2 %). Earlier, 36 compounds comprising 70.9 % of sesquiterpenes and 6.4 % monoterpene hydrocarbons were identified in the *E. purpurea* flower-head essential oil in Iran (Mirjalili et al. 2006). Germacrene D (57 %) was the major component.

Rutin and nicotiflorin (3-*O*-rutinoside campherol) were isolated from the flowers, the latter flavonoid being dominant (Kurkin et al. 2011). The major anthocyanins of *Echinacea purpurea* and *E. pallida* were identified as cyanidin 3-*O*-(β-D-glucopyranoside) and cyanidin 3-*O*-(6-*O*-malonyl-β-D-glucopyranoside) (Cheminat et al. 1989). Cyanidin 3-*O*-(β-D-glucopyranoside) (9.8 mg) and cyanidin 3-*O*-(6″-*O*-β-D-glucopyranoside) (14.3 mg) were obtained from 160 mg crude flower extract with a purity of 95.1 and 98.2 %, respectively (Li et al. 2012).

The profile of phenolic compounds (mean concentration μg/ml) in *E. purpurea* flower was determined as 19–1,212 μg caftaric acid, 0–208 μg chlorogenic acid, 11–179 μg caffeic acid, 0–13 cynarin, 9–734 μg cichoric acid, 0 μg echinacoside, and 0–39 μg tet 8/9 (dodeca-2E,4*E*,8*Z*,10*E*/*Z*-tetraenoic acid isobutylamide) (Vimalanathan et al. 2005). In *Echinacea purpurea* cultivars Magnus and White Swan and line CLS-P2, harvested dry flower heads contained highest cichoric acid content and followed by caftaric acid and chlorogenic acid (Chen et al. 2009). The contents of cynarin and echinacoside in flower heads were relatively low as compared to cichoric acid, caftaric acid or chlorogenic acid. Total caffeoyl derivatives content were 125.3, 116.7 and 145.5 mg/g dry weight for line CLS-P2, Magnus and White Swan, respectively. The alkamides dodeca-2*E*,4*E*,8*Z*,10*E*-tetraenoic acid isobutylamide (alkamide 8) and dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide (alkamide 9) were also found in the flower heads, but their content was much lower than in the roots. No statistically significant differences in flower-head alkamides 8 and 9 content were found among the tested *E. purpurea* cultivars and lines.

The extraction yields of phenolics of freeze-dried *E. purpurea* flowers were significantly

affected by the ethanol concentrations at 25 °C with water extraction giving the highest extraction yield (39.8 %) (Tsai et al. 2011). When the ethanol volume percentage in the solvent was increased from 25 % up to 95 %, the extraction yields were decreased from 36.9 to 3.3 %. Water extraction yielded 1,656 mg/g extract of caftaric acid, 0.14 mg chlorogenic acid, 0.53 mg echinoside, 37.23 mg cichoric acid, total caffeic acid derivatives 54.45 mg and total phenolics 97.07 mg. For caftaric acid, ethanol extraction (50 %) yielded the highest 67.07 mg down to 16.35 mg (ethanol 95 %); for chlorogenic acid, ethanol (75 %) gave 2.84 mg down to 0.53 mg at ethanol 95 %; for echinacoside, ethanol (75 %) gave 1.07 mg down to 0.54 mg at ethanol 95 %; for cichoric acid, ethanol extraction (50 %) yielded the highest 180.29 mg down to 42.54 mg (ethanol 95 %). For total caffeic acid derivatives, ethanol extraction (50 %) yielded the highest 250.79 mg down to 59.96 mg (ethanol 95 %). For total phenolics, ethanol extraction (50 %) yielded the highest 441.33 mg down to 104.47 mg (ethanol 95 %). The total phenols, individual and total caffeic acid derivatives contents of extracts were enhanced by elevated extraction temperatures ranged from 25 to 65 °C.

The content of cichoric acid and caftaric acids in dried *E. purpurea* flowers were found to be significantly affected by the drying methods used (Kim et al. 2000b). Although significant loss of cichoric acid was observed when flowers were stored at high moisture, vacuum microwave-dried flowers with a low-moisture content retained the highest levels of cichoric acid and caftaric acid similar to freeze-dried flowers. Flowers that were air-dried at 25 °C retained about 50 %, while those air-dried D at 70 °C had lowest retention of these acids. Although flowers air-dried at 40 °C retained relatively high amounts of cichoric acid and caftaric acid, the time (55 hours) required to reach optimal drying was considerably longer than that (47 minutes) for vacuum microwave drying. They also found that individual alkamide concentrations in roots and leaves were affected by the drying methods used (Kim et al. 2000a). To preserve higher levels of total alkamides, freeze-drying was found to be the best method, vacuum microwave drying was a superior method for drying roots than air-drying at 70 °C, while air-drying at 50 °C was the preferred method for drying leaves of *E. purpurea*.

Fruit (Achene)/Seed Phytochemicals

Two major alkamide peaks were identified in *E. purpurea* achenes as undeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide and dodeca-2*E*,4*E*,8*E*,10*E/Z* tetraenoic acid isobutylamide (8/9) (He et al. 1998). The isomer pair, tetraene 8/9, was purified as a standard for quantification of alkamide content in *E. purpurea* achenes and roots.

Seed oil yields of *E. angustifolia*, *E. pallida* and *E. purpurea*, harvested in 1998 and 1999, ranged from 13 to 23 % (Oomah et al. 2006). Vitamin E content of the oils ranged from 29 to 85 mg/100 g oil, with α-tocopherol constituting 83 % of the total tocopherol. The oil was highly polyunsaturated and abundant in linoleic, oleic and palmitic acids, together comprising 95 % of the total fatty acids. *E. purpurea* seed oils contained 66.5 % linoleic, 21.4 %, oleic and 8 % palmitic acids in the 1998 year harvest and 75.6 % linoleic, 12.2 % oleic and 7 % palmitic acids in the 1999 harvest. Fruit (achenes) of *E. purpurea* was found to contain 33.6 % light yellow fatty oil comprising 78.4 % unsaturated fatty acids and 21.6 % saturated fatty acids; the major components were linoleic acid (58.2 %) and oleic (20.2 %) acid, and the equivalent iodine number was 121 (Vandyshev et al. 2009). Eighteen components were identified in *E. purpurea* seed oil, comprising 90.4 % of total area with petroleum ether solvent and 96 % with solvent *n*-hexane solvent (Diraz et al. 2012). The most abundant fatty acids were palmitic acid, stearic acid, oleic acid, and linoleic acid. The fatty acid profile using petroleum ether and *n*-hexane solvents were, respectively, as follows: oleic acid C18:1 (48 %, 29 %), palmitic acid C16:0 (16.6 %, 9.2 %), linoleic acid C18:2 (13.3 %; 51 %) , oxocol C13 (0.1 %, 0 %), myristic acid C14:0 (0.3 %, 0.2 %), pentadecanoic acid C15:0 (0.1 %, 0.1 %), palmitoleic acid C16:1

(1 %, 0.4 %), carbonic acid C17:0 (0.2 %, 0.1 %), heptadecanoic acid C17:1 (0.2 %, 0 %), stearic acid C18:0 (5 %, 2.5 %) elaidic acid C18:1 (0.7 %, 0 %), linolelaidic acid C18:2 (0.8 %, 0 %), arachidic acid C20:0 (0.5 %, 0.6 %), gamma-linolenic acid C18:3 (0 %, 0.5 %), eicosenoic acid C20:1 (0.3 %, 0.5 %), behenic acid C22:0 (1.3 %, 0.7 %), tricosanoic acid C23:0 (0.1 %, 0.1 %), lignoceric acid C24:0 (0.6 %, 0.3 %) and oxiraneoctanoic acid C26 (0.8 %, 0.8 %). Oxocol, heptadecenoic acid, elaidic acid and linolelaidic acid could not be defined with solvent *n*-hexane.

Leaf Phytochemicals

Volatiles in the headspace of *E. purpurea* leaf tissues were acetaldehyde, dimethyl sulphide, propanal, 2-methylbutanal, 3-methylbutanal, 2-ethylfuran, pentanl, α-pinene, α-thujene, camphene, hexanal, β-pinene, sabinene/ β-thujene, pentanal, 2-methyl-4-pentenal, β-myrcene, α-terpinene, limonene, 2-hexanal (*cis*), 2-hexenal (*trans*), ocimene, γ-terpinene, *trans*-ocimene, *p*-cymene, hexyl acetate, α-terpinolene, 3-hexen-1-ol-acetate, 1-hexanol, *allo*-ocimene 3-hexen-1-ol (*cis*), α-ylangene, γ-cadinene, *trans*-caryophyllene, calarene/α-copaene, germacrene D/α-cubebene, 5-ethyl-2(5*H*)-furanone, δ-cadinene, βα-cubebine/γ-cadinene and 2,2,3,3-tetramethyl hexane (Mazza and Cottrell 1999). Major volatiles in headspace of leaf tissues were myrcene 27 %, β-pinene 1.9 %, α-pinene 12.1 %, dimethyl sulphide <1.0 %

Total phenolic contents reported for *E. purpurea* (leaf) were 15.15 mg GAE/100 g DW (Wojdyło et al. 2007). Major phenolic compounds (mg/100 g DW) found were phenolic acids, 620 mg caffeic acid, 115 mg neochlorogenic acid, 19.5 mg *p*-coumaric acid and 17.9 mg ferulic acid, and flavonoids, 12.4 mg quercetin.

In *Echinacea purpurea* cultivars Magnus and White Swan and line CLS-P2, harvested dry leaves contained highest cichoric acid content and followed by caftaric acid and echinacoside (Chen et al. 2009). The contents of chlorogenic acid and cynarin in leaves were relatively low as compared to cichoric acid, caftaric acid and chlorogenic acid. Among the five caffeoyl derivatives examined, CLS-P2 leaves had greater cichoric acid, caftaric acid, cynarin and echinacoside levels than Magnus and White Swan. Total caffeoyl derivatives content were 61.73, 31.75 and 20.02 mg/g dry weight for line CLS-P2, cultivar Magnus and cultivar White Swan, respectively. Line CLS-P2 had the highest dodeca-2E,4*E*,8*Z*,10*E*-tetraenoic acid isobutylamide (alkamide 8) and dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide (alkamide 9) content in dry leaves among the tested cultivars and line. The profile of phenolic compounds (mean concentration μg/ml) in *E. purpurea* leaf and stem was determined as 0–1,174 μg caftaric acid, 0–63 μg chlorogenic acid, 0–421 μg caffeic acid, 0–5 cynarin, 0–6,001 μg cichoric acid, 0 μg echinacoside and 0.19 μg tet 8/9 (dodeca-2E,4*E*,8*Z*,10*E*/*Z*-tetraenoic acid isobutylamide) (Vimalanathan et al. 2005).

Stem Phytochemicals

Volatiles in the headspace of *E. purpurea* stem tissues were acetaldehyde, dimethyl sulphide, 2-methylpropanal and acetone, 2-methylbutanal, 3-methylbutanal, α-pinene, geranyl acetate, camphene, hexanal, β-pinene, sabinene/ β-thujene, unknown, 2-methyl-4-pentenal, β-myrcene, α-terpinene, limonene, 2-hexenal (*trans*), ocimene, γ-terpinene, *trans*-ocimene, α-terpinolene, 3-hexen-1-ol-acetate, 1-hexanol, *allo*-ocimene, 3-hexen-1-ol (*cis*), 2-hexen-1-ol (*trans*), α-cubebene/α-copaene, α-ylangene, α-ylangene, germacrene D/α-cubebene, δ-cadinene and βα-cubebine/γ-cadinene (Mazza and Cottrell 1999). Major volatiles in headspace of stem tissues were myrcene 45 %, β-pinene 4.4 %, α-pinene 33.7 % and dimethyl sulphide <1.0 %.

Root Phytochemicals

Volatiles in the headspace of *E. purpurea* roots were acetaldehyde, dimethyl sulphide, 2-methylpropanal and acetone, 2-propenal,

2-methylbutanal, 3-methylbutanal, ethanol, 1-methylpropyl acetate, trichloroacetic acid, α-pinene, camphene, hexanal, β-pinene, 2-methyl-1-propanol, sabinene/ β-thujene, α-phellandrene, α-terpinene, heptanal, limonene, 2-methyl-1-butanol, 3-methyl-1-butanol, ocimene, *p*-cymene, hexyl acetate, unknown, 6-methyl-5-hepten-2-one, 1-hexanol and 1-octen-3-ol, benzaldehyde (Mazza and Cottrell 1999). Major volatiles in headspace of root tissues were 0%, β-pinene 0.2 %, α-pinene 0.6 %, α-phellandrene 16.7 % and dimethyl sulphide 14.7 %. The seventeen lipophilic, volatile to semivolatile components, including the 11 alkamides known to *E. purpurea* roots, were identified (Hudaib et al. 2002). Cucumber mosaic cucumovirus infection was found to be responsible for significant variations in the relative compositions of the major constituents, in particular germacrene D, dodeca-2*E*, 4*E*, 8*Z*, 10*Z*(*E*)-tetraenoic acid isobutylamide *cis*/*trans* isomers, undeca-2*Z*, 4*E*-diene-8, 10-diynoic acid isobutylamide and dodeca-2*E*, 4*Z*-diene-8, 10-diynoic acid isobutylamide.

Root extracts of *E. purpurea* root were found to contain (μg/ml) chlorogenic acid (0.0157 μg), caftaric acid (0.1568 μg), cafeic acid (trace), cichoric acid (1.0147 μg) alkamides 1 undeca-2*E*-4*Z*-diene-8,10-diynoic acid isobutylamide (0.056 μg), undeca-2*Z*-4*E*-diene-8,10-diynoic acid isobutylamide (0.0159 μg), doceca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide (0.0130 μg), undeca-2*E*,4*Z*-diene-8,10-diynoic acid 2-methylbutylamide (trace), dodeca-2*E*,4*E*,10*E*-trien-8-ynoic acid isobutylamide (0.0156 μg), dodeca-2*E*,4*E*-diene-8,10-diynoic acid 2-methylbutylamide (0.0092 μg), dodeca-2*E*,4*E*,8*Z*,10*E*-tetraenoic acid isobutylamide (0.2912 μg), dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide (0.0396 μg), dodeca-2*E*,4*E*,8*Z*, trienoic acid isobutylamide (0.0102 μg) and undeca-2*E*-ene-8,10-diynoic acid isobutylamide (0.0106 μg) (Bauer et al. 1988; Bauer and Reminger 1989; Binns et al. 2002b; Perry et al. 2001; Hall 2003; Senchina et al. 2006; Pietta et al. 1998; Gotti et al. 2002; Pomponio et al. 2002; Solco 2007). No cynarin and echinacoside were detected in the roots. Five alkylamides, undeca-2*E*,4*Z*-dien-8,10-diynoic acid isobutylamide, dodeca-2*E*,4*Z*-dien-8,10-diynoic acid isobutylamide, dodeca-2*E*,4*E*,10*E*-trien-8-ynoic acid isobutylamide, dodeca-2*E*,4*E*,8*Z*-trienoic acid isobutylamide and dodeca-2*E*,4*Z*-dien-8,10-diynoic acid 2-methylbutylamide, were isolated from the roots (Bauer et al. 1988). Nine alkamides were identified in the root of *E. purpurea* (He et al. 1998) similar to the fingerprint reported by Bauer and Remiger (1989). Several minor alkamides were also tentatively identified.

The following alkamides were identified in fresh and dry root extracts of *E. purpurea* (Spelman et al. 2009): undeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide (A); undeca-2*Z*,4*E*-diene-8,10-diynoic acid isobutylamide (B); undeca-2*E*-ene-8,10-diynoic acid isobutylamide (C); undeca-2*E*,4*Z*-diene-8,10-diynoic acid 2-methylbutylamide (D); undeca-2*Z*,4*E*-diene-8,10-diynoic acid 2-methylbutylamide (*E*, new); dodeca-2*Z*,4*E*-diene-8,10-diynoic acid isobutylamide (F); dodeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide (G); dodeca-2*E*,4*E*,10*E*-triene-8-ynoic acid isobutylamide (H); dodeca-2*E*,4*E*,8*Z*,10*E*-tetraenoic acid isobutylamide (I); dodeca-2*E*-ene-8,10-diynoic acid isobutylamide (J, used as standard); dodeca-2*E*,4*E*, 8*E*,10*Z*-tetraenoic acid isobutylamide (K); dodeca-2*E*,4*E*, 8*Z*,10*Z*-tetraenoic acid isobutylamide (L, used as standard); dodeca-2*E*,4*E*,8*Z*-trienoic acid isobutylamide (M); dodeca-2*E*,4*E*-dienoic acid isobutylamide (N); dodeca-2*E*,4*E*-dienoic acid isobutylamide (O); trideca-2*E*,7*Z*-diene-8,10-diynoic acid isobutylamide (P); dodeca-2*E*,4*Z*-diene-8,10-diynoic acid 2-methylbutylamide (Q); and dodeca-2,4,8,10-tetraenoic acid 2-methylbutylamide (R). Quantities of the isomeric alkylamides K, L and M and alkylamide J in ethanol extracts of *E. purpurea* root were determined in terms of concentrations of the isomeric tetraenes (compounds K, L and M) and dodeca-2*E*-ene-8,10-diynoic acid isobutylamide (compound J) per ml of solvent. The three different *Echinacea* root extracts, fresh 1:2, dry 1:11 and dry 1:5, all contained these alkylamides. However, the dry 1:5 extract contained the greatest amount of these compounds. All three extraction techniques investigated here (fresh 1:2, dry 1:5 and dry 1:11) resulted in very similar

alkylamide profile and gave similar yields of alkylamides and of total dissolved solids. The similarity in alkylamide content in fresh 1:2 and dry 1:11 extracts indicated that drying of root material at 50 °C did not result in a loss of alkylamides. It was concluded that either fresh or dried roots could be used to prepare extracts with high alkylamide content, although the overall yield was slightly lower for fresh extracts.

Caffeic acid derivatives, caftaric acid, chlorogenic acid, caffeic acid, cichoric acid and alkamides: undeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide; undeca-2*Z*,4*E*-diene-8,10-diynoic acid isobutylamide; dodeca-2*Z*,4*E*-diene-8,10-diynoic acid isobutylamide; undeca-2*E*,4*Z*-diene-8,10-diynoic acid 2-methylbutylamide; dodeca-2*E*,4*E*,10*E*-triene-8-ynoic acid isobutylamide; trideca-2*E*,7*Z*-diene-10,12-diynoic acid isobutylamide; dodeca-2*Z*, 4*E*-diene-8,10-diynoic acid isobutylamide; dodeca-2*E*,4*Z*-diene-8,10-diynoic acid 2-methylbutylamide; dodeca-2*E*,4*E*, 8*E*,10*Z*-tetraenoic acid isobutylamide, dodeca-2*E*, 4*E*,8*Z*-trienoic acid isobutylamide; and dodeca-2*E*,4*E*-dienoic acid isobutylamide, were detected in the roots and extracts (Luo et al. 2003). Three alkamides and nitidanin diisovalerianate were identified, together with 14 known alkamides and one sesquiterpene from the roots of *Echinacea purpurea* (Hohmann et al. 2011). Cichoric acid and verbascoside predominated in extracts of *E. purpurea* roots (Sloley et al. 2001). A total of 16 alkamides, three ketoalkenes, two ketoalkynes and four phenolic acids (echinacoside, cichoric acid, caftaric acid and chlorogenic acid) were identified in aqueous ethanol (70 %) root extracts of *Echinacea purpurea* and *Echinacea pallida* (Thomsen et al. 2012). The major alkamides in the roots of *E. purpurea* were at their lowest concentration in the middle of autumn and early winter, while all of the major phenolic acids were at their highest concentrations in spring. In *E. purpurea* root extract, the major alkamide, dodeca-2*E*, 4*E*, 8*Z*, 10*E*/*Z*-*tetraenoic* acid isobutyl amide, was not significantly affected by storage at any of the temperatures (−20, 25 and 40 °C), but cichoric acid content declined significantly at both 25 and 40 °C as compared to low-temperature storage (Livesey et al. 1999). In the root powder, the major alkamide showed a significantly reduced level at 25 and 40 °C, while cichoric acid did not decline significantly.

Biomass accumulation and production of caffeic acid derivatives (caftaric acid, chlorogenic acid and cichoric acid) in *Echinacea purpurea* adventitious root cultures was optimal under incubation temperature of 20 °C among the different incubation temperatures tested (10, 15, 20, 25 and 30 °C) (Wu et al. 2007a). Biomass of adventitious roots was highest in cultures grown under dark, while accumulation of caffeic acid derivatives was optimum in the cultures grown under 3/21 hours light and dark cultural regimes. Studies found that 15-day-old hairy root culture stimulated every 5 days by ultrasound for 6 minutes produced the highest amount of caffeic acid derivatives (CADs) after 30 days of culture among all ultrasound treatment experiments (Liu et al. 2012). The obvious increase of CADs production in *E. purpurea* hairy roots stimulated by ultrasound was related to the increase of both rolB-regulated endogenous indole-3-acetic acid biosynthesis and phenylalanine ammonium lyase (PAL) activity.

In *Echinacea purpurea* cultivars Magnus and White Swan and line CLS-P2, harvested dry roots contained highest cichoric acid content and then followed by caftaric acid, cynarin, echinacoside and chlorogenic acid (Chen et al. 2009). The caffeoyl derivatives were 16.53, 19.71 and 27.40 mg/g dry weight for CLS-P2, Magnus and White Swan, respectively. Compared to flowers and leaves, roots contained the highest content of alkamides, dodeca-2*E*,4*E*,8*Z*,10*E*-tetraenoic acid isobutylamide (alkamide 8) and dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide (alkamide 9). White Swan accumulated considerably higher alkamides 8 and 9 content in dry roots than Magnum and line CLS-P2.

Highly water-soluble fructans were isolated from *E. purpurea* roots (Wack and Blaschek 2006). The fructans represented linear inulin-type fructans with almost exclusively β-(2 → 1)-linked fructosyl units, terminal glucose

and terminal fructose. Small proportions of β-(2→1,2→6)-linked branch point residues were detected. 80 % ethanol-insoluble fructan from *E. purpurea* showed an average mean degree of polymerization of 35, 60 % ethanol-insoluble fructan of 44, and 40 % ethanol-insoluble fructan of 55.

Commercial *Echinacea* extracts are manufactured primarily from three *Echinacea* species, namely, *Echinacea purpurea* (herb, roots or seeds), *E. angustifolia* (roots) and *E. pallida* (roots) (Mahady et al. 2001). Current recommendations for use of these products include oral administration for the prophylaxis and treatment of the common cold, bronchitis, influenza and bacterial and viral infections of the respiratory tract. However, based on existing data products containing pressed juice or hydroalcoholic extracts, *Echinacea purpurea* (leaf juice and roots) and *E. pallida* (roots) had the most convincing data supporting their use. According to Spelman et al. (2009), *Echinacea purpurea*, a top-selling botanical medicine, is currently of considerable interest due to immunomodulatory, antiinflammatory, antiviral and cannabinoid receptor 2 (CB_2)-binding activities of its alkylamide constituents. It is an immunostimulating drug, containing multiple bioactive substances such as polysaccharides, caffeic acid derivatives (caffeic acid, cichoric acid, caftaric acid, chlorogenic acid), alkamides and glycoproteins (Manček and Kreft 2005). Among the many pharmacological properties reported for *E. purpurea* extracts, immunomodulation of macrophages had been demonstrated most convincingly (Barrett 2003). Several dozen clinical studies—including a number of blind randomized trials—had reported health benefits. The most robust data were from studies testing *E. purpurea* extracts in the treatment for acute upper respiratory infection. Although indicative of modest benefit, these studies were limited both in size and in methodological quality. Although a great deal of moderately good-quality scientific data regarding *E. purpurea*, effectiveness in treating illness or in enhancing human health exist, much has not yet been proven beyond a reasonable doubt. Numerous studies had shown that *E. purpurea* exhibited immunostimulating, antimicrobial, antiinflammatory, antioxidant, cytochrome enzyme inhibitory, antiandrogenic, cannabinoidomimetic, radioprotective and antitumorous activities (Gupta et al. 2012).

Antioxidant Activity

The mechanisms of antioxidant activity of extracts derived from *E. angustifolia*, *E. pallida* and *E. purpurea* roots included free radical scavenging and transition metal chelating (Hu and Kitts 2000). Root extracts of these *Echinacea* spp. were capable of scavenging hydroxyl, DPPH and ABTS radicals. These root extracts delayed the formation of conjugated diene hydroperoxide induced by the thermal decomposition of 2, 2′-azobis(2-amidinopropane) dihydrochloride and protracted the lag phase of peroxidation of soybean liposomes. These root extracts also suppressed the oxidation of human low-density lipoprotein, as evaluated by reduced agarose electrophoretic mobility following oxidative modification by Cu^{2+}.

Studies showed that *E. purpurea* extracts had antioxidant activity similar to that of ascorbic acid but had no serious effect on inhibiting chicken's peripheral blood mononuclear cells viability (Lee et al. 2009), In 2,2-diphenyl-1-picril hydrazyl radical (DPPH) scavenging capacity, the ED_{50} for the extract was measured at 0.23 mg/ml. The superoxide anions scavenging capacity of the extract was nearly equivalent to ascorbic acid (91.1 % vs. 93.0 %) at the same concentration of 1.6 mg/ml, and ED_{50} was 0.32 and 0.13 mg/ml, respectively. Reducing power of the extract increased linearly with its concentration, and the concentration at 2.0 mg/ml reached about 65 % of ascorbic acid at 0.3 mg/ml. The chelating capacity of ferrous iron (Fe^{2+}) was 70 % as good as that of the synthetic metal chelater EDTA when added to 5.0 mg/ml of *E. purpurea* extract. The polysaccharides content of the extract was 159.8 mg/g dry weight (DW), and total phenolic compound was 11.0 mg gallic acid equivalent/g

DW. Microculture tetrazolium assays showed extracts had 92 % cell viability at 1.6 mg/ml for chicken's peripheral blood mononuclear cells (PBMCs) and 84 % for RAW 264.7 macrophages, neither reaching the IC_{50} level.

Extracts of the roots and leaves of *E. purpurea* were found to have antioxidant properties in a free-radical scavenging assay and in a lipid peroxidation assay (Sloley et al. 2001). The methanol root extract of *E. purpurea*, *E. pallida* and *E. angustifolia* exhibited DPPH antioxidant activity with EC_{50} values of 134, 167 and 231 μg/ml, respectively (Pellati et al. 2004). The radical scavenging activity of *Echinacea* root extracts reflected their phenolic content. The total phenolic content was 23.23 mg/g for *E. purpurea*, 17.83 mg/g for *E. pallida* and 10.49 mg/g for *E. angustifolia*. Caftaric acid, chlorogenic acid, caffeic acid, cynarin, echinacoside and cichoric acid were identified and quantified in *Echinacea* roots and derivatives. Pure echinacoside had the highest capacity to quench DPPH radicals (EC_{50} = 6.6 μM), while caftaric acid had the lowest (EC_{50} = 20.5 μM).

The antioxidant activity of three extracts, one alkamide fraction, four polysaccharide-containing fractions, and three caffeic acid derivatives from *Echinacea purpurea* root was evaluated by measuring their inhibition of in-vitro Cu(II)-catalyzed oxidation of human low-density lipoprotein (LDL) (Dalby-Brown et al. 2005). Among the extracts the 80 % aqueous ethanol extract exhibited ten times longer lag phase prolongation (LPP) than the 50 % ethanol extract, which in turn exhibited a longer LPP than the water extract. The antioxidant activity of the tested *Echinacea* extracts, fractions and isolated compounds was dose dependent. Synergistic antioxidant effects of *Echinacea* constituents were found when cichoric acid (major caffeic acid derivative in *E. purpurea*) or echinacoside (major caffeic acid derivative *in Echinacea pallida* and *Echinacea angustifolia*) was combined with a natural mixture of alkamides and/or a water extract containing the high molecular weight compounds.

The extracts of the stems, leaves and roots of *Echinacea purpure*a and their constituent cichoric acid were found to be efficient scavengers of DPPH radicals with an activity comparable to that of rosmarinic acid, a well-characterized antioxidant (Thygesen et al. 2007). The efficacy of the extracts in the reaction with DPPH correlated well with the amount of cichoric acid present in the various extracts. The alkamides alone showed no antioxidant activity in any of the tests. Alkamides present in the extract increased, however, the antioxidative effect of cichoric acid in the peroxidation lipid emulsion assay. Antioxidant activity in terms of TEAC (μM trolox/100 g DW) of *E. purpurea* leaves reported was 12.3 μM for ABTS, 75 μM for DPPH and 94.6 μM for FRAP (ferric reducing antioxidant power) assays (Wojdyło et al. 2007). Total phenolic contents reported were 15.15 mg GAE/100 g DW. The DPPH scavenging reached 93.6 %, and the values of EC_{50} were (34.16) μg/ml and (65.48) μg/ml for the extracts obtained by the classical and ultrasound extractions, respectively (Stanisavljević et al. 2009).

At level of 10 μg/ml, the scavenging abilities of tested samples on DPPH radicals were in the descending order of ascorbic acid > BHA (butylated hydroxyanisole) > flower extract > α-tocopherol (Tsai et al. 2011). At level of 30 μg/ml, the flower extract and α-tocopherol showed 90.82 and 93.10 % scavenging abilities, respectively. The radical scavenging ability of *E. purpurea* flower extract could be attributable to the caffeic acid derivatives, especially cichoric acid with two adjacent hydroxyl groups of its phenolic rings showed the highest radical scavenging ability. The order of potency against DPPH radicals was the following: echinacoside > cichoric acid > chlorogenic acid > caffeic acid > caftaric acid. At the level of 100 μg/ml, the reducing power of samples was in the descending order of ascorbicacid > BHA > flowerextract > α-tocopherol. The ascorbic acid, BHA, and flower extract attained the same maximum reducing power (2.3 AU) at 100, 200 and 400 μg/ml, respectively. The flower extracts exerted an 81.88 % ferrous ions chelating effect at 3 mg/ml concentration when compared with the EDTA (ethylenediaminetetraacetic acid) concentration of 10 μg/ml.

Immunomodulatory Activity

Studies found that the main immunostimulatory activity of *Echinacea* resided in the water-soluble materials rather than the lipoidal small molecules (Pillai et al. 2007). The use of flow cytometry demonstrated a link between the polysaccharides in *Echinacea* and the biologic immunostimulatory effect. *E. purpurea*, *E. pallida* and *E. angustifolia* leaves, stems, flowering tops and roots all produced substantial immunostimulatory activity. In-vitro and in-vivo studies indicated that the therapeutic effects of *Echinacea* were due to a stimulation of cellular immune response (Mahady et al. 2001).

In-Vitro Studies

Purified polysaccharides (EPS) prepared from *Echinacea purpurea* were shown to strongly activate macrophages that developed pronounced extracellular cytotoxicity against tumour targets (Stimpel et al. 1984). The splenic lymphocytes from mice treated with *E. purpurea* and *Hypericum perforatum* at the two dose levels used (30 and 100 mg/kg/day) were shown to be significantly more resistant to apoptosis than those from mice treated only with the vehicle (Di Carlo et al. 2003). Further, mice treated with these natural substances showed a decrease in Fas-Ag expression and an increase in Bcl-2 expression.

The 4-*O*-methyl-glucuronoarabinoxylan, isolated from *E. purpurea* showed immune-stimulating activity in several in-vitro immunological test systems (Wagner et al. 1984, 1985; Proksch and Wagner 1987). The fucogalactoxyloglucan of mean molecular weight 25,000 isolated from *E. purpurea* cell culture enhanced phagocytosis in vitro and in-vivo (Wagner et al. 1988). The arabinogalactan specifically stimulated macrophages to excrete the tumour necrosis factor (TNF). The arabinogalactan protein (AGP) from pressed juice of the aerial parts of *Echinacea purpurea* demonstrated binding to lymphocytes, monocytes and granulocytes of different donors (Thude et al. 2006). A high molecular weight arabinogalactan protein (AGP) from the pressed juice of *Echinacea purpurea*, known to exhibit immunomodulatory properties in vitro, was characterized (Volk et al. 2007). Normal human peripheral blood macrophages cultured in concentrations of *Echinacea purpurea* fresh pressed juice as low as 0.012 μg/ml produced significantly higher levels of IL-1, TNF-α, IL-6 and IL-10 than unstimulated cells (Burger et al. 1997). The high levels of IL-1, TNF-α and IL-10 induced by very low levels of echinacea were consistent with an immune-activated antiviral effect. Echinacea induced lower levels of IL-6 in comparison to the other cytokines measured. Echinacea herb and root powders were found to stimulate murine macrophage cytokine secretion as well as to significantly enhance the viability and/or proliferation of human peripheral blood mononuclear cells in vitro (Rininger et al. 2000). In contrast, echinacea extracts chemically standardized to phenolic acid or echinacoside content and fresh pressed juice preparations were found to be inactive as immunostimulatory agents but did display, to varying degrees, antiinflammatory and antioxidant properties.

Studies showed that *E. purpurea* root and leaf–stem extract exhibited opposite (enhancing vs. inhibitory) modulatory effects on the expression of the CD83 marker in human dendritic cells (DCs) (Wang et al. 2006) Downregulation of mRNA expression of specific chemokines (e.g., CCL3 and CCL8) and their receptors (e.g., CCR1 and CCR9) was observed in stem- and leaf-treated DCs. Other chemokines and regulatory molecules (e.g., CCL4 and CCL2) involved in the c-Jun pathway were found to be upregulated in root-treated DCs. In another study, following 48 hours exposure of dendritic cells from C57Bl/6 mice to *E. purpurea* root and leaf extracts, it was found that the polysaccharide-rich root extract increased the expression of MHC class II, CD86 and CD54 surface biomarkers whereas the alkylamide-rich leaf extract inhibited expression of these molecules (Benson et al. 2010). Production of IL-6 and TNF-α increased in a concentration-dependent manner with exposure to the root, but not leaf, extract. In contrast, the leaf but not root extract inhibited the enzymatic activity of cyclooxygenase-2. The leaf but not

root extract inhibited the antigen-specific activation of naïve CD4+ T cells from OT II/Thy1.1 mice. These results suggested that *E. purpurea* could be immunostimulatory, immunosuppressive and/or antiinflammatory depending on the plant part and extraction method.

E. purpurea extracted in a solvent mixture of 95:5 ethanol/water dose-dependently inhibited interleukin IL-2 production in human Jurkat T cells (Sasagawa et al. 2006). This IL-2 inhibitory activity correlated with the presence of alkylamides but not caffeic acid derivatives. *E. purpurea* extract was both IL-2 suppressive and cytotoxic at 50 and 100 μg/ml. Lower concentrations from 6.25 to 25 μg/ml significantly decreased IL-2 production, but not cell viability. Alkylamides at concentrations found in a 50 μg/ml extract decreased IL-2 production by approximately 50 %, but not cell viability in a dose-dependent manner. *Echinacea* and several of its phytochemical components were found to have opposing effects on NFκB expression by Jurkat cells (a human T-cell line) (Matthias et al. 2008). In the absence of stimulation, *Echinacea* and its components exerted no significant effect on basal NFκB expression levels. In the presence of endotoxin (LPS), NFκB expression was decreased. However, this decrease was significantly reversed by treatment with cichoric acid, an *Echinacea* root extract (prepared from both *Echinacea angustifolia* and *Echinacea purpurea*) and the alkylamide fraction derived from this combination. For the phorbol myristate acetate stimulation of Jurkat cells, effects on NFκB expression were mixed. Depending on the concentration, cichoric acid and a 2,4-diene alkylamide significantly induced NFκB levels, whereas a 2-ene alkylamide caused a significant inhibition. In contrast, both the *Echinacea* and the mixed alkylamide fraction exerted no effect.

Pugh et al. (2012) found that differences in total bacterial load within *Echinacea purpurea* samples were strongly correlated with in-vitro macrophage activity (NF-κB activation in THP-1 cells) and content of bacterial lipopolysaccharides in the extracts. The results added to the growing body of evidence that bacteria within *Echinacea* were the main source of components responsible for enhancing innate immune function.

Animal Studies

Polysaccharides purified from large-scale *Echinacea purpurea* plant cell cultures were found to activate human phagocytes in vitro and in vivo and to induce acute-phase C reactions (Roesler et al. 1991b). These substances enhanced the spontaneous motility of polymorphonuclear leukocytes (PMN) under soft agar and increased the ability of these cells to kill staphylococci. Monocytes were activated to secrete tumour necrosis factor alpha (TNF-α) and interleukins IL-6 and IL-1, whereas class II expression was unaffected. Intravenous application of the polysaccharides to test subjects immediately induced a fall in the number of PMN in the peripheral blood, indicating activation of adherence to endothelial cells. This decline was followed by a leukocytosis due to an increase in the number of PMN and a lesser increase of monocytes. The acute-phase C-reactive protein (CRP) was induced, probably due to activation of monocytes and macrophages to produce IL-6. Subsequent in-vivo studies found that the purified polysaccharides (EP) from *Echinacea purpurea* plant cell cultures enhanced mice phagocytes' activities thus protecting against systemic infections with *Listeria monocytogenes* and *Candida albicans* (Roesler et al. 1991a). They confirmed their hypothesis that macrophages (Mφ) from different organ origin could be activated to produce IL-1, TNFα and IL-6 to produce elevated amounts of reactive oxygen intermediates and to inhibit growth of *Candida albicans* in-vitro and that in-vivo the substances could induce increased proliferation of phagocytes in spleen and bone marrow and migration of granulocytes to the peripheral blood. In a subsequent study, EP was found effective in activating peritoneal macrophages isolated from animals after administration of cyclophosphamide (CP) or cyclosporin A (CsA) (Steinmüller et al. 1993). EP-treated macrophages exhibited increased production of tumour necrosis factor-alpha (TNF) and enhanced cytotoxicity against tumour target WEHI 164 as well as against the intracellular parasite

Leishmania enrietti. After a CP-mediated reduction of leukocytes in the peripheral blood, the polysaccharides induced an earlier influx of neutrophil granulocytes as compared to PBS (phosphate buffer saline)-treated controls. EP treatment of mice, immunosuppressed with CP or CsA, restored their resistance against lethal infections with the predominantly macrophage-dependent pathogen *Listeria monocytogenes* and predominantly granulocyte-dependent *Candida albicans*.

The results of studies suggested that oral gavage with *Echinacea* preparations containing optimal concentrations of cichoric acid, polysaccharides and alkylamides were potentially effective in stimulating an in-vivo, nonspecific immune response in normal male Sprague–Dawley rats (Goel et al. 2002a, b). Among the components the alkylamides at the dose level of 12 μg/kg body weight/day significantly increased the phagocytic activity as well as phagocytic index of the alveolar macrophages. The alveolar macrophages obtained from this alkylamide-administered group also produced significantly more TNF-α and nitric oxide after an in-vitro stimulation with LPS than any other active component or the control. The immunomodulatory effects of alkylamides appeared to be more pronounced in lungs than in spleen. Studies demonstrated *Echinacea purpurea* extracts to be potent activators of natural killer (NK) cells cytotoxicity (Gan et al. 2003). NK cytotoxicity was augmented 100 % at the concentration of 0.1 μg/ml of *Echinacea* in a short time (4-hour) assay. *Echinacea* augmented the frequency of NK target conjugates and activated the programming for lysis of NK cells. In another study, dietary administration of *E. purpurea* (14 days) to aging, normal mice or thyroxin injection revealed that *E. purpurea*, but not thyroxin, had the capacity to increase natural killer (NK) cell numbers, in aging mice, reflecting increased new NK cell production in their bone marrow generation site, leading to an increase in the absolute numbers of NK cells in the spleen, their primary destiny (Currier and Miller 2009). The *E. purpurea*-mediated increase in NK cell numbers was also paralleled by an increase in their antitumour, cytolytic functional capacity. In a recent study levamisole and *Echinacea purpurea* separately and together exerted a stimulant effect on the immune system in rats (Sadigh-Eteghad et al. 2011). The gamma globulin level, white blood cells, neutrophil and monocyte counts and phagocyte activity increased significantly in comparison with normal saline group during the study. In the group that received *Echinacea* and levamisole simultaneously, these effects were synergistically increased.

Male rats were orally treated with two different doses (30 and 100 mg/kg) of extract of *Echinacea purpurea* (EP), *Hypericum perforatum* (HP) and *Eleutherococcus senticosus* (ES) drugs for 3 or 15 days (Di Carlo et al. 2005). A 3-day treatment was not able to modify prolactin serum levels, whereas a 15-day treatment with EP and HP at the higher dose significantly inhibited prolactin production; prolactin had been reported to play an important role in immune system regulation. The treatment with ES was ineffective. They suggested that a possible mechanism for this effect could be that both *Echinacea purpurea* and *Hypericum perforatum* extracts displayed a direct dopaminergic activity, although an involvement of the GABAergic system could not be excluded.

Clinical Studies

Year-and-a-half old, dried *Echinacea* roots were found to retain cytokine-modulating capabilities in an in-vitro human older adult model of influenza vaccination (Senchina et al. 2006). In this model, peripheral blood mononuclear cells were collected from subjects 6 months postvaccination and stimulated in vitro with the two type A influenza viruses contained in the trivalent 2004–2005 vaccine with a 50 % alcohol tincture prepared from the roots of one of seven *Echinacea* species: *E. angustifolia*, *E. pallida*, *E. paradoxa*, *E. purpurea*, *E. sanguinea*, *E. simulata* and *E. tennesseensis*. Four species (*E. angustifolia*, *E. purpurea*, *E. simulata*, *E. tennesseensis*) augmented interleukin IL-10 production, diminished IL-2 production, and had no effect on interferon IFN-gamma production. Parnham (1996) reported squeezed sap of *E. purpurea*, widely used in self-medication, to be well tolerated on long-term oral administration with no adverse

event in healthy adults. In contrast, parenteral administration of the squeezed sap of *E. purpurea* (Echinacin®) may be associated with symptoms of immunostimulation (shivering, fever, muscle weakness). Echinacin® had little or no effect on lymphocyte responses but had been reported to cause transient lymphopenia in some patients with infections of various etiologies. In a double-blind placebo-controlled crossover design study with two treatment periods of 14 days involving 40 healthy male volunteers (age range 20–40 years), oral administration of *Echinacea purpurea* pressed juice for 1 and 2 weeks had only minor effects on two out of 12 lymphocyte subpopulations determined in the study (Schwarz et al. 2005). The small differences observed in the number of CD8+-T lymphocytes and natural killer cells were only of questionable physiological relevance.

Echinacea purpurea was found to have immunomodulatory property. Ritchie et al. (2011) found that a subgroup of volunteers who showed low pretreatment levels of the cytokines MCP-1, IL-8, IL-10 or IFN-γ ($n=8$) showed significant stimulation of these factors upon Echinaforce® treatment (*E. purpurea*) (30–49 % increases), whereas the levels in subjects with higher pretreatment levels remained unaffected. Volunteers who reported high stress levels ($n=7$) and more than 2 colds per year experienced a significant transient increase in interferon IFN-γ upon Echinaforce® treatment (>50 %). Subjects with low cortisol levels ($n=11$) showed significant downregulation of the acute-phase proteins interleukin IL1-β, IL-6, IL-12 and TNF-α by Echinaforce® (range, 13–25 %), while subjects with higher cortisol levels showed no such downregulation. The authors concluded that Echinaforce® thus regulated the production of chemokines and cytokines according to current immune status, such as responsiveness to exogenous stimuli, susceptibility to viral infection and exposure to stress.

Review Studies

In a review of immunomodulatory efficacy of preparations containing extracts of *Echinacea*, 26 controlled clinical trials (18 randomized, 11 double blind) were identified by Melchart et al. (1994). Their study indicated that preparations containing extracts of *Echinacea* could be efficacious immunomodulators. However, present evidence was still insufficient for clear therapeutic recommendations as to which preparation to use and which dose to employ for a specific indication.

Antiviral Activity

The roots of *E. purpurea* were found to induce a substance showing interferon-like activity (Skwarek et al. 1996). Biological activity studies showed that the protective titre (the largest dilution which protected cells by 50 % against virus infection) of the interferon-like materials was 1:6–1:15. *Echinacea purpurea* and *Panax ginseng* extracts at concentrations ≥0.1 or 10 μg/kg, respectively, significantly enhanced natural killer cell function against human erythromyeloblastoid leukaemia cell line, K562 cells in healthy subjects and chronic fatigue syndrome or acquired immunodeficiency syndrome (AIDS) patients (See et al. 1997). Similarly, the addition of either herb significantly increased antibody-dependent cellular cytotoxicity (ADCC) against human herpesvirus 6 infected H9 cells of peripheral blood mononuclear cells (PBMC) from all subject groups. Thus, extracts of *Echinacea purpurea* and *Panax ginseng* enhanced cellular immune function of PBMC both from normal individuals and patients with depressed cellular immunity. Extracts of 8 taxa of the genus *Echinacea* were found to have antiviral activity against herpes simplex (HSV) virus type I in vitro when exposed to visible and UVA light (Binns et al. 2002a). *n*-Hexane extracts of roots containing alkenes and amides were more active in general than ethyl acetate extracts containing caffeic acids. *Echinacea purpurea n*-hexane root extract (MIC = 0.12 mg/ml) was one of the most potent inhibitors of HSV.

Aqueous extracts of *E. purpurea* root contained a relatively potent activity against herpes simplex virus (HSV) and influenza virus (FV) but not against rhinovirus (RV) (Hudson et al. 2005).

These fractions had low amounts of caffeic acids and alkamides. The ethyl acetate fraction contained significant but weak activity against both HSV and FV and contained significant levels of cichoric acid. All aqueous fractions of *E. purpurea* aerial parts contained potent activity against herpes simplex virus and influenza virus (Vimalanathan et al. 2005). The antiviral activity could partly be attributed to polysaccharide and cichoric acid components; their individual contributions could not account for the total antiviral activity. Additionally, the ethanol- and ethyl acetate-soluble fractions from leaves and stem contained an uncharacterized but potent antiviral photosensitizer, which was absent from the flower extract. None of the fractions, however, contained anti-rhinovirus.

Studies showed that exposure of a cultured line of human bronchial epithelial cells to rhinovirus 14 infection stimulated the release of at least 31 cytokine-related molecules, including several important chemokines known to attract inflammatory cells. Most of these effects were reversed by simultaneous exposure to either of the two *Echinacea* extracts (Sharma et al. 2006a). Rhinovirus infection of BEAS-2B cell line resulted in a more dramatic increase in multiple transcription factors including proinflammatory factors examined, such as NFkB, AP-1, AP-2 and STATs 1–6 (Sharma et al. 2006b). However, when rhinovirus-infected cells were treated with either of the two *Echinacea* extracts, transcription factors levels were reduced to low levels, although the pattern of the reductions was different for the two extracts. The results could help to explain the beneficial effects of *Echinacea* consumption. All the viruses tested, rhinoviruses 1A and 14, influenza virus, respiratory syncytial virus, adenovirus types 3 and 11, and herpes simplex virus type 1, induced substantial secretion of IL-6 and IL-8 (CXCL8), in addition to several other chemokines, in a line of human bronchial epithelial cells (BEAS-2B) (Sharma et al. 2009). In every case, however, *Echinacea* (Echinaforce, an ethanol extract of herb and roots of *E. purpurea*) inhibited this induction. The *Echinacea* preparation also showed potent virucidal activity against viruses with membranes, indicating the multifunctional potential of the herb. The results supported the concept that certain *Echinacea* preparations could alleviate 'cold and flu' symptoms, and possibly other respiratory disorders, by inhibiting viral growth and the secretion of proinflammatory cytokines.

In a separate in-vitro study, human H1N1-type IV, highly pathogenic avian IV (HPAIV) of the H5- and H7-types, as well as swine origin IV (S-OIV, H1N1) were all inactivated in cell culture assays by the *Echinacea purpurea* (Echinaforce®, EF) preparation at concentrations ranging from the recommended dose for oral consumption to several orders of lower magnitude (Pleschka et al. 2009). Detailed studies with the H5N1 HPAIV strain indicated that direct contact between EF and virus was required, prior to infection, in order to obtain maximum inhibition in virus replication. Hemagglutination assays showed that the extract inhibited the receptor-binding activity of the virus, suggesting that the extract interferes with the viral entry into cells. Recent studies reported that Echinaforce® the standardized extract of *Echinacea purpurea* exhibited immunomodulation and broad antiviral effects against respiratory tract viruses (Schapowal 2012). Haemagglutinin and neuraminidase were blocked. In contrast to Oseltamivir no resistance was caused by Echinaforce®. A randomized, double-blind, placebo-controlled study over 4 months confirmed that Echinaforce® supported the immune resistance and acted directly against a series of viruses. He reported Echinaforce® to be efficacious and safe in respiratory tract infections for long-term and short-term prevention as well as for acute treatment.

An open-label, fixed-sequence study of 15 HIV-infected patients showed that co-administration of *E. purpurea* root extract containing capsules with etravirine (a nonnucleoside reverse transcriptase inhibitor of HIV) was safe and well tolerated in HIV-infected patients (Moltó et al. 2012). The geometric mean ratio for etravirine coadministered with *E. purpurea* relative to etravirine alone was 1.07 for the maximum concentration, 1.04 for the area under the concentration-time curve from 0 to 24 hours

and 1.04 for the concentration at the end of the dosing interval. The data suggested that no dose adjustment for etravirine was necessary.

Rhinoviruses, influenza viruses, herpes viruses and calcivrus were found to be susceptible to *E. purpurea* ethanol extract and aqueous extract; respiratory syncytial virus, coronavirus (mouse) were susceptible only to *E. purpurea* ethanol extract, and polio virus was not susceptible to both extracts (Hudson et al. 2005; Vimalanathan et al. 2005; Pleschka et al. 2009; Hudson 2012).

Echinacea and Respiratory Tract Infection

In-Vitro Studies

A standardized *Echinacea* extract (Echinaforce) was found to have dual action against several important respiratory bacteria, a killing effect and an antiinflammatory effect (Sharma et al. 2010). It readily inactivated *Streptococcus pyogenes*, often associated with sore throat and more severe pulmonary infections, *Haemophilus influenzae* and *Legionella pneumophila*, and reversed their proinflammatory responses. *Staphylococcus aureus* (methicillin-resistant and sensitive strains) and *Mycobacterium smegmatis* were less sensitive to the bactericidal effects of *Echinacea* however, but their proinflammatory responses were still completely reversed. In contrast some other pathogens tested, including *Candida albicans*, were relatively resistant. The results supported the concept of using a standardized *Echinacea* preparation to control symptoms associated with bacterial respiratory infections.

The alkylamides undeca-2*Z*,4*E*-diene-8,10-diynic acid isobutylamide, dodeca-2E,4*E*,8*Z*, 10*E*/*Z*-tetraenoic acid isobutylamide, dodeca-2*E*,4*E*-dienoic acid isobutylamide, and undeca-2*E*-ene-8,10-diynoic acid isobutylamide from *E. purpurea* suppressed production of TNF-α and PGE2 from RAW 264.7 macrophage-like cells infected with the H1N1 influenza A strain PR/8/34 (Cech et al. 2010). Dodeca-2*E*,4*E*-dienoic acid isobutylamide was especially effective at inhibiting production of these mediators and also strongly inhibited production of G-CSF, CCL2/MCP-1, CCL3/MIP-1α and CCL5/RANTES. In contrast, the ethanol extracts (75 %), prepared from *E. purpurea* dormant roots, displayed a range of effects from suppression to stimulation of mediator production. Analysis of the extracts revealed slight variations in concentration of alkylamides, caftaric acid and cichoric acid, but the activity of the extracts did not strongly correlate with concentrations of these compounds. The in-vitro studies suggested *E. purpurea* extracts to have the potential for use in alleviating the symptoms and pathology associated with infections with influenza A.

Clinical/Human Studies

Some herbal preparations, including *Echinacea purpurea*, had been reported to improve cold symptoms in adults but ineffective in children (Fashner et al. 2012). Randolph et al. (2003) found that the overall gene expression pattern at 48 hours to 12 days after taking *Echinacea* product for cold and flu by six healthy nonsmoking subjects (18–65 years of age)was consistent with an antiinflammatory response. The expression of interleukin-1 beta, tumour necrosis factor-alpha, intracellular adhesion molecule and interleukin-8 was modestly decreased up through day 5, returning to baseline by day 12. The expression of interferon-alpha steadily rose through day 12, consistent with an antiviral response. The data presented a gene expression response pattern that was consistent with *Echinacea*'s reported ability to reduce both the duration and intensity of cold and flu symptoms.

Mixed results have been obtained in clinical studies on the efficacy of *E. purpurea* in combating respiratory tract infections. In a randomized, double-blind, placebo-controlled study, 246 of 559 recruited healthy, adult volunteers contracted a common cold and took 3 times daily 2 tablets of either Echinaforce® (*Echinacea purpurea* preparation from 95 % herba and 5 % radix), *Echinacea purpurea* concentrate (same preparation at 7 times higher concentration), special *Echinacea purpurea* radix preparation (totally different from that of Echinaforce®) or placebo until they felt healthy again but not longer than 7 days

(Brinkeborn et al. 1999). It was found that Echinaforce® and its concentrated preparation were significantly more effective than the special *Echinacea* extract or placebo. All treatments were well tolerated. Among the *Echinacea* groups the frequency of adverse events was not significantly higher than in the placebo group. They concluded that *Echinacea* concentrate as well as Echinaforce® represented a low-risk and effective alternative to the standard symptomatic medicines in the acute treatment of common cold.

In a randomized, double-blind, placebo-controlled trial, 282 subjects aged 18–65 years, a total of 128 subjects contracted a common cold (59 echinacea, 69 placebo) (Goel et al. 2004). The total daily symptom scores were found to be 23.1 % lower in the echinacea group than in placebo in those who followed all elements of the study protocol. Throughout the treatment period, the response rate to treatments was greater in the echinacea group. A few adverse event profiles were observed in both groups. The researchers concluded that early intervention with a standardized formulation of echinacea resulted in reduced symptom severity in subjects with naturally acquired upper respiratory tract infection. In a clinical study, Echinilin (a formulation prepared from freshly harvested *Echinacea purpurea* plants and standardized on the basis of three known active components: alkamides, cichoric acid and polysaccharides) or placebo was administered to volunteers at the onset of their cold for a period of 7 days, with eight doses (5 ml/dose) on day 1 and three doses on subsequent days (Goel et al. 2005). The decrease in total daily symptomatic score was more evident in the echinacea group than in the placebo group. These effects of echinacea were associated with a significant and sustained increase in the number of circulating total white blood cells, monocytes, neutrophils and natural killer cells. In the later part of the cold, the echinacea treatment suppressed the cold-related increase in superoxide production by the neutrophils. The results suggested that Echinilin, by enhancing the nonspecific immune response and eliciting free radical scavenging properties, may have led to a faster resolution of the cold symptoms.

Jawad et al. (2012) conducted a 4-month randomized, double-blind, placebo-controlled trial to investigate the safety (risk) and efficacy (benefit) of *Echinacea purpurea* (95 % herba and 5 % root) extract in the prevention of common cold episodes with 755 healthy subjects. *Echinacea* extract found to reduce the total number of cold episodes, cumulated episode days within the group, and painkiller-medicated episodes. *Echinacea* inhibited virally confirmed colds and especially prevented enveloped virus infections. *Echinacea* showed maximal effects on recurrent infections, and preventive effects increased with therapy compliance and adherence to the protocol. A total of 293 adverse events occurred with echinacea and 306 with placebo treatment. Nine and 10 % of participants experienced adverse events, which were at least possibly related to the study drug (adverse drug reactions). Thus, the safety of *Echinacea* was noninferior to placebo. The study concluded that compliant prophylactic intake of *E. purpurea* over a 4-month period appeared to provide a positive risk to benefit ratio

In a randomized, placebo-controlled, double-blind study, treatment with fluid extract of *Echinacea purpurea* (widely used for the prevention and treatment of colds and respiratory infections), did not significantly decrease the incidence, duration or severity of colds and respiratory infections compared to placebo (Grimm and Müller 1999). During the 8-week treatment period, 35 (65 %) of 54 patients in the echinacea group and 40 (74 %) of 54 patients in the placebo group had at least one cold or respiratory infection. The average number of colds and respiratory infections per patient was 0.78 in the echinacea group, and 0.93 in the placebo group. There were no significant differences between treatment groups in the number of infections in each category of severity. Side effects were observed in 11 patients (20 %) of the echinacea group and in seven patients (13 %) of the placebo group. In a randomized, double-blind placebo-controlled trial of 175 adults travelling back from Australia to America, Europe or Africa for a period of 1–5 weeks on commercial flights via

economy class, supplementation with standardized *Echinacea* tablets, taken before and during travel, may have preventive effects against the development of respiratory symptoms during travel involving long-haul flights (Tiralongo et al. 2012). In another study, 128 patients were enrolled within 24 hours of cold symptom onset in a randomized, double-blind, placebo-controlled design wherein patients received either 100 mg of *E. purpurea* (freeze-dried pressed juice from the aerial portion of the plant) or a lactose placebo 3 times daily until cold symptoms were relieved or until the end of 14 days, whichever came first (Yale and Liu 2004). No statistically significant difference was observed between treatment groups for either total symptom scores or mean individual symptom scores. The time to resolution of symptoms was not statistically different. The efficacy of *E. purpurea* in reducing common cold was not confirmed.

In a multicenter randomized placebo controlled trial, *Echinacea purpurea* was found ineffective for treating upper respiratory tract infections in children aged 2–11 years (Mainous 2004). There was no significant difference in duration or severity of symptoms with *Echinacea purpurea* compared with placebo in children with upper respiratory tract infection. In another randomized, double-blind, placebo-controlled trial of 407 children aged 2–11 years including 337 upper respiratory tract infections (URIs) treated with echinacea and 370 with placebo, *Echinacea purpurea* was found not effective in treating URI symptoms in these children, and its use was associated with an increased risk of rash (Taylor et al. 2003).

Review Studies

Scoop et al. (2006) conducted a meta-analysis on the therapeutic effectiveness of *Echinacea* in the treatment and the prevention of colds, wherein 3 suitable studies were selected for pooling of data, and 231 were excluded from the analysis because they related to studies of spontaneous common colds. The meta-analysis suggested that standardized extracts of *Echinacea* were effective in the prevention of symptoms of the common cold after clinical inoculation, compared with placebo. However, more prospective, appropriately structured clinical studies were required to confirm. Although *Echinacea* preparations tested in clinical trials differed greatly, there was some evidence that preparations based on the aerial parts of *Echinacea purpurea* might be effective for the early treatment of colds in adults but results were not fully consistent (Linde et al. 2006). Beneficial effects of other *Echinacea* preparations and for preventative purposes might exist but had not been shown in independently replicated, rigorous, randomized trials. A meta-analysis of 14 studies provided published evidence supporting *Echinacea*'s benefit in decreasing the incidence and duration of the common cold (Shah et al. 2007). Woelkart et al. (2008) stated that *Echinacea* preparations were more effective than no treatment, more effective than placebo or similarly effective to other treatments in the prevention and the treatment of the common cold. In a more recent review on the efficacy of *Echinacea* in cold prevention, Hart and Dey (2009) reiterated that in view of the residual uncertainty and the gaps between the evidence and the ways that this was summarized on webpages, it may prove difficult for consumers to assimilate the evidence. As well as undertaking high-quality trials in complementary medicine, there was a need to ensure precision in the reporting of uncertainty.

Antimicrobial Activity

Echinacea (including *E. purpurea*) were found to have phototoxic antimicrobial activity against fungi, including clinically relevant pathogenic fungi. Results showed that hexane extracts of *Echinacea* variably inhibited growth of yeast strains of *Saccharomyces cerevisiae*, *Candida shehata*, *C. kefyr*, *C. albicans*, *C. steatulytica* and *C. tropicalis* under near UV irradiation (phototoxicity) and to a lower extent without irradiation (conventional antifungal activity) (Binns et al. 2000). The presence of polyacetylenes and alkylamides in extracts of different organs was confirmed in *Echinacea purpurea* and was related to phototoxic activity. Significant phototoxicity was demonstrated by pure

trideca-1-ene-3,5,7,9,10-pentayne from *E. purpurea* roots, while only minor phototoxicity was induced by the other two *E. purpurea* acetylenic compounds undeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide and dodeca-2*E*,4*E*,8*Z*,10*E*/*Z*-tetraenoic acid isobutylamide. Phototoxic activity of *Echinacea* spp. was primarily attributed to the ketoalkenes and ketoalkynes abundantly present in the roots. Root extracts of the eight *Echinacea* species including *E. purpurea* showed antifungal activity against most of the pathogenic fungi (*Trichophyton tonsurans*, *T. mentagrophytes*, *Microsporum gypseum*, *Pseudallescheria boydii*, *Cryptococcus neoformans* and two *Candida albicans* isolates) (Merali et al. 2003). Recent studies on *Echinacea purpurea* had revealed that certain standardized preparations contain potent and selective antiviral and antimicrobial activities (Hudson 2012). In addition, they displayed multiple immunomodulatory activities, comprising stimulation of certain immune functions such as phagocytic activity of macrophages and suppression of the proinflammatory responses of epithelial cells to viruses and bacteria, which are manifested as alterations in secretion of various cytokines and chemokines. *E. purpurea* dried aerial part ethanol extract showed a considerable growth inhibition on *Candida albicans* and *Saccharomyces cerevisiae*, while no growth inhibition zones were observed for *Aspergillus niger* (Stanisavljević et al. 2009). In-vitro studies showed a standardized preparation of *Echinacea purpurea* (Echinaforce®) could provide a safe twofold benefit to acne individuals by inhibiting proliferation of the Gram-positive bacterium *Propionibacterium acnes* and reversing the bacterial-induced inflammation (Sharma et al. 2011). *E. purpurea* completely reversed the bacterial increase in secretion of substantial amounts of several proinflammatory cytokines, including IL-6 and IL-8 (CXCL8), and brought the cytokine levels back to normal.

Antiinflammatory Activity

Root extracts of the three commercial species of *Echinacea* (*E. purpurea*, *E. pallida* var. *angustifolia*, *E. pallida* var. *pallida*) inhibited the 5-lipoxygenase (5-LOX) enzyme (Merali et al. 2003). The results show that *Echinacea* spp. had significant antiinflammatory activity. Alcohol extracts of *Echinacea angustifolia*, *Echinacea pallida* and *Echinacea purpurea* significantly inhibited NO production by lipopolysaccharide (LPS)-activated the RAW 264.7 macrophage cell line (Zhai et al. 2009). Arginase activity of RAW 264.7 cells stimulated with 8-bromo-cAMP was significantly increased by alcohol extracts of all three *Echinacea* species. The polar fraction containing caffeic acid derivatives enhanced arginase activity, while the lipophilic fraction containing alkamides exhibited a potential of inhibiting NO production and iNOS expression. The results suggested that the antiinflammatory activity of *Echinacea* might be due to multiple active metabolites, working together to switch macrophage activation from classical activation towards alternative activation.

At 100 g/ml, several *E. purpurea* alkamides, isolated from *E. purpurea* roots, inhibited cyclooxygenase COX-I and COX-II enzymes in the range of 36–60 % and 15–46 %, respectively, as compared to controls (Clifford et al. 2002). Chicca et al. (2009) demonstrated that ethanol *E. purpurea* radix and herba extracts elicited synergistic pharmacological effects on the endocannabinoid system in vitro. Supra-additive action of *N*-alkylamide combinations was observed at the level of intracellular calcium release as a function of cannabinoid receptor type-2 (CB_2) activation. Likewise, synergism of the radix and herba tinctures was observed in LPS-stimulated cytokine expression from human PBMCs. While the expression of the antiinflammatory cytokine IL-10 was significantly superstimulated, the expression of the proinflammatory TNF-α protein was inhibited more strongly upon combination of the extracts. They concluded that *N*-alkylamides in the extracts acted in concert to exert pleiotropic effects modulating the endocannabinoid system by simultaneously targeting the CB_2 receptor, endocannabinoid transport and degradation. Cannabinoid type-1 (CB_1) and CB_2 receptors belong to the family of G protein-coupled receptors and are the primary targets of

the endogenous cannabinoids *N*-arachidonoyl ethanolamine and 2-arachidonoyl glycerol (Gertsch et al. 2006). CB_2 receptors are believed to play an important role in distinct pathophysiological processes, including metabolic dysregulation, inflammation, pain and bone loss.

A mitogen-induced murine skin inflammation study suggested that alkamides were the active antiinflammatory components present in *Echinacea* plants (Hou et al. 2010). Mixed alkamides and the major component, dodeca-2*E*,4*E*,8*Z*,10*Z*(*E*)-tetraenoic acid isobutylamides (8/9), were then isolated from *E. purpurea* root extracts for further bioactivity elucidation. In macrophages, the alkamides significantly inhibited cyclooxygenase 2 (COX-2) activity and the lipopolysaccharide-induced expression of COX-2, inducible nitric oxide synthase and specific cytokines or chemokines [i.e., TNF-α, interleukin (IL)-1α, IL-6, MCP-1, MIP-1β] but elevated heme oxygenase-1 protein expression. Cichoric acid, however, exhibited little or no effect. In another study, three alkamides and nitidanin diisovalerianate were identified, together with 14 known alkamides and one sesquiterpene from the roots of *Echinacea purpurea* (Hohmann et al. 2011). Their interaction with G-protein-coupled cannabinoid receptors was examined on rat brain membrane preparations. Both partial and inverse agonist compounds for cannabinoid (CB1) receptors were identified among the metabolites, characterized by weak to moderate interactions with the G-protein signalling mechanisms. Upon co-administration with arachidonyl-2′-chloroethylamide, a number of them proved capable of inhibiting the stimulation of the pure agonist, thereby demonstrating cannabinoid receptor antagonist properties. In an earlier study, alkylamides, anandamide and SR144528 were found to potently inhibit lipopolysaccharide-induced inflammation in human whole blood and exerted modulatory effects on cytokine expression, but these effects were not exclusively related to CB_2 binding (Raduner et al. 2006). The alkylamides dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide (A1) and dodeca-2*E*,4*E*-dienoic acid isobutylamide (A2) bound to the CB_2 receptor more strongly than the endogenous cannabinoids. A1, A2, anandamide, the CB2 antagonist SR144528 ($Ki < 10$ nM), and also the non-CB_2-binding alkylamide undeca-2*E*-ene,8,10-diynoic acid isobutylamide all significantly inhibited lipopolysaccharide-induced tumour necrosis factor alpha, IL-1beta and IL-12p70 expression (5–500 nM) in a CB2-independent manner.

Anticancer Activity

Animal studies found that dietary administration with *E. purpurea* preparations significantly decreased prostate weight of rats and increased lymphocyte numbers after 8 weeks (Skaudickas et al. 2003). *Echinacea purpurea* root hexane extract reduced cell viability of human pancreatic cancer MIA PaCa-2 and colon cancer COLO320 cell lines in a concentration- and time-dependent in vitro (Chicca et al. 2007). *E. purpurea* flower extract and cichoric acid significantly inhibited proliferation in a dose- and time-dependent manner human colon cancer cells Caco-2 and HCT-116 (Tsai et al. 2012). Cichoric acid treatment decreased telomerase activity in HCT-116 cells. Further, cichoric acid effectively induced apoptosis in colon cancer cells, which were characterized by DNA fragmentation, activation of caspase-9, cleavage of PARP and downregulation of β-catenin.

Anti-teratogenic Activity

Studies found that *E. purpurea* could stimulate immune system of mice more than levamisole and had better prophylactic effect against the teratogenic effect of phenytoin as evidenced by lower incidence of phenytoin-induced cleft palate, but it was not significant (Mahabady et al. 2006). Cleft palate incidence was 16, 5.3 and 3.2 % in fetuses of mice that received only phenytoin, phenytoin with levamisole, and phenytoin with *Echinacea* extract, respectively. Mean weight and length of fetuses of animals that received levamisole and *Echinacea* extract were significantly greater than those that received only phenytoin.

Hepatoprotective Activity

Studies showed that dodeca-2*E*,4*E*,8*Z*,10*Z*(*E*)-tetraenoic acid isobutylamides (Alk-8/9), isolated from *Echinacea purpurea* roots, dose-dependently induced heme oxygenase (HO)-1 protein expression in lipopolysaccharide-stimulated murine macrophages that was likely regulated by the JNK-mediated pathway through increasing SAPK/JNK phosphorylation, c-Jun protein expression, and phosphorylation and transcription factor AP-1 binding consensus DNA activity (Hou et al. 2011). Further, Alk-8/9 markedly induced c-Jun and HO-1 protein expression and suppressed serum aminotransferase activities, TNF-α expression, and hepatocyte damage in liver tissues of lipopolysaccharide/D-galactosamine-treated mice. The results suggested a potential application of *Echinacea*, a top-selling herbal supplement, as a hepatoprotective agent.

Antimutagenic Activity

The 50 % ethanol flower extract did not show toxicity and mutagenicity towards *Salmonella typhimurium* TA98 and TA100 with or without S9 mix (Tsai et al. 2011). The ethanol extract at 0.25–5 mg/plate exhibited a dose-dependent inhibitory effect against the mutagenicity of 2-aminoanthracene. They concluded that freeze-dried *E. purpurea* flower ethanol extract exhibited good antioxidant and antimutagenic activities.

Radioprotective Activity

E. purpurea administration significantly ameliorated the detrimental reduction effects of gamma rays on peripheral blood haemoglobin and the levels of red blood cells, differential white blood cells and bone marrow cells and antioxidant activity in mice (Abouelella et al. 2007). The radioprotection effectiveness was similar to the radio recovery curativeness in comparison to the control group in most of the tested parameters. The radioprotection efficiency was greater than the radio recovery in haemoglobin level during the first 2 weeks, in lymphoid cell count and thiobarbituric acid-reactive substances (TBARs) level at the fourth week and in superoxide dismutase (SOD) activity during the first 2 weeks, as compared to the levels of these parameters in the control group.

Actoprotective/Adaptogenic Activity

Purple coneflower tincture was found to improve both the work capacity and the endurance characteristics of white male mice in the conventional forced swim test (Kurkin et al. 2006). The actoprotective effect was attributed to a phenylpropanoid, echinacoside.

In a double-blind design placebo-controlled and self-administered study of 24 men (24.9 ± 4.2 years) for 4 weeks, oral *Echinacea* supplementation resulted in significant increases in erythropoietin (EPO), VO2max (maximal oxygen uptake) and running economy compared to placebo (Whitehead et al. 2012).

Anti-Tyrosinase Activity

Cichoric acid extracted from *E. purpurea* flowers was found to have significant tyrosinase inhibition activity in a broad range of concentration (10–20 mg/ml) (Jiang et al. 2012).

Trypanocidal Activity

Various *Echinacea* extracts could inhibit the proliferation of three species of trypanosomatids: *Leishmania donovani*, *Leishmania major* and *Trypanosoma brucei* (Canlas et al. 2010). The standardized ethanol extract of *E. purpurea* (L.) Moench reversed the proinflammatory activity (production of cytokines IL-6 and IL-8) of *Leishmania donovani* in human bronchial epithelial cells and in human skin fibroblasts.

Larvicidal Activity

Several alkamides isolated from *E. purpurea* roots exhibited mosquitocidal activity causing 100 % mortality of *Aedes aegypti* larvae (Clifford et al. 2002).

Herb–Drug/Herb–Herb Interaction Activity

Studies showed *Echinacea* alkylamides were degraded in a time- and NADPH-dependent manner in microsomal fractions suggesting they were metabolized by cytochrome P450 (P450) enzymes in human liver (Matthias et al. 2005b). There was a difference in the susceptibility of 2-ene and 2,4-diene pure synthetic alkylamides to microsomal degradation with (2*E*)-*N*-*isobutylundeca*-2-ene-8,10-diynamide metabolized to only a tenth the extent of (2*E*,4*E*,8*Z*,10*Z*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide under identical incubation conditions. Alkylamide metabolites were detected and found to be the predicted epoxidation, hydroxylation and dealkylation products. These findings suggested that *Echinacea* may affect the P450-mediated metabolism of other concurrently ingested pharmaceuticals.

Cytochrome P450 enzymes (P450s) appeared to be the principal system responsible for the metabolism of *Echinacea* components and most of the main hepatic and some extrahepatic isoforms appeared to be involved (Toselli et al. 2009). Epoxide formation, N-dealkylation and hydroxylation were reported as the main metabolic pathways mediated by P450s and interactions with P450s determined the circulating concentrations and duration of action of these phytochemicals as well as any potential interactions with other chemicals. In-vivo studies in rats showed that *E. purpurea* may interact cytochrome P450 enzymes and induce significant herb–drug interactions which may alter pharmacotherapy (Mrozikiewicz, et al. 2010). The *Echinacea* ethanol extract could potently inhibit the expression of CYP3A1 (41 %) and CYP3A2 (25 %) mRNAs. A weaker inhibitory effect was observed for CYP2D2 by 15 % and CYP2C6 by 18 % after long application of the *Echinacea* ethanol extract. CYP2D2 and CYP2C6 activities were also inhibited by extract but in a lesser degree than CYP3A1 activity. The findings suggested that *Echinacea* extract may influence the P450-mediated metabolism of different drugs and may initiate chemical carcinogenesis by activation of some compounds to their carcinogenic metabolites.

The multiherbal product Sambucus Force containing *Echinacea purpurea* and *Sambucus nigra* as its main constituents was found to inhibit CYP3A4 activity with IC_{50} value of 1,192 (1,091–1,302) μg/ml (Schrøder-Aasen et al. 2012). The inhibitory potency appeared exclusively to be exerted by *E. purpurea*, implicating an insignificant inhibition by *S. nigra*. *Echinacea purpurea* acted differently in the multiherbal product, which showed a dual inhibition profile with both an uncompetitive (substrate-dependent) inhibition and a time-dependent (substrate-independent) inhibitory mechanism. These mechanistic differences were suggested to be caused by herb–herb interactions in the multiherbal product.

Allergy Problems

A woman with atopy experienced anaphylaxis after taking a commercial extract of *Echinacea*; hypersensitivity was confirmed by skin prick and RAST testing (Mullins 1998). Regular ingestion of *Echinacea* by up to 5 % of surveyed patients with atopy, combined with detection of *Echinacea*-binding IgE in atopic subjects (19 % by skin testing; 20 % with moderate to strong reactivity by RAST testing), indicated the possibility of severe allergic reactions, even with first-time use, due to cross-reactivity with other structurally similar allergens.

Toxicity and Safety Studies

According to the review of Huntley et al. (2005), despite the voluminous data availability on the efficacy of *Echinacea* (*Echinacea* spp. namely

E. angustifolia, *E. pallida* and *E. purpurea*), safety issues and the monitoring of adverse events had not been focused on. Short-term use of *Echinacea* was reported to be associated with a relatively good safety profile, with a slight risk of transient, reversible, adverse events. The major adverse events reported with *Echinacea* products are allergic reactions, ranging from contact dermatitis to anaphylaxis (Mahady et al. 2001). Patients with an allergy to plants in the daisy family (Asteraceae) should be instructed not to use products containing *Echinacea.* The use of *Echinacea* products during pregnancy and lactation would appear to be ill-advised in light of the paucity of data in this area. According to the review by Perri et al. (2006) there was good scientific evidence from a prospective cohort study that oral consumption of *Echinacea* during the first trimester did not increase the risk for major malformations. Low-level evidence based on expert opinion showed oral consumption of *Echinacea* in recommended doses to be safe for use during pregnancy and lactation. *Echinacea* was non-teratogenic when used during pregnancy. However more quality studies were needed to determine its safety.

After 4 weeks of oral administration of expressed juice of *E. purpurea* in doses amounting to many times, the human therapeutic dose laboratory tests and necropsy findings presented no evidence of any toxic effects in rats (Mengs et al. 1991). Tests for mutagenicity carried out in microorganisms and mammalian cells in-vitro and in mice all gave negative results. In an in-vitro carcinogenicity study, *E. purpurea* did not produce malignant transformation in hamster embryo cells.

Pharmacokinetic Studies

Studies showed that alkylamides from *Echinacea* species can readily be transported across Caco-2 monolayers indicating that they can be transported across the intestinal barrier and may contribute to the in-vivo effects of *Echinacea preparations* (Jager et al. 2002; Matthias et al. 2004) but not caffeic acid conjugates (Matthias et al. 2004).

Studies of nine healthy volunteers found that alkamides were rapidly absorbed and were measurable in plasma 20 minutes after *Echinacea* (*E. purpurea* and *E. angustifolia*) tablet ingestion after standard high-fat breakfast and remained detectable for up to 12 hours (Matthias et al. 2005a). The maximal concentrations for the sum of alkamides in human plasma were reached within 2.3 hours post ingestion and averaged 336 ng eq/ml plasma. No obvious differences were observed in the pharmacokinetics of individual or total alkamides. Caffeic acid conjugates could not be identified in any plasma sample at any time after tablet ingestion.

Alkamides dodeca-2*E*,4*E*,8*Z*,10*E*/*Z*-*tetraenoic* acid isobutylamides were found to be rapidly absorbed and measurable in plasma 10 minutes after administration of 0.21 and 0.9 mg *Echinacea purpurea* phytotherapeutic lozenges and remained detectable for 3 hours for the 0.21 mg lozenges and >3 hours for the 0.9 mg lozenges; 0.07 mg lozenges were measurable 20 minutes after administration and remained detectable for only 2 hours after the administration (Guiotto et al. 2008). A significant dose-independent downregulation of the proinflammatory cytokines IL-12p70, IL-8, IL-6, IL-10 and TNF was observed after 24 hours. The results demonstrated that pharmacokinetics of dodeca-2*E*,4*E*,8*Z*,10*E*/*Z* -tetraenoic isobutylamides were linear and that absorption was very rapid ($t_{1/2}$=6 minutes) with apparently no lag time, thus indicating the possibility that a fraction of the drug was absorbed through the oral mucosa. In an earlier study, after oral ingestion, the arithmetic mean *C*(max) of dodeca-2*E*,4*E*,8*Z*,10*E*/*Z* -tetraenoic acid isobutylamides absorbed for *Echinacea purpurea* tincture was 0.40 ng/ml serum with 30 minutes *t*(max), while for the *Echinacea* tablet the *t*(max) of tablets was 45 minutes with a *C*(max) of 0.12 ng/ml (Woelkart et al. 2006). Both *E. purpurea* preparations led to the same effects on the immune system according to the concentration of proinflammatory cytokines TNF-alpha and IL-8. Twenty-three hours after oral application a significant downregulation of TNF-alpha and IL-8 in LPS pre-stimulated whole blood was found. However, no significant changes in the concentration of IL-6 were observed.

The alkylamide, undeca-2-ene-8,10-diynoic acid isobutylamide, a constituent of *E. purpurea* (Goel et al. 2011) and dodeca-2*E*,4*E*,8*Z*,10*E*/*Z* - tetraenoic acid isobutylamides (DTAI), the most abundant alkylamide in *E. purpurea*, were successfully quantified in the patients plasma after ingestion of *E. purpurea* extract by LC–MS/MS assay (Goey et al. 2012).

Traditional Medicinal Uses

Echinacea spp. are native to North America and were traditionally used by the Indian tribes for a variety of ailments, including mouth sores, colds and snakebites (Kindscher 1989). Traditional uses of *E. purpurea*, *E. angustifolia* and *E. pallida* include the following: respiratory infections, colds and flu, bronchitis, strep throat, toothache; urinary tract infections, herpes sores and gonorrhoea; skin disorders, staph infections, cold sores, ulcers, wounds, burns, insect bites, eczema, allergies and others; and rheumatoid arthritis (Hudson 2012).

Other Uses

Dried *Echinacea purpurea* (EP) can be used as a feed additive to improve the meat quality and oxidative status in Arbor Acres broilers (Lee et al. 2013). The addition of 0.5 and 1.0 % EP significantly increased water-holding capacity and decreased storage loss of breast and thigh fillets at 35 days old. Results for Trolox equivalent antioxidant capacity, catalase and superoxide dismutase were significantly higher for the 0.5, 1.0 and 2.0 % EP supplemental groups than control group in serum. Liver and spleen tissues results showed that the antioxidative enzyme activities were higher with EP powder at 35 days of age.

Studies showed *E. purpurea* to have potential as immunostimulatory feed additive against Newcastle disease virus in laying hens and in fattening pigs by intermittent application (Böhmer et al. 2009). The performance of laying hens was not impacted with feed additive application of pressed *E. purpurea* (aerial parts) juice in ethanol or fermented juice. Significant changes were found in the number of lymphocytes, phagocytosis rate and Newcastle Disease Virus (NDV) antibody titre. The number of lymphocytes was highest in the group receiving ethanol juice for five consecutive days. Phagocytosis was reduced in both groups provided with ethanol juice (2 or 5 days). Highest NDV antibody titres were seen in the groups receiving fermented juice for 2 days. Additionally, phagocytosis of granulocytes was determined in fattening pigs (80–100 kg) after 5 days of *Echinacea* application with ethanol or fermented juice. A significant increase was found with both *Echinacea* formulations. The number of lymphocytes was also increased significantly in the groups provided with *Echinacea*.

Comments

Purple coneflower is easily propagated either from seeds or vegetatively by division, root cuttings and basal cuttings. It blooms throughout spring and summer and is pollinated by butterflies and bees.

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Helianthus annuus

Scientific Name

***Helianthus annuus* L.**

Synonyms

Helianthus annuus subsp. *jaegeri* (Heiser) Heiser, *Helianthus annuus* subsp. *lenticularis* (Douglas ex Lindley) Cockerell, *Helianthus annuus* var. *lenticularis* (Douglas ex Lindley) Steyermark, *Helianthus annuus* var. *macrocarpus* (DC.) Cockerell, *Helianthus annuus* subsp. *texanus* Heiser, *Helianthus annuus* var. *texanus* (Heiser) Shinners, *Helianthus aridus* Rydberg, *Helianthus cultus* Ventsl., *Helianthus erythrocarpus* Bartl., *Helianthus indicus* L., *Helianthus jaegeri* Heiser, *Helianthus lenticularis* Douglas, *Helianthus lenticularis* Douglas ex Lindley, *Helianthus macrocarpus* DC., *Helianthus macrocarpus* DC. & A.DC., *Helianthus multiflorus* Hook., *Helianthus ovatus* Lehm., *Helianthus platycephalus* Cass., *Helianthus pumilus* Pers., *Helianthus tubaeformis* Nutt.

Family

Asteraceae

Common/English Names

Annual Sunflower, Common Sunflower, Hopi Sunflower, Sunflower

Vernacular Names

Afrikaans: Sonneblom
Albanian: Lule Dielli
Arabic: Abbâd Esh Shams, Azriyun, Azaryun
Brazil: Girassol
Catalan: Corona De Rei, Corona De Reina, Girasol, Heliantem, Mira-Sol, Sol Coronat
Chinese: Kui Hua, Xiang Mu Kui, Zhang Ju, Xiang Ri Kui
Corsican: Girasole
Croatian: Džirasol, Jednogodišnji Suncokret, Krumpir Morski, Ljubomir, Suncokret
Czech: Slunečnice Roční
Danish: Almindelig Solsikke, Solsikke
Dutch: Engelse Zonnebloem, Jaarlijkse Zonnebloem, Zonnebloem
Esperanto: Sunflora
Estonian: Harilik Päevalill, Päevalill
Finnish: Auringonkukka, Auringon Ruusu, Isoauringonkukka
French: Grand Soleil, Hélianthe Annuel, Soleil, Tournesol
German: Echte Sonnenblume, Gewöhnliche Sonnenblume, Sonnenblume
Hawaiian: Nānālā, Pua Nānālā
Hungarian: Napraforgó
India: Beliphul (Assamese), Surajmukhi (Bengali), Hurduja, Hurhuja, Suraj-Mukhi, Surajmukhi, Surij-Makkhi, Surjmukhi, Surij-Makkhi, Surij-Mukkhi (Hindi), Adityabhakti, Arka Pushpa, Aoorya Kaanthi Hoo, Hothu Thirugu Hoo Surya-Kanti-Bija, Suryakanti, Surya Kanthi Hoovu, (Kannada), Suryakanti, Suryappu,

DOI 10.1007/978-94-007-7395-0_24,

Suryya-Kantam-Vitta (Malayalam), Numitlei (Manipuri), Brahmoka, Soorajmaka, Soorya Kamala, Sooryaphula, Ssurajmaka, Suryaphula, Surya-Phul, Urya-Kamal (Marathi), Nihawipar (Mizoram), Adityabhakta, Arkakantha, Sauvarcala, Suriamukhi, Suryamukhi, Suryavarta, Suvarcala, Suvarchala (Sanskrit), Aditya-Bhakti-Chettu, Arukkopalam, Atavan, Atittiyaparani, Attikankam, Curiya Kanti, Curiyakantam, Curiyakanti, Curiyakantacceti, Cutu, Kanti, Kokamantukacceti, Kokapantakam, Kokapantukam, Kolluppanitacceti, Kolluppanitam, Kotaikantitacceti, Kotaikkantitam, Muntakanayakacceti, Muntakanayakam, Nayirutirumpi, Nayiruvananki, Nerankatti, Nerrankatticceti, Nontakiri, Nontakiricceti, Panippakaicceti, Polututirumpi, Polututirumpicceti, Polutuvananki, Putavakanti, Putavakanticceti, Raviputpam, Shuriya-Kanti-Virai, Suryakanti, Suriyakanthi, Suryakanthi, Takanopalam, Tanu, Tanuvankam, Tinakaracceti, Tinakaran, Tivakaram, Uroci, Urocicceti, Vacciravalli, Vinmani, Vinmanicceti (Tamil), Aadithya Bhakti Chettu, Aditya-Bhakti, Aditya-Bhakti-Chettu, Adityabhaktichettu, Podduthirugudu Chettu, Poddatringudachettu, Poddutiruguduchettu, Proddutiruguduchettu, Proddathringudda Chettu, Sooryakaanthamu Surya-Kanti-Vittulu, Surya Kanthi, Surya-Vartamu, Suryakanti (Telugu), Azriyun (Urdu)

Indonesia: Bunga Matahari

Italian: Corona Del Sole, Girasole, Girasole Commune

Japanese: Himawari, Koujitsuki

Korean: Hae Ba Ra Gi

Latvian: Vasaras Saulgrieze

Lithuanian: Tikroi Saulėgrąža

Malaysia: Bunga Matahari

Niuean: Matalā

Norwegian: Solsikke, Solvendel

Persian: Aftabi, Azriyun, Guli-Aftab, Tukhme-Gule-Aftab-Parst, Vartaj, Vartraj

Philippines: Mirasol (Tagalog)

Polish: Słonecznik Roczny, Słonecznik Zwyczajny

Portuguese: Giganta, Girassol, Gyrasol, Heliantho, Tornesol Vastifloro

Russian: Podsolnechnik, Podsolnečnik Odnoletnij, Podsolnechnik Maslichnyi

Samoan: Mata O Le Lā, Mata O Le Lā

Slovašcina: Navadna Sonènica, Sonènica Navadna

Slovencina: Slnečnica Ročná

Spanish: Alizet, Copa De Júpiter, Flor De Sol, Flor Del Sol, Giganta, Gigantean, Girasols, Girassol, Girasol, Heliantemo, Mirasol, Mirasol Común, Pipa, Rosa De Hiericó, Rosa De Jericó, Sol De Las Indias, Tornasol, Trompeta De Amor, Yerba Del Sol

Swahili: Alizeti

Swedish: Solros

Thai: DtôN Bua Tong, DtôN Chon Dtà-Wan, Má-Lét Taan Dtà-Wan, Taan Dtà-Wan

Turkish: Ay Çiç., Gün Çiç., Güne Bakan

Vietnamese: Hoa Mặt Trời, Hướng Dương, Quỳ

Origin/Distribution

Sunflower is indigenous to the Americas—North America and Mexico. Lentz et al. (2008) presented archaeological, linguistic, ethnographic and ethnohistoric data indicating sunflower to be a pre-Columbian domesticate by ca. 2600 B.C. in Mexico. Sunflower cultivation was widespread in Mexico and extended as far south as El Salvador by the first millennium B.C., and was well known to the Aztecs, and is still in use by traditional Mesoamerican cultures today.

Studies on chloroplast variation by Wills and Burke (2006) confirmed a single origin of domesticated sunflower (*Helianthus annuus*). Evidence was provided that the extant domesticated sunflowers were the product of a single domestication event somewhere outside of Mexico. Evidence from multiple evolutionarily important loci and from neutral markers supported a single domestication event for extant cultivated sunflower in eastern North America (Blackman et al. 2011).

Agroecology

Sunflower prefers a mild temperature regime and is grown in many semiarid regions of the world at 0–3,000 m altitude. It is suited to most dryland

and irrigated farming systems but is not highly drought tolerant. It will grow in a wide range of temperatures 17–33 °C conditions with an optimum of 21–26 °C. It is quite frost hardy at the seedling stage, but subzero temperatures will injure and kill maturing plants. Sunflower grows best in full sun and is insensitive to day length. It is adaptable to a wide range of soils from sand to clay but thrives best in well-drained, moist and fertile soil with lots of organic matter. Sunflower is low in salt tolerance.

Edible Plant Parts and Uses

The seeds, flower petals and tender leaf petioles are edible (Hedrick 1972; Harrington 1974; Facciola 1990; Garland 1993; Barash 1997; Roberts 2000). Flower petals can be eaten raw or cooked but are best eaten in the young bud stage when it has an artichoke flavour. Young flower buds can be lightly boiled or steamed and eaten.

Sunflower 'whole seed' (fruit) are sold as a snack food after roasting within heated ovens with or without salt added and also used in confectionary. The roasted seeds or its roasted hulls can be used as a coffee and drinking chocolate substitute. Sunflower seeds can be grounded into flour and processed into a peanut butter alternative, SunButter, especially in China, Russia, the United States, the Middle East and Europe. In Germany, it is used together with rye flour to make a sunflower whole seed bread called 'Sonnenblumenkernbrot'. The germinated seed can be blended with water and left to ferment to make seed yoghurt. The sprouted seed can be eaten raw. The leaf petioles are boiled and mixed in with other foodstuffs.

Sunflower oil, extracted from the seeds, is used primarily as salad and cooking oil or in margarine for cooking. Sunflower oil is generally considered a premium oil because of its light colour, high level of unsaturated fatty acids and lack of linolenic acid, bland flavour and high smoke points.

Flour free from chlorogenic acid and high protein concentrate obtained from sunflower seeds could be added to wheat flour in as high a proportion as 65 % in weight to prepare cookies containing 16 g/100 g high-quality protein, 80–90 % in relation to casein, and with adequate sensorial properties (Bourges et al. 1980).

Botany

Annual, erect, coarse herb, 100–300 cm, branched or unbranched with tap root. Stems green and fleshy, usually hispid. Leaves large, mostly cauline; alternate on petioles 2–20 cm long; lamina cordate to ovate, 10–40 by 5–40 cm, base subcordate or cordate, margins serrate, lower surface usually hispid, occasionally gland-dotted (Plate 1). Flowering heads 1–9 on peduncles 2–20 cm long. Involucres hemispheric or broader, 15–30 cm across (Plates 1, 2 and 3). Phyllaries 20–100+, ovate to lanceolate-ovate,

Plate 1 Flowers and leaves

Plate 2 Close-up of sunflowers

Plate 3 Sunflower with unusually large central disc

Plate 4 Sunflower seeds (achenes)

13–25 × 3–8 mm, margins usually ciliate, abaxial surfaces hirsute to hispid, rarely glabrate or glabrous, usually gland-dotted. Paleae 9–11 mm, 3-toothed (middle tooth long-acuminate). Ray florets sterile, yellow 13–100+; laminae 25–50 mm. Disk florets 150–1,000+; corollas 5–8 mm (throats swollen at bases), lobes usually reddish, sometimes yellow; anthers brownish to black, appendages yellow or dark, style branches yellow. Achene 3–15 mm, glabrate with pappi of 2 lanceolate scales plus 0–4 obtuse scales, dark gray with white stripes (Plates 4 and 5).

Plate 5 Close-up of sunflower seeds

Nutritive/Medicinal Properties

Seed Nutrient/Phytochemicals

Quinic and isochlorogenic acids were identified in sunflower's seeds (Mourgue et al. 1975). Caffeic acid, the most predominant phenolic acid, along with *p*-hydroxybenzoic, *p*-coumaric, cinnamic, *m*-hydroxybenzoic, vanillic and syringic acids, was identified in both acid and base hydrolysates of sunflower seeds with only slight variations in concentrations among the cultivars (Leung et al. 1981). Relatively larger amounts of these acids were detected in the basic hydrolysates except in the cases of *p*-hydroxybenzoic, vanillic and syringic acids, indicating that these acids may exist in glycosidic form to a larger extent than in ester form in the cultivars examined. The principal phenolic constituents of sunflower seeds were chlorogenic acid (CGA), smaller quantities of caffeic acid, cinnamic, coumaric, ferulic, sinapic and hydroxy-cinnamic and traces of vanillic, syringic and hydroxybenzoic acids were also present (Pedrosa et al. 2000). Total tocopherol in *H. annuus* seeds (32 accessions) was determined as 389.8 mg/kg seed comprising mainly 97.9 mg α-tocopherol, 1.8 mg β-tocopherol and 0.3 mg γ-tocopherol (Velasco et al. 2004).

Six different phenolic compounds were extracted from sunflower seeds and kernels (Žilić et al. 2010). Chlorogenic acid was the most abundant phenol. The chlorogenic acid content strongly correlated with total phenols ($R^2 = 0.93$). Other marked phenolics were caffeic acid, ferulic acid, rosmarinic acid, myricetin and rutin. The total tocopherols were significantly higher in kernels than in seeds of all sunflower hybrids. Concentrations in sunflower seeds ranged from

200.67 to 220.05 μg/g and from 256.62 to 267.49 μg/g in sunflower kernels where α-tocopherol was the dominant isomer in all samples. The α-tocopherol content was 98 % of averaged of the total tocopherols in all analyzed samples. β+γ-tocopherols were present in sunflower samples in amounts of 1.28–1.61 % of the total tocopherols. The level of δ-tocopherol was not significant in all sunflower samples and ranged from 0.42 to 0.52 % of the total tocopherols.

Seed reserve storage proteins of sunflowers were found to be globulins and albumins stored in protein bodies (Baudet and Mossé 1977; Buttrose and Lott 1978; Durante et al. 1989). The native globulin protein showed an apparent molecular weight of 300 K, but a 190 K band was present in some selfed sunflower lines (Durante et al. 1989). The globulin fraction amounted to 70–80 % of the total protein, light albumins constituted 20 % and 5–10 % for heavy albumins (Baudet and Mossé 1977). 'Light' albumins appeared as a rather homogeneous constituent with a low molecular weight of 11,000–1,600 (Raab and Schwenke 1975; Baudet and Mossé 1977) and an amino acid composition showing high amounts of methionine, cystine, arginine and glutamine (Baudet and Mossé 1977). 'Heavy' albumins possessed a molecular weight of 48,000 and a very different amino acid composition with a high level of lysine (Baudet and Mossé 1977). The major seed globulin called helianthinin was found to be an 11S protein with an oligomeric structure and 300 K MW (Schwenke et al. 1974, 1975) and to consist of 6 subunits (Plietz et al. 1978). Helianthinin was found to contain high contents of glutamic (26 %) and aspartic (14 %) acid and arginine (9.7 %) as well as a low content of sulphur-containing amino acids (Schwenke et al. 1979). 59 % of the acidic amino acids were present in an amidated form. The globulin contained 12 disulphide bridges per molecule. Low molecular weight (10,000–18,000) methionine-rich albumin was also found in sunflower seeds (Kortt and Caldwell 1990). The major albumins (4–8) contain high contents of glutamine/glutamic acid, asparagine/aspartic acid, arginine and cysteine, characteristic of the 2S class of seed storage proteins. One exception was the small glutamine/glutamic acid content of albumin 6. Two of the sunflower albumins (7 and 8) with Mr 10,000 were methionine-rich proteins containing 16 residues percent methionine as well as 8 residues percent cysteine. The methionine-rich 2S sunflower seed protein was found to consist of a single polypeptide chain of 103 amino acids (molecular mass 12,133 Da) which contained 16 residues of methionine and 8 residues of cysteine (Kortt et al. 1991). The sunflower protein exhibited 34 % identity with the methionine-rich Brazil nut 2S protein. Helianthinin was found to be the most abundant storage protein of sunflower seeds; two populations of the monomeric form of helianthinin with denaturation temperatures of 65 and 90 °C were found (González-Pérez et al. 2004). The structural and interfacial properties of five different fractions of sunflower seed storage proteins, namely, lipid transfer protein (LTP), the methionine-rich 2S albumin SFA8 (sunflower albumin 8) and three mixtures of non-methionine-rich 2S albumins called Alb1 and Alb2 proteins (sunflower albumins 1 and 2), were characterized (Berecz et al. 2010). Heating affected all of the protein fractions, with SFA8 and LTP becoming more surface active than the native proteins after heating and cooling. LTP appeared to be less thermostable. SFA8 generated the greatest elastic modulus and formed the most stable emulsions, whereas LTP showed poorer emulsification properties. The mixed 2S albumin fractions showed moderate levels of surface activity but had the poorest emulsification properties among the proteins studied.

Peroxisome membrane proteins (PMPs) were found in sunflower seed cotyledons (Jiang et al. 1994). Six prominent nondenatured PMP complexes and ten prominent sodium dodecyl sulfate (SDS)-denatured polypeptides were identified in the membranes of the three types of peroxisomes: glyoxysomes, transition peroxisomes and leaf-type peroxisomes in the cotyledons.

The four most abundant anthocyanins in the hulls of purple sunflower seeds were identified as cyanidin3-glucoside, cyanidin3-malonylglucoside, cyanidin 3-xyloside and cyanidin 3-malonylxyloside (Mazza and Gao 1993). From the exudate of

germinating sunflower seeds was isolated a stereoisomer of diversifolide, 4,15-dinor-3-hydroxy-1(5)-xanthene-12,8-olide (designated sundiversifolide) with allelopathic activity (Ohno et al. 2001).

Analyses carried out in the United States reported that dried sunflower seed kernels have the following proximate composition (per 100 g edible portion): water 4.73 g, energy 584 kcal (2,445 kj), protein 20.78 g, total lipid 51.46 g, ash 3.02 g, carbohydrates 20.00 g, total dietary fibre 8.6 g, total sugars 2.62 g, Ca 78 mg, Fe 5.25 mg, Mg 325 mg, P 660 mg, K 645 mg, Na 9 mg, Zn 3.14 mg, Cu 0.824 mg, Mn 1.626 mg, Se 8.2 µg, vitamin C 1.4 mg, thiamine 0.555 mg, riboflavin 0.333 mg, niacin 2.832 mg, pantothenic acid 0.976 mg, vitamin B-6 0.366 mg, total folate 423 µg, choline 95.8 mg, vitamin A 53 IU, vitamin E (α-tocopherol) 0.05 mg, vitamin K (phylloquinone) 9 µg, β-carotene 32 µg, total saturated fatty acids 0.254 g, total monounsaturated fatty acids 0.303 g, total polyunsaturated fatty acids 0.627 g, phytosterols 124 mg, tryptophan 0.247 g, threonine 0.928 g, isoleucine 1.053 g, leucine 1.964 g, lysine 1.671 g, methionine 0.213 g, cystine 0.334 g, phenylalanine 1.103 g, tyrosine 0.827 g, valine 1.161 g, arginine 2.411 g, histidine 0.664 g, alanine 1.070 g, aspartic acid 2.916 g, glutamic acid 4.437 g, glycine 1.095 g, proline 1.099 g and serine 1.195 g (USDA 2012).

Sunflower oil is the non-volatile oil expressed from the seeds. British Pharmacopoeia Commission (2005) listed the following profile: palmitic acid (4–9 %), stearic acid (1–7 %), oleic acid (14–40 %) and linoleic acid (48–74 %). Sunflower oil also contains lecithin, tocopherols, carotenoids and waxes and has a high vitamin E content. It is a combination of monounsaturated and polyunsaturated fats with low saturated fat levels.

The seed lipids from five sunflower mutants, two with high-palmitic acid contents, one of them in high-oleic background and three with high-stearic acid contents, were found to have increased saturated fatty acid content with high levels of triacylglycerols (Alvarez-Ortega et al. 1997). No difference between mutants and standard sunflower lines (controls) was found in minor fatty acids: linolenic, arachidic and behenic. In the high-palmitic mutants, palmitoleic acid (16:1n−7) and some palmitolinoleic acid (16:2n−7, 16:2n−4) were present. Phosphatidylinositol, the lipid with the highest palmitic acid content in controls, also had the highest content of palmitic or stearic acids, depending on the mutant type. The triacylglycerol (TAG) composition of oils from new high-saturated sunflower lines was found to be characterized by triacylglycerol species with asclepic (*cis*,delta11-octadecenoic acid, isomer of oleic acid), araquidic or behenic acids (Fernández-Moya et al. 2000). The TAG molecular species that contained asclepic acid instead of oleic acid were found to have a longer retention time.

High-palmitoleic-acid sunflower mutant was found to have contents of unusual acyl chains up to 20 % (12 % of 16:1delta9, 5 % of 16:2delta9,12 and 6 % of 18:1delta11), whereas these fatty acids were found in negligible amounts in common sunflower cultivars (Salas et al. 2004). The high-palmitoleic-acid phenotype was associated with a concerted reduction in the fatty acid synthase II activity with respect to the control lines and an increase of stearoyl-ACP desaturase activity with respect to the high-palmitate mutant line. The high-palmitic, low-palmitoleic sunflower mutant lines CAS-18 and CAS-25 (with a high-oleic background) had been selected from the high-stearic mutant CAS-3 (Serrano-Vega et al. 2005). In these high-palmitic lines, desaturation of palmitic acid and the synthesis of palmitoleic acid and its derivatives (asclepic and palmitolinoleic acids) were reduced, and stearic content increased. Introducing a FA thioesterase from a high-palmitic line (e.g., CAS-5) into the high-stearic CAS-3 increased the stearic acid content from 27 to 32 % in the new high-stearic line CAS-31. Seed oils from new recombinant high-stearic sunflower lines CAS-29 and CAS-30 were found to contain up to 34.5 % of stearic acid, whereas CAS-15 and CAS-33 with a high-oleic-acid background contained only 24.9 and 17.4 % of stearic acid, respectively (Fernández-Moya et al. 2005).

As seen from above, there are various types of sunflower oils produced which differs in the

levels and composition of fatty acid profiles. The USDA (2012) has analyzed the nutrient composition (per 100 g values) of various types of vegetable sunflower oils in the United States:

(a) High-oleic (70 % and over) vegetable sunflower oil: energy 884 kcal (3,699 kJ); vitamin E (α-tocopherol) 41.08 mg; vitamin K (phylloquinone) 5.5 μg; total fat 100 g; total saturated fatty acids 9.748 g, 15:0 (pentadecanoic) 0.800 g, 16:0 (palmitic) 3.62 g, 18:0 (stearic) 4.32 g, 22:0 (behenic) 1.00 g; total monounsaturated fatty acids 83.594 g, 18:1 undifferentiated (oleic) 82.63 g, 20:1 (gadoleic) 0.964 g; total polyunsaturated fatty acids 3.798 g, 18:2 undifferentiated (linoleic) 3.606 g, 18:3 undifferentiated (linolenic) 0.192 g

(b) Mid-oleic, vegetable sunflower oil, industrial, principal frying and salad oils: energy 884 kcal (3,699 kJ); vitamin E (α-tocopherol) 41.08 mg; vitamin K (phylloquinone) 5.4 μg; Fe 0.03 mg; choline 0.2 mg; total fat 100 g; total saturated fatty acids 9.009 g, 14:0 (myristic) 0.057 g, 16:0 (palmitic) 4.219 g, 17:0 (margaric) 0.037 g, 18:0 (stearic) 3.564 g, 20:0 (arachidic) 0.297 g, 22:0 (behenic) 0.836 g; total monounsaturated fatty acids 57.334 g, 16:1 undifferentiated (palmitoleic) 0.095 g, 16: 1 c 0.095 g, 18:1 undifferentiated (oleic) 57.029 g, 18:1 c 57.029 g, 20:1 (gadoleic) 0.0.211 g; total polyunsaturated fatty acids 28.962 g, 18:2 undifferentiated (linoleic) 28.924 g, 18:2 n−6 c.c 28.705 g, 18:2i 0.219 g, 18:3 undifferentiated (linolenic) 0.037 g, 18:3 n−3 c.c.c (α linoleic) 0.037 g; total *trans*-fatty acids 0.219 g

(c) Linoleic (approx. 65 %) vegetable sunflower oil: energy 884 kcal (3,699 kJ); vitamin E (α-tocopherol) 41.08 mg; vitamin K (phylloquinone) 5.4 μg; choline 0.2 mg; total fat 100 g; total saturated fatty acids 10.300 g, 16:0 (palmitic) 5.900 g, 18:0 (stearic) 4.500 g; total monounsaturated fatty acids 19.500 g, 18:1 undifferentiated (oleic) 19.500 g; total polyunsaturated fatty acids 65.700 g, 18:2 undifferentiated (linoleic) 65.700 g; phytosterols 100 mg

(d) Linoleic (less than 60 %) vegetable sunflower oil: energy 884 kcal (3,699 kJ); vitamin E (α-tocopherol) 41.08 mg; vitamin K (phylloquinone) 5.4 μg; Fe 0.03 mg; total fat 100 g; total saturated fatty acids 10.100 g, 16:0 (palmitic) 5.400 g, 18:0 (stearic) 3.500 g; total monounsaturated fatty acids 45.400 g, 16:1 undifferentiated (palmitoleic) 0.200 g, 18:1 undifferentiated (oleic) 45.300 g; total polyunsaturated fatty acids 40.100 g, 18:2 undifferentiated (linoleic) 39.800 g, 18:3 undifferentiated (linolenic) 0.200 g; phytosterols 100 mg

(e) Linoleic (hydrogenated) vegetable sunflower oil: energy 884 kcal (3,699 kJ); vitamin E (α-tocopherol) 41.08 mg; β-tocopherol 1.69 mg; γ-tocopherol 9.09 mg; δ-tocopherol 2.04 mg; vitamin K (phylloquinone) 5.4 μg; total fat 100 g; total saturated fatty acids 13.00 g, 16:0 (palmitic) 7.100 g, 18:0 (stearic) 5.500 g; total monounsaturated fatty acids 46.200 g, 18:1 undifferentiated (oleic) 46.200 g; total polyunsaturated fatty acids 40.100 g, 18:2 undifferentiated (linoleic) 35.300 g, 18:3 undifferentiated (linolenic) 0.900 g; phytosterols 10 mg

As a frying oil, sunflower oil behaves as a typical vegetable triglyceride. In cosmetics, it has smoothing properties and is considered noncomedogenic. Only the high-oleic variety possesses shelf life suitable for commercial cosmetic formulation.

Flower Phytochemicals

Total carotenoids in *H. annuus* cv. Sunrich orange flower was 1023.8 ug/g FW, in cv. Sonia (orange flowers) 1599.6 ug/g FW, in cv. Sunrich lemon (yellow flowers) 305.2 ug/g FW, and in cv. Valentine (yellow flowers) 143.8 ug/g FW (Kishimoto et al. 2007).

Sixty-nine compounds were identified in the essential oils of leaves and flowers of sunflower plants. Significant percentage variations were recorded between the leaves and flowers oil content. The monoterpenes were the major compounds present in both essential oils examined.

α-Pinene content was higher in flowers (72.6 %) than in leaves (28.6 %). The content of sabinene was about two times higher in leaves than in flowers.

Lipids in sunflower pollens rich in omega-3 linolenic acid including triglycerides, free fatty acids, phosphatidylethanolamines, phosphatidic acids and phosphatidylcholines were highly phagostimulatory (Lin and Mullin 1999). Other important phagostimulatory components included a hydroxycinnamic acid-polyamine amide, N(1),N(5),N(10)-tri[(*E*)-*p*-coumaroyl] spermidine and a flavonol, quercetin β-3-*O*-glucoside. The major component of sunflower pollen lipids was the seco-triterpene helianyl octanoate, followed by new β-diketones as second major group of compounds that included -phenyl-β-diketones (Schulz et al. 2000). Further lipid classes present were related hydroxyketones and diols and also present were β-dioxoalkanoic acids which most likely were biogenetic precursors of the diketones. Also, the composition of the pollen coat resembled the total extract, but lacked dioxoalkanoic acids and certain estolides. Sunflower pollen coat was found to be richer in lipids (8 %) than stigma (2.2 %) on fresh weight basis (Shakya and Bhatla 2010). Neutral lipids were preferentially found localized in the pollen coat. Neutral esters and triacylglycerols (TAGs) were the major lipidic constituents in pollen grains and stigma, respectively. Lignoceric acid (24:0) and *cis*-11-eicosenoic acid (20:1) were specifically expressed only in the pollen coat. Lipase activity was expressed both in pollen grains and stigma, while stigma exhibited a better expression of acyl-ester hydrolase activity than that of observed in both the pollen fractions. Expressions of two acyl-ester hydrolases (41 and 38 kDa) were found to be specific to pollen coat.

The saponified sunflower ligule extract afforded two esters of *ent*-kaur-16en-19-oic and *ent*-trachyloban-19-oic acids with thujanol (Pyrek 1984). The following diterpenoids were also identified: *ent*-kaur-16-en-19-al; *ent*-trachyloban-19-al; *ent*-kauran-16β-ol; *ent*-kauran-16α-ol; *ent*-kauran-16β, 19-diol; *ent*-atisan-16α-ol; and *ent*-atisan-16β-ol. Loliolide acetate was also isolated from an acetylated portion of the same extract. Three bisdesmosidic triterpenoid saponins, helianthoside 1 (1), 2 (2) and 3 (3), and monodesmoside 4 were isolated from sunflower flowers (Bader et al. 1991). Germacranolides 3-*O*-methylniveusin A and 1,10-*O*-dimethyl-3-dehydroargophyllin B diol, the eudesmanoic acid eudesma-1,3,11(13)-trien-12-oic acid and the diterpene 7-oxo-trachyloban-15α, 19-diol and 5-hydroxy-4,6,4′-trimethoxyaurone were isolated from the flower epicuticle of sunflower (Alfatafta and Mullin 1992). Two antifungal benzopyran derivatives, 6-acetyl-2,2-dimethyl-1,2-benzopyran (1) and 6-acetyl-7-hydroxy-2,2-dimethyl-1,2-benzopyran (2), were isolated from the ethanol extract of sunflower receptacles (Satoh et al. 1996).

Floral chemicals with insect feeding-deterrent activity included the following: sesquiterpene lactones (e.g., argophyllin A, 3-*O*-methylniveusin A and germacranolide angelates), diterpenes (grandifloric acid and its 15-angelate) and phenolics, flavonoids (nevadensin and quercetin β-7-*O*-glucoside) and dicaffeoylquinic acids (Mullin et al. 1991) and sesquiterpenes, germacranolides 3-*O*-methylniveusin A and 1,10-*O*-dimethyl-3-dehydroargophyllin B diol, the eudesmanoic acid eudesma-1,3,11(13)-trien-12-oic acid, the diterpene 7-oxo-trachyloban-15α, 19-diol and hydroxy-4,6,4′-trimethoxyaurone (Alfatafta and Mullins 1992).

Eleven diterpene compounds were obtained from the flower disc of *H. annuus* and identified as *ent*-kaurane-2α, 16α-diol (1) and *ent*-kaurane-15α,16α-epoxy-17-al-19-oic acid (2) and nine known diterpenes, *ent*-kaurane-16P-ol (3), phyllocladan-16β-ol (4), *ent*-atisan-16α-ol (5), grandifloric acid (6), angeloylgrandifloric acid (7), *ent*-kaurane-16-en-19-oic acid (8), *ent*-kaurane-17-hydroxy-15-en-19-oic acid (9), *ent*-kaurane-16β, 17-dihydroxy-19-oic acid (10) and ciliaric acid (11) (Suo et al. 2007). Two new oleanane-type triterpene glycosides, named helianthosides 4 (4) and 5 (5), along with four known triterpene glycosides, helianthosides 1 (1), 2 (2), 3 (3) and B (6), were isolated from an n-butanol-soluble fraction of a methanol extract

of sunflower (*Helianthus annuus*) petals (Ukiya et al. 2007).

Eight fatty acid esters of triterpene alcohols (1–8), four free triterpene alcohols (9, 12, 17 and 18), four diterpene acids (19–22), two tocopherol-related compounds (23 and 24), four estolides (25–28), three syn-alkane-4,6-diols (29–31), one 1,3-dioxoalkanoic acid (32) and one aliphatic ketone (33), along with the mixture of free fatty acids, were isolated from the diethyl ether extract of the pollen grains of sunflower (Ukiya et al. 2003b). Sunpollenol and five other rearranged 3,4-seco-tirucallane-type triterpenoids (1–6) were isolated from the diethyl ether extract of the pollen grains of sunflower (Ukiya et al. 2003a). Two new diterpenes, 2β, 16β-*ent*-kaurane diol and 15α, 16α-epoxy-17β-al-*ent*-kaurane-19-oic acid, were isolated from *Helianthus annuus* (Suo et al. 2006).

Barker (1997) and Foster et al. (2003) found that nonpolar (pentane) and moderately polar (dichloromethane) extracts of sunflower bracts contained compounds that stimulated oviposition by females banded sunflower moth (BSFM) *Cochylis hospes*. Two diterpenoid alcohols *ent*-kauran-16α-ol and *ent*-atisan-16α-ol were isolated from a dichloromethane extract of pre-bloom sunflowers heads and found to stimulate female BSFM. Two diterpenoid alcohols, *ent*-kauran-16α-ol (1) and *ent*-atisan-16α-ol (2), along with *ent*-trachyloban-19-oic acid (3) and *ent*-kaur-16-en-19-oic acid (4), were isolated from pre-bloom sunflower heads as oviposition stimulants for the female BSFM (Morris et al. 2005). Compounds 3 and 4 failed to stimulate significant egg laying at any of the dosages tested. Three diterpenoids, grandifloric acid (1), 15β-hydroxy-*ent*-trachyloban-19-oic acid (2) and 17-hydroxy-16α-*ent*-kauran-19-oic acid (3), were isolated from polar fractions of pre-bloom sunflower head extract and found to stimulate oviposition by female BSFM (Morris et al. 2009).

Sesquiterpenes and sesquiterpene lactones such as germacrolides and heliangolides were found as major natural compounds in linear and capitate glandular trichomes of sunflower, *Helianthus annuus* (Göpfert et al. 2005, 2009, 2010). The key enzymes of sesquiterpene lactone biosynthesis in the glandular trichomes of sunflower anthers were identified as two germacrene A synthases HaGAS1 and HaGAS2 (Göpfert et al. 2009) which also occurred in the roots. In addition using reverse transcription-PCR experiments, a third germacrene A synthase, HaGAS3, was identified (Göpfert et al. 2010). The new enzyme occurred in plant tissues not linked to the presence of specific trichomes (e.g., cotyledons) and was absent in roots. The experiments showed that independently regulated pathways for the first cyclic sesquiterpene, germacrene A, were present in sunflower.

Sixty-nine compounds were identified in the essential oils of leaves and flowers of sunflower cultivars Carlos and Florom 350 plants grown in Tuscany, Italy (Ceccarini et al. 2004). The monoterpenes were the major compounds present in both essential oils examined. α-Pinene content was higher in flowers (72.6 %) than in leaves (28.6 %). The content of sabinene was about 2 times higher in leaves than in flowers. There were no significant differences between the essential oil compositions of the oils obtained from the same organs of the two cultivars. Pinene, *cis*-verbenol and β-gurjunene were in both the main volatiles but with significant quantitative differences; moreover, Florom oil was characterized by a greater variety of constituents (Cioni et al. 2005). The fixed oil and the waxes composition showed a general qualitative homogeneity, for both cultivars, even though marked quantitative differences were observable.

Sunflower flower was found to contain ubiquitin, a 76-amino acid protein, the most conserved polypeptide (Binet et al. 1989). Accumulation of polyubiquitin genes (UbB1 and UbB2) were found to be mainly induced by heat stress or during flower development (Binet et al. 1991a, b). Accumulation levels of the 0.7- and 1.6-kb mRNAs (monoubiquitin and hexaubiquitin, respectively) actually decreased during late embryogenesis. In contrast, tetraubiquitin (1.3 kb) mRNAs were approximately eight- to tenfold more abundant in mature seeds than in young embryos (Almoguera et al. 1995).

Leaf Phytochemicals

Sunflower leaf tissues contained allagochrome and chlorogenic acid (Habermann 1967). Sesquiterpene lactones niveusin C (I) and 15-hydroxy-3-dehydrodesoxyfruticin (II) were found in the young leaves (Spring and Hager 1982; Spring et al. 1982b, 1986). In leaves grown in high-intensity light (100 W/m^{-2}), the concentration of sesquiterpene lactone (SQL) I increased sixfold and of SQL II 19-fold compared to leaves in low-intensity light (5 W/m^{-2}) (Spring et al. 1986). Sesquiterpene lactones niveusin C, argophyllin B, 15-hydroxy-3-dehydrodesoxyfruticin and three germacranolides of the niveusin A-type were identified in the resinous content of multicellular capitate glandular trichomes of sunflower leaves (Spring et al. 1987, 1989). Seven sesquiterpene lactones 4,5-dihydroniveusin A, argophyllin B, argophyllin A, 15-hydroxy-3-dehydrodesoxyfruticin, niveusin B, 1,2-anhydridoniveusin A and an unidentified epoxide were isolated from sunflower leaves (Chou and Mullin 1993).

The medium polar fractions from sunflower leaf aqueous extracts afforded five guaianolides, the annuolides A–E (Macías et al. 1993b). From the medium polar active fractions, a sesquiterpene heliannoul A was isolated (Macías et al. 1993b). From the moderately polar fractions of sunflower leaf aqueous extract, 3 sesquiterpenes heliannuols B–D were isolated (Macías et al. 1994).

From an aqueous sunflower leaf extract, six new heliannuols were isolated: three 7,10-heliannanes, heliannuols F (1), I (4) and J (5), and three 7,11-heliannanes, heliannuols G (2), H (3) and K (6) (Macías et al. 1999c). Allelopathic sesquiterpene lactones found in the leaves included the following: 1,2-anhydrido-4,5-dihydroniveusin A, annuithrin, annuolides A,C,F,G, 8β-angeloyloxycumambranolide, helivypolides A–B, melampolides, heliangolides, *cis,cis*-germacranolides and *trans,trans* germacranolides (Macías et al. 1996a). Eleven allelopathic compounds (trivial and systematic names) were isolated from the leaves: heliannuol A (7*R*,11-heliannane-5,10*S*-diol), heliannuol B (7*R*,10*R*-heliann-8(9)-ene-5,11-diol), heliannuol C (8*S**,11-heliann-7(14)-ene-5,10*R**-diol), heliannuol D (7*R*,10*R*-helianane-5,11-diol), heliannuol E (8*R*,10*R*-heliann-7(14)-ene-5,11-diol), heliannuol F (5,11-dihydroxy-7*S*,10*R*-heliannan-8-one), heliannuol G (7*S*,11-heliann-9(10)-ene-5,8*R*-diol), heliannuol H (7*S*,11-heliann-9(10)-ene-5,8*S*-diol), heliannuol I (7*R*,8*S*-epoxy-7,10*R*-heliannane-5,11-diol), heliannuol J (7*S*,8*R*-epoxy-7,10*R*-heliannane-5,11-diol) and heliannuol K (5-hydroxy-7*R*,11-heliannan-10-one) (Macías et al. 2000). Five allelochemicals, chlorogenic, caffeic, syringic, vanillic and ferulic acids, were identified in the leaves (Ghafar et al. 2001). It has been found that total phenols in the leaves were more (0.0316 mM/g) as compared to the stem (0.016 mM/g).

Sesquiterpene lactones annuolide E and leptocarpin, and the sesquiterpenes heliannuols A, C, D, F, G, H, I and L, helibisabonol A and helibisabonol B and bisnorsesquiterpene, annuionone E, were isolated from CH_2Cl_2 leaf extract (Macías et al. 2002b). (±)-Helibisabonol A, a new sesquiterpene with phytotoxic activity, was isolated from sunflower leaves (Macías et al. 2002a). The polar bioactive fractions of the aqueous sunflower leaf extract yielded 10 lignans and a phenylpropanoid: pinoresinol (1), siringaresinol (2), medioresinol (3), buddlenol E (4), lariciresinol (5), 7-hydroxylariciresinol (6), neo-olivil (8), dihydro-dehydrodiconiferilic alcohol (9), l-(4′-hydroxy-3′-methoxyphenyl)-2-[4″-(3hydroxypropyl)-2″-methoxyphenoxy]-propane-l,3-diol (10) and 3-(4-hydroxy-3,5-dimethoxyphenyl) propan-l-ol (11) (Macías et al. 2004b). Compound **7** tanegool was isolated as a natural aglycone. The polar bioactive fractions of *Helianthus annuus* cv. Stella and SH-222 yielded eight apocarotenoids, annuionones A to H (Macías et al. 2004a). From the medium polar active fraction of leaf aqueous extract, allelopathic spiroterpenes heliespirones C–E were isolated (Macías and Galindo 2005).

Annuionone H was isolated from sunflower aqueous leaf extract (Anjum and Bajwa 2005). Six sesquiterpene lactones (annuolide H, helivypolides F, H, I and J, and helieudesmanolide A), 1,2-anhydroniveusin A, 1-methoxy-4,5-dihydroniveusin and 15-hydroxy-3-dehydrodeoxyfruticin were isolated from sunflower leaves (Macías et al. 2006a). From the medium, polar bioactive fractions of sunflower leaf aqueous

extract heliespiranes with a novel spiro heterocyclic sesquiterpene skeleton, namely, heliespirones B and C, were isolated (Macías et al. 2006b).

Stem/Root Phytochemicals

Sunflower stems yielded small quantity of trachyloban-19-oic and (−)-kaur-16-en-19-oic acids trachyloban-19-oic and (−)-kaur-16-en-19-oic acids with antimicrobial property (Mitscher et al. 1983). The following main volatile components were found in the headspace profile of sunflower stems: α-pinene (86.2 %), β-pinene (4.1 %), butyl acetate (2.3 %) camphene (1.9 %) (Buchbauer et al. 1993). Other important components (<1 %) included the following: acetic acid, α-thujune, limonene, β-phellandrene, (*E*)-2-hexen-1-ol, 3-heptanol, decanal, octanol, benzaldehyde, noanol, 2-nonanol, linalool, bornyl acetate, geranyl acetate, β-caryophyllene and vanillin. Minor headspace constituents of sunflower stems included anisole, butanol, ethyl acetate, fenchone, hexanal, *Z*-3-hexenol, hexyl acetate, pentanol, propyl acetate, α-terpineol, β-thujone and 2-undecanol. Three alleochemicals were found in the stem (chlorogenic, ferulic and vanillic acids) and only one (ferulic acid) in the roots (Ghafar et al. 2001).

Aerial Parts/Plant/Seedling Phytochemicals

A sesquiterpene lactone, annuithrin, a germacranolide with an α-methylene-γ-lactone moiety, was isolated from sunflower (Spring et al. 1981). From the ethanol sunflower extract, a new germacranolide with an α-methylene-γ-lactone moiety, the heliangolide niveusin B and its ethoxy derivative, was isolated (Spring et al. 1982a). A furanoheliangolide derivative, 4,5-dihydroniveusin A, as well as niveusin B, argophyllin A and B, diterpene acid, grandifloric acid, ciliaric acid and 17-hydroxy-*ent*-isokaur-15(16)-en-19-oic acid were isolated from a Texas population of *Helianthus annuus* (Melek et al. 1985). The sesquiterpene (−)-heliespinore A, a potential allelopathic agent, was isolated from sunflower var. SH-222 (Macías et al. 1998a). Two allelochemicals, namely, sesquiterpene lactones, helivypolide D and helivypolide E and the bisnorsesquiterpene, annuionone D, were isolated from sunflower (Macías et al. 1999a). The polar bioactive fractions of *Helianthus annuus* cv. Stella and SH-222 yielded eight apocarotenoids, annuionones A to H (Macías et al. 2004a). Structures for annuionone A, B and E were revised. Five flavonoids, namely, the flavonol tambulin, the chalcones kukulcanin B and heliannone A and the flavanones heliannones B and C, were isolated from sunflower cultivar VYP (Macías et al. 1997). Three ionone-type bisnorsesquiterpenes annuionones A–C and the norbisabolene, helinorbisabone, were isolated from sunflower (Macías et al. 1998b). Two bioactive flavonoids heliannone A (1) and (R,S)-heliannone B (2) were identified from *Helianthus annuus* cultivars (Rao et al. 2001). The following allelochemicals were reported from sunflowers: (±)-heliannuol D (Vyvyan and Looper 2000), heliannuol C (Biswas et al. 2006), heliannuols A and K (Ghosh et al. 2007), heliannuol A and D (Tuhina et al. 2002) and natural enatiomers of (−)-heliespirone A and (+)-heliespirone C (Miyawaki et al. 2012). An *ent*-kaurane glucoside named helikauranoside A was isolated together with three known *ent*-kaurane-type diterpenoids: (−)-kaur-16-en-19-oic acid, grandifloric acid and paniculoside IV from sunflower aerial parts (Macías et al. 2008).

Three polyacetylenes, 8-(β-D-glucopyranosyloxy)-3-hydroxy-1,9,14-pentadecatriene-4,6-diyne, termed 'helian' (1), 8-acetoxy-3-hydroxy-1,9,14-pentadecatriene-4,6-diyne (2), and 3,8-dihydroxy-1,9,14-pentadecatriene-4,6-diyne (3), were isolated from sunflower seedlings (Hong et al. 2009). Compounds 1 and 2, having a β-glucose and an acetoxy group at C-8, respectively, showed a weak effect on the growth of roots and shoots of rice (*Oryza sativa*) and cress (*Lepidium sativum*), while compound 3, having a free hydroxyl group at C-8, exhibited a growth promoting effect on the roots and shoots of rice and cress.

Some of the reported pharmacological properties of sunflowers are discussed below.

Antioxidant Activity

Of the three antioxidant assays used, the aqueous extract of striped sunflower seed cotyledon at 30 µg/ml showed a higher antioxidant capacity value (FRAP, 45.27 µmol; DPPH, 50.18 %; ORAC, 1.5 Trolox equivalents) than the ethanol extract (FRAP, 32.17 µmol; DPPH, 15.21 %;ORAC, 0.50 Trolox equivalents) (Giada and Mancini-Filho 2009). When compared with the synthetic antioxidant butylated hydroxyltoluene, the antioxidant capacity of the aqueous extract varied from 45 to 66 %, according to the used assay. Different concentrations (50–250 ppm) of α-tocopherol and myricetin exhibited synergistic antioxidant effect during autoxidation of triacylglycerols of sunflower oil (TGSO) at 100 °C (Marinova et al. 2008). The best synergistic effect was achieved with an equal molar ratio of α-tocopherol and myricetin and at total concentration of the mixtures lower than 10×10^{-4} M. Myricetin was found to be a more effective and stronger antioxidant than α-tocopherol. Studies found that sunflower oil with high content of oleic and palmitic acid (HOHPSO) and containing γ-tocopherol as the most abundant natural antioxidant had a very high stability at frying temperatures and that mixtures of HOHPSO-α and HOHPSO-γ would be an excellent alternative to fulfill the frying performance required by the processors and the vitamin E content claimed by the consumers (Marmesat et al. 2008).

Antiinflammatory Activity

Oleanane-type triterpene glycosides, helianthosides 1–6, isolated from the petals exhibited marked inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1.7 nmol/ear) in mice with ID_{50} values in the range 65–262 nmol/ear (Ukiya et al. 2007). Three diterpene acids, grandiflorolic, kaurenoic and trachylobanoic acids, isolated from the petroleum ether extract of sunflower exhibited antiinflammatory activity on the generation of inflammatory mediators in lipopolysaccharide (LPS)-activated RAW 264.7 macrophages (Díaz-Viciedo et al. 2008). At non-toxic concentrations, these compounds reduced, in a concentration-dependent manner, nitric oxide (NO), prostaglandin E(2) (PGE(2)) and tumour necrosis factor (TNF-alpha) production, as well as expression of inducible nitric oxide synthase (NOS-2) and cyclooxygenase-2 (COX-2). All diterpenoids displayed significant in-vivo antiinflammatory activity and suppressed the 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-mouse ear edema. Also, inhibition of myeloperoxidase (MPO) activity, an index of cellular infiltration, was observed. Results of studies suggested that oral administration of aqueous sunflower seed extract to ovalbumin-induced asthmatic mice exhibited considerable potential in reducing the asthma-like symptoms (Heo et al. 2008). The extract induced a decrease in CD4+ cell number, interleukins IL-4/IL-13 expression and IgE secretion levels in the lungs.

Immunomodulatory Activity

Triterpenoid saponins from several plants including sunflower exhibited mitogenic effects on murine spleen and thymus cells, as well as on human mononuclear cells in-vitro (Plohmann et al. 1997). The activity of murine bone marrow macrophages was stimulated in a chemiluminescence assay, and an induction of cytotoxic macrophages and a TNF-alpha release from murine macrophages were observed. Water and hydroethanol extracts of sunflower plant residues were found to modulate the immune functions of isolated ovine neutrophils when tested for adhesion and superoxide production induced with PMA (Farinacci et al. 2008).

Antiviral Activity

Among the 24 terpenoids and lipids (1–4, 6–9, 12 and 19–33) and 6 free triterpene triols (10, 11 and 13–16),

derived from their fatty acid esters (2, 3 and 5–8) by alkaline hydrolysis of sunflower pollens, 21 compounds possessing a di- or a polycyclic ring system in the molecule (1–4, 6–16 and 19–24) showed potent inhibitory effects on Epstein–Barr virus early antigen (EBV-EA) induction (91–100 % inhibition at 1 × 10(3) mol ratio/TPA) by the tumour promoter, 12-*O*-tetradecanoylphorbol-13-acetate (TPA), in Raji cells (Ukiya et al. 2003b). Six new rearranged 3,4-seco-tirucallane-type triterpenoids (1–6) isolated from the diethyl ether extract of the pollen grains of sunflower exerted potent inhibitory effects on the induction of Epstein–Barr virus early antigen (EBV-EA) induced by the tumour promoter 12-*O*-tetradecanoylphorbol 13-acetate (TPA) in Raji cells (97–100 % inhibition at 1 × 10(3) mol ratio/TPA) (Ukiya et al. 2003a).

Antimicrobial Activity

Annuithrin, a germacranolide from sunflower, exhibited antibacterial activity (Spring et al. 1981). Sesquiterpene lactones niveusin C (1) and 15-hydroxy-3-dehydrodesoxyfruticin (II), isolated from sunflower leaves, exerted an antibiotic effect on Gram-negative and Gram-positive bacteria as well as on some fungi (Spring et al. 1982b). The minimal inhibitory concentration (MIC) of compound II (15-hydroxy-3-dehydrodesoxyfruticin), for example, was 15 µg/ml for *Bacillus brevis* and 95 µg/ml for the fungus *Eremothecium ashbyi*. Heliangolides from sunflower, niveusin B and its ethoxy derivative exhibited antimicrobial activity (Spring et al. 1982a). Sesquiterpene lactones from noncapitate sunflower trichomes were found to possess antimicrobial activity (Spring et al. 1992). Two benzopyran derivatives, 6-acetyl-2,2-dimethyl-1,2-benzopyran (1) and 6-acetyl-7-hydroxy-2,2-dimethyl-1,2-benzopyran (2), from the ethanol extract of sunflower receptacles exhibited antifungal activity against *Pyricularia oryzae* as the test fungus (Satoh et al. 1996). A lipid transfer protein isolated from germinating sunflower seeds (Ha-AP10) displayed strong antimicrobial activity against a model fungus and a weak inhibitory effect on the growth of *Alternaria alternata*, a fungus known to naturally attack sunflower seeds (Gonorazky et al. 2005).

Anticancer Activity

Annuithrin, a germacranolide from sunflower, inhibited DNA/RNA synthesis in cells of the ascitic form of Ehrlich carcinoma (Spring et al. 1981). Sesquiterpene lactones niveusin C (1) and 15-hydroxy-3-dehydrodesoxyfruticin (II), isolated from sunflower leaves, exhibited cytotoxic effects on mouse myeloma cells (NS-1) (Spring et al. 1982b). Compound II causes a 50 % inhibition of cell proliferation (ED_{50}) at a concentration of 170 nM, compound I (niveusin C) at 220 nM. The LD_{50} values were 0.15 µg/ml for II and 1.24 µg/ml for I, respectively. By measuring 14C-labelled thymidine, uridine and leucine incorporation into murine cells of the ascitic form of Ehrlich carcinoma (EAC), it was shown that compounds I and II inhibited DNA and RNA synthesis but did not affect the translation processes involved in protein synthesis. Furthermore, it could be shown that the exocyclic methylene group in the molecules of I and II played an important role in triggering the described inhibitory effects. Saponins from *H. annuus* exhibited cytotoxic activities in the murine T-cell lymphoma YAC-1 and in the β-galactosidase-transfected murine mastocytoma P815-tumour cell models (Bader et al. 1996). Recently, some of the diterpenes compounds isolated from the sunflower head showed cytotoxic activities on cancer cell lines—SF-268, MCF-7 and HepG2 cell lines (Suo et al. 2007).

Antidiabetic Activity

In a protein-reducing sugar model, the sunflower sprout exhibited the strongest inhibitory effects against the formation of advanced glycation end products (AGEs) (Sun et al. 2012). At a concentration of 1.0 mg/ml, its inhibitory rate achieved 83.29 %, which was stronger than that of aminoguanidine (1 mM), a well-known

synthetic antiglycative agent (with an inhibitory rate of 80.88 %). The antioxidant capacity of sunflower sprout was also much stronger than other sprout samples in terms of free radical scavenging and reducing properties. An active ingredient contributing to the observed activities was identified as cynarin (1,5-dicaffeoylquinic acid). Given the key roles of AGEs and oxidation in the pathogenesis of diabetes, the sunflower sprouts rich in cynarin may be regarded as a beneficial food choice for diabetic patients.

Antihypertensive Activity

Sunflower seed proteins were found to be a potential source of angiotensin I converting enzyme (ACE) inhibitory peptides when hydrolyzed with pepsin and pancreatin (Megías et al. 2004). This ACE inhibitory peptide had the sequence Phe-Val-Asn-Pro-Gln-Ala-Gly-Ser and corresponded to a fragment of helianthinin, the 11S globulin from sunflower seeds.

An arginase inhibitor was isolated from sunflower seeds (Reifer and Morawska 1963). Animal studies reported that treatment with arginase inhibitor could improve vascular function and lower hypertension (Bagnost et al. 2008, 2010) and ameliorate endothelial dysfunction in cardiovascular disorders (Pokrovskiy et al. 2011).

Antihyperchlolesteromic Activity

Sunflower oil of any kind has been shown to have cardiovascular benefits. Numerous animal and clinical studies suggested that diets combined with a low-fat content and high levels of oleic acid lowered cholesterol which, in turn, mitigated the risk of heart disease. Dietary studies of adult men and women showed that two test diets, one rich in high-oleic- and low-erucic-acid rapeseed oil (total energy content of fat, 38 %; saturates, 12.4 %; monounsaturates, 16 %; n−6 polyunsaturates, 6 %; and n−3 polyunsaturates, 2 %) and another rich in sunflower oil (total energy content of fat, 38 %; saturates, 12.7 %; monounsaturates, 10 %; n−6 polyunsaturates, 13 %; and n−3 polyunsaturates, 0 %), reduced serum total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol levels from baseline (Valsta et al. 1992). Very low-density lipoprotein (VLDL) cholesterol and total, VLDL, and LDL triglyceride levels were lower during the sunflower oil diet compared with the rapeseed oil diet. Total high-density lipoprotein (HDL) cholesterol levels remained unchanged by both diets. The consumption of rapeseed oil resulted in a more favourable HDL2 to LDL cholesterol ratio and an apolipoprotein A–I to B ratio. Another randomized crossover dietary intervention study of 14 healthy males (35–55 years old) and 14 healthy postmenopausal women (50–60 years) reported that a monounsaturated enriched sunflower oil (MO) diet (40–42 % of energy from fat, with 26–28 % from monounsaturated fat and 40–45 % of energy from carbohydrate) resulted in slower oxidation of LDL and higher HDL cholesterol, suggesting that the MO diet could decrease CHD risk compared to the low-fat, high-carbohydrate diet (22–25 % of energy from total fat, 7–8 % of energy from monounsaturated fat and 55–60 % of energy from carbohydrate) (Ashton et al. 2001). A randomized ABB/BAA extra-period crossover study of 15 men and women aged 35–69 by Allman-Farinelli et al. (2005) found that a diet rich in high-oleic-acid sunflower oil favourably altered low-density lipoprotein cholesterol, triglycerides and fasting factor VII coagulant activity. A significant increase in both plasma phospholipid and neutral lipid oleic acid occurred on the MUFA (sunflower) diet. Sunflower oil presented another useful source of MUFA for diets aimed at prevention of heart disease.

Feeding studies of male Syrian golden hamsters showed that monounsaturated fatty acid (MUFA)-rich dietary fats, for example, 18:1-rich sunflower oil, rapeseed oil and olive oil, were comparable in their hypocholesterolemic potential and caused similar effects on plasma cholesterol as polyunsaturated (PUFA)-rich oils (18:2-rich sunflower oil) when the dietary cholesterol intake was moderate (Trautwein et al. 1999). A double-blinded, randomized, three-period crossover, controlled feeding study of

adults suggested that a balanced diet in which small quantities of saturated fats replaced with sunflower oil had detectable cholesterol-reducing benefits (Binkoski et al. 2005). Total cholesterol decreased 4.7 % and low-density lipoprotein cholesterol decreased 5.8 % on the sunflower oil diet versus the average American diet. There was no effect of the experimental diets on triglyceride levels, rate of oxidation, total dienes, lipid hydroperoxides or alpha-tocopherol. The fact that there were no differences in the resulting oxidation products suggested there were no adverse effects on low-density lipoprotein oxidation. Thus, the results suggested that lower cholesterol levels can be attained by balances of polyunsaturated and monounsaturated fatty acids and sunflower oil may help with this balance.

Sunflower protein hydrolysates were found to decrease the micellar cholesterol solubility from bile acids and therefore may reduce in vivo cholesterol absorption (Megías et al. 2009). It was shown that a combination of different characteristics such as peptide size or hydrophobicity may be responsible of the inhibitory activity of generated peptides.

Skin Moisturizing Activity

Studies reported that topical application of 9 botanical extracts including sunflower oleodistillate improved skin hydration, reduced the transepidermal water loss and/or promoted keratinocyte differentiation in humans in vivo (Casetti et al. 2011). The authors concluded that the botanical extract displayed skin-barrier-reinforcing properties that may be used in dermocosmetics for dry skin.

Proteinase Inhibitory Activity

Sunflower seed was found to contain high amount of trypsin inhibitor (Roy and Bhat 1974). Two proteinaceous cysteine proteinase inhibitors (cystatins) referred to as Sca and Scb were homogenously purified from sunflower seeds (Kouzuma et al. 1996). The proteins Sca and Scb consisted of 83 and 101 amino acid residues with *M*(r) of 9,330 and 11,187, respectively. Papain and ficin were strongly inhibited by both Sca and Scb. Rat cathepsin H was inhibited strongly by Scb and slightly by Sca. One major and two minor groups of trypsin inhibitors were identified in sunflower seeds; the former also inhibited chymotrypsin (Konarev et al. 2000). Three groups of trypsin/subtilisin inhibitors were also present in seeds, together with three inhibitors of ficin. The molecular weights of two trypsin inhibitors were determined to be about 1,500 and 2,500, while the three trypsin/subtilisin inhibitors varied from about 1,500–6,000. Sunflower trypsin inhibitor-1(SFTI-1) a bicyclic peptide trypsin inhibitor from sunflower seeds comprised 14 amino acid residues with one disulfide bond and a cyclic backbone and was deemed as the most potent known Bowman–Birk trypsin inhibitor and the only naturally occurring cyclic one (Korsinczky et al. 2001; Marx et al. 2003). Both the cyclic and acyclic variants of SFTI-1 inhibited trypsin with very high potencies. Enzymatic cyclization of SFT-1 afforded an acyclic permutant of SFTI-1 designated SFTI-1[6,5], which also functioned as an inhibitor of trypsin and which could be enzymatically backbone-cyclized by incubation with bovine beta-trypsin.

Allergy Problem

Sesquiterpene lactones (STL) of the sunflower, occurring in fragile multicellular capitate glandular hairs, were shown to display marked sensitizing capacity in guinea pigs (Hausen and Spring 1989). The strongest response was induced by the hemiketal form of 1-*O*-methyl-4,5-dihydroniveusin A. The STL content of 50 capitate glands was sufficient to elicit a marked response in the guinea pigs. The authors asserted that touching a sunflower plant (with up to 1,000 capitate glands per cm^2) may lead to the release of sufficient STL to sensitize humans, and these substances could be considered to be responsible for the cases of allergic contact dermatitis described in sunflower growers since 1906. Four allergens named allergens a, b, c and d were puri-

fied from sunflower pollens (de la Hoz et al. 1994). Under native conditions, allergen a has a mol. mass of 32, allergen b has one of 24 and allergens c and d each have one of 55 kDa. Cross-reactivity among the four allergens and with the whole extract was very high, and each allergen recognized IgE in a high proportion of patients sensitized to sunflower pollen. In a study of the general population living in sunflower-growing regions suffering from seasonal summer allergy, cross-reactivity studies between *H. annuus* and other Compositae suggested that sunflower pollen was the main allergen involved in the hypersensitivity reaction of those patients (Jiménez et al. 1994). Bronchial challenge tests performed on 8 of the 32 patients confirmed the clinical implication of *Helianthus* pollen in suspected subjects. Thirteen patients with RAST values > or = class 2 showed 2 IgE-binding fractions at 34.0 and 42.8 kDa in 65 % of sera and 3 IgE-binding fractions at pI 4.9, 9.6 and 10.2 in 54 % of sera. A 34-kDa major allergen was purified.

The sunflower seed methionine-rich 2S albumin (SSA) was found to be an IgE-binding protein responsible for anaphylactic reactions in some sunflower seed-sensitive subjects (Kelly and Hefle 2000). Thus, subjects allergic to sunflower seed whose IgE binds to SSA are at risk of developing allergic reactions if they consume SSA. Sunflower seed was found to contain several IgE-binding proteins ranging in size from 10 to 50 kDa, including regions of the high-methionine 2 S albumin SFA-8/SSA (Kelly et al. 2000). The methionine-rich 2 S albumin seed protein from sunflower was found to be allergenic (Pantoja-Uceda et al. 2002).

Phytotoxic/Allelopathic Activity

Phytoxic/allelopathic chemicals from sunflowers can be used as a source of biological herbicides for pest management in sustainable agriculture (Macías et al. 1996b). The biological activity of annuithrin, a germacranolide, was confirmed by growth inhibition in straight-growth tests (Spring et al. 1981). Sesquiterpene lactones niveusin C (1) and 15-hydroxy-3-dehydrodesoxyfruticin (II), isolated from sunflower leaves, strongly inhibited indole-3-acetic acid (IAA)-induced elongation growth of *Avena sativa* L. coleoptile segments and *Helianthus annuus* L. hypocotyl segments (Spring and Hager 1982). Heliangolides from sunflower, niveusin B and its ethoxy derivative exhibited inhibitory activity in the *Avena* coleoptile tests (Spring et al. 1982a).

All five guaianolides, annuolides A–E, from sunflower leaves, possessed potential allelopathic activity, in particular over dicotyledon species when tested for their effects on the germination and growth of the dicotyledon *Lactuca sativa* and the monocotyledon *Hordeum vulgare* species (Macías et al. 1993a, b). Allelopathic bioassay suggested that the sesquiterpenes heliannuols B–D may be involved in sunflower defense against dicot plants (Macías et al. 1994). Sunflower guaianolides generally had no effect on the germination and growth of *L. sativum* and *Lycopersicon esculentum*, except for C-10 epimers 8β-angeloyloxycumambranolide and annoulide G where inhibitory effects were found on the shoot length of *L. esculentum* (Macías et al. 1996a). The conformational changes due to functionalization within germacranolides influenced principally root and shoot growth. Heliangolides exerted greater effect on root and shoot length of dicotyledon species, presumably due to conformational flexibility and the presence of electrophylic groups.

Five flavonoids (the flavonol tambulin, the chalcones kukulcanin B and heliannone A and the flavanones heliannones B and C) were found to influence, principally, the shoot growth of *Lycopersicon esculentum* and *Hordeum vulgare* seedlings, but germination and radical length were affected by the chalcones (Macías et al. 1997). Three ionone-type bisnorsesquiterpenes annuionones A–C and the norbisabolene, helinorbisabone, isolated from sunflower exhibited clear selectivity (parameters and species) with monocotyledon species with an average of inhibition of −45 % on the germination of *Allium cepa* and an average of stimulation of 50 % on the root growth of *A. cepa* and *Hordeum vulgare*

in a range of concentrations of 10^{-5}–10^{-9} (Macías et al. 1998b).

From an aqueous sunflower leaf extract, six new heliannuols were isolated: three 7,10-heliannanes, heliannuols F (1), I (4) and J (5), and three 7,11-heliannanes, heliannuols G (2), H (3) and K (6) (Macías et al. 1999c). The sesquiterpenes heliannuol A and helibisabonol A and the sesquiterpene lactone leptocarpin, from the leaves, inhibited the growth of etiolated wheat coleoptiles (Macías et al. 2002b). Annuionone H from sunflower leaves was found to be a potent plant growth inhibitor that could be exploited for the development of an herbicide model (Anjum and Bajwa 2005). Helivypolide F and 15-hydroxy-3-dehydrodeoxyfruticin, isolated from the leaves, were found to be the most phytotoxic when assayed in standard target species (STS) (*Lepidium sativum*, *Allium cepa*, *Lactuca sativa*, *Lycopersicon esculentum* and *Triticum aestivum*) from 5×10^{-4} to 10^{-5} M (Macías et al. 2006a). Both compounds possessed a carbonyl group at C-3 conjugated with two double bonds. Helikauranoside A, from sunflower aerial parts, was found to be the most active (−84 % at 10^{-3} M; −56 % at 10^{-4} M) in the etiolated wheat coleoptile bioassay (Macías et al. 2008). The results suggested that this compound may be involved in defense mechanisms of sunflower.

Traditional Medicinal Uses

Sunflower seeds have diuretic and expectorant properties and have been employed with success in the treatment of bronchial, laryngeal and pulmonary infections, coughs and colds in traditional medicine (Grieve 1971; Bown 1995; Foster and Duke 1998). In Europe, sunflower has been used as a treatment for pulmonary infections; a preparation of the seeds has been widely used for cold and coughs. Sunflower has been used in Chinese folk medicine for treatment of hypertension, carcinoma of stomach and asthma. In China the seeds are administered in dysentery. A tincture prepared from the seed, with rectified spirit of wine, is employed for intermittent fevers and ague, in place of quinine. In the Caucasus, the seeds have served as a substitute for quinine in the treatment of malaria. The flowering head and seeds are febrifuge, nutritive and stomachic. A tea made from the flowers is used in the treatment of malaria and lung complaints. An infusion of the flowers has been used to kill flies. A tincture of the flowers and leaves has been recommended in combination with balsamics in the treatment of bronchiectasis. A tincture of the bark and flowers is employed for intermittent fevers and fevers that are not responsive to quinine. Sunflower oil is used in aromatherapy. In Portugal, sunflower pith has been used in making moxa, which was used in the cauterization of wounds and infections.

The leaves have astringent, diuretic and expectorant properties. A tea made from the leaves is used in the treatment of high fevers, and the crushed leaves are used as a poultice on sores, swellings, snakebites and spider bites. In Brazil the leaves are used as a substitute for *Datura stramonium* in the treatment of asthma. A decoction of the roots has been used as a warm wash on rheumatic aches and pains and as a remedy for diabetes mellitus.

In North America, sunflowers were widely used by the various native tribes for a myriad of ailments (Moerman 1968). The plant was used as a 'spider medicine' and dermatological aid. A sunflower infusion was used for chest pains and pulmonary disorders; the plant was used as a disinfectant to prevent prenatal infections caused by solar eclipse. Sunflower seeds were used as appetite stimulant and a dry seed decoction eaten by women to protect suckling children. A salve of pulverized seeds and root is used to prevent injury from a horse falling on a person. A poultice of the roots is used to treat snakebites and root decoction used to alleviate rheumatism. A flower infusion was used for kidney ailments. Powdered sunflower leaves were used alone in an ointment on sores and swellings. A poultice of warm ashes was applied on the stomach for worms and leaf decoction used for high fevers and as a wash for horses' sores caused by screwworms. The Zuni men cured rattle snakebites by chewing the

fresh or dried roots and then sucking the wounds (Camazine and Bye 1980).

Other Uses

Sunflower is cultivated for its seed, which is primarily processed into an edible and industrial oil, and for food and birdseed. The seed is also processed into flour. Varieties used for non-oilseed purposes are characterized by a larger seed size and require slightly different management practices. During processing, seed is divided into (1) larger seed for in-shell roasting, (2) medium for dehulling and (3) small for birdseed. Sunflower oil has been used in certain paints, varnishes, candles and plastics because of good semidrying properties without colour modification associated with oils high in linolenic acid. In eastern Europe and the USSR where sunflower oil is plentiful, the oil is used commonly in the manufacture of soaps and detergents (Putnam et al. 1990). Sunflower oil is also used as a carrier oil for aromatherapy, as a pesticide carrier and in the production of agrochemicals, surfactants, adhesives, plastics, fabric softeners, lubricants and coatings.

Sunflower oil contains 93 % of the energy of US number 2 diesel fuel (octane rating of 37) and has been extensively researched for its potential as an alternate biofuel source in diesel engines (Putnam et al. 1990). Blends of sunflower oil and diesel fuel are expected to have greater potential than the burning of pure vegetable oil. Recent research has emphasized on improvement in the transesterification process of sunflower oil to produce biodiesel. Ethyl acetate was employed as an acyl acceptor for immobilized lipase-catalyzed preparation of biodiesel from crude sunflower oil (Modi et al. 2007). The maximum yield of ethyl esters was 92.7 % with crude sunflower oil under optimum conditions. Pessoa et al. (2010) employed enzymatic transesterification of ethanol (ethanolysis) of the sunflower oil for production of biodiesel. Enzymatic transesterification of sunflower oil to biodiesel was conducted in a solvent-free system (Ognjanovic et al. 2009). The use of methyl acetate as an acyl receptor in a solvent-free condition resulted in high fatty acid methyl ester (FAME) yield (95.65 %) and increased the half-life of the immobilized lipase by about 20.1 times as compared to methanol as an acyl receptor. Umdu and Sekir (2012) found that transesterification of sunflower oil at 50 °C and methanol/oil molar ratio of 9, 85 % CaO/Al_2O_3 sol-gel showed the highest biodiesel yield, ~96.6 %, but 60 % CaO/Al_2O_3 had the highest turnover frequency, 0.028 s(−1). Tsai et al. (2013) used non-catalytic transesterification of refined sunflower oil with supercritical methanol, in the presence of carbon dioxide for biodiesel production. The FAME yield could be achieved up to about 0.70 at 593.2 K and 10.0 MPa in 23 minutes with methanol–oil of 25:1 in molar ratio.

The plant is also a popular ornamental and a good bee foraging plant. It is also cultivated as a silage plant, especially in Central Europe. The cake remaining after the seeds have been processed for oil is used as a livestock feed. Non-dehulled or partly dehulled sunflower meal has been substituted successfully for soybean meal in isonitrogenous (equal protein) diets for ruminant animals, as well as for swine and poultry feed (Putnam et al. 1990).

Studies showed that sunflower cake (SFC) being a natural composite has potential to be used as a plastic substitute (Geneau-Sbartaï et al. 2008). SFC contains several components like lignocellulosic fibres [40 %/dry matter (DM)], which essentially come from the husk of sunflower seed, that can act as fillers. It also has other biopolymers like globulins (30 % of the 30 % of sunflower seed proteins/DM of SFC) that can be shaped as a thermoplastic-like material. These proteins have also viscoelastic properties. Moreover, SFC has similar rheological properties and other physicochemical properties compatible with shaping or moulding behaviours of plastic-processing machinery. Studies reported that sunflower oil cake could be used without any additives to make biodegradable, water-resistant and exceptionally cheap mouldable composite materials (Rouilly et al. 2006). Sunflower oil cake has potential for biomethane production (Fernández-Cegrí et al. 2012). The overall methane yield was highest for sunflower oil cake pretreated hydrothermally at 100 °C; however,

this value was only 6.5 % higher than that achieved after pretreatment at 25 °C.

The stems are used as a source of cellulose and for the production of fiber mats and a high-quality writing paper. The Chinese have used this fibre for the manufacturing of fabrics. Other countries are experimenting with the use of fibre in paper. The pith of the stems is used for purposes such as making lifesaving appliances and slides for microscopes. Pectin is obtained from the receptacle and straw. The dried stems make an excellent fuel; the ash is rich in potassium and is returned to the soil. Both the dried stems and the empty seed receptacles make excellent kindling material. The seed hulls could be used for litter for poultry or returned to the soil or composted. In Russia, the hulls are utilized in manufacturing ethyl alcohol and furfural, in lining plywood and in growing yeast.

Sunflower also produces latex and is being researched to improve their suitability as an alternative crop for producing hypoallergenic rubber. A yellow dye is obtained from the ray flowers. A purple and a black dye were obtained from the seed of certain varieties that were grown by the Hopi Indians of S.W. North America to dye basketry materials. Sunflowers can be grown as a spring-sown green manure; they produce a good bulk of material. Phytoxic/allelopathic chemicals from sunflowers can be used as a source of biological herbicides for pest management in sustainable agriculture (Macías et al. 1996b).

Sunflower chemicals have insecticidal properties. Sunflower floral chemicals with feeding deterrency for adult western corn rootworm, *Diabrotica virgifera virgifera*, decreased in the order sesquiterpenes >> diterpenes > flavonoids > dicaffeoylquinic acids (Mullin et al. 1991). Argophyllin A and 3-*O*-methylniveusin A, both sesquiterpene lactone angelates, were the most potent. The diterpenoic acid grandifloric acid and its 15-angelate and the flavonoids nevadensin and quercetin β-7-*O*-glucoside were much poorer antifeedants, although more abundant components of sunflower. The highly active antifeedant germacranolide angelates exhibited structural features and injected neurotoxic symptoms in adult rootworm similar to picrotoxinin, a gamma-aminobutyric acid-gated chloride channel antagonist, suggesting a link between sesquiterpene neurotoxicity and GABA. Sesquiterpenes from sunflower flowers germacranolides 3-*O*-methylniveusin A and 1,10-*O*-dimethyl-3-dehydroargophyllin B diol, the eudesmanoic acid eudesma-1,3,11(13)-trien-12-oic acid and the diterpene 7-oxo-trachyloban-15α, 19-diol and hydroxy-4,6,4′-trimethoxyaurone were strongly antifeedant to adult western corn rootworm, *Diabrotica virgifera virgifera* (Alfatafta and Mullins 1992). Seven sesquiterpene lactones 4,5-dihydroniveusin A, argophyllin B, argophyllin A, 15-hydroxy-3-dehydrodesoxytifruticin, niveusin B, 1,2-anhydridoniveusin A, and an unidentified epoxide, from sunflower leaves, exhibited antifeedant activity on western corn rootworm, *Diabrotica virgifera virgifera* (Chou and Mullin 1993). Lipids in sunflower pollens rich in omega-3 linolenic acid including triglycerides, free fatty acids, phosphatidylethanolamines, phosphatidic acids and phosphatidylcholines were highly phagostimulatory to the adult western corn rootworm *Diabrotica virgifera virgifera* (Lin and Mullin 1999). Other important phagostimulatory components included a hydroxycinnamic acid-polyamine amide, N(1),N(5),N(10)-tri[(*E*)-*p*-coumaroyl]spermidine and a flavonol, quercetin β-3-*O*-glucoside.

Biodegraded products of sunflower flower heads (BPSH) were found to be useful for plant growth (Kaya et al. 2006). Growth of *Phaseolus vulgaris*, *Cicer arietinum* and *Triticum vulgare* seedlings was enhanced at a concentration of 10 % BPSH and decreased at 100 % concentration. As a result, at concentrations up to 10 %, the product was found to be beneficial for growth of plants. A bioactive compound with antibacterial activity was isolated and purified from sunflower leaf extract (Sankaranarayanan et al. 2008). It showed activity against *Xanthomonas oryzae* pv. *oryzae* and induced auxin, gibberellins and cytokinin in *Oryza sativa* and *Phaseolus mungo.*

Comments

Leading sunflower seed-producing countries (in tonnes production) are the following: Russian Federation (9,697,450), Ukraine (8,670,500),

Argentina (3,671,750), France (1,882,450), Romania (1,789,330), China (1,700,000), Bulgaria (1,439,700), Hungary (1,374,780), Turkey (1,335,000), Spain (1,084,300) and the United States (924,550) (FAO 2012).

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Matricaria chamomilla

Scientific Name

***Matricaria chamomilla* L.**

Family

Asteraceae

Synonyms

Camomilla deflexa Gilib. (Inval.), *Chamaemelum suaveolens* E.H.L. Krause, *Chamaemelum vulgare* Bubani, *Chamomilla chamomilla* (L.) Rydb. (Illeg.), *Chamomilla courrantiana* (DC.), *Chamomilla officinalis* K. Koch, *Chamomilla patens* Gilib. (Inval.), *Chamomilla recutita* (L.) Rauschert, *Chamomilla recutita* subsp. *bayeri*, *Chamomilla vulgaris* Gray, *Chrysanthemum chamomilla* (L.) Bernh., *Chrysanthemum suaveolens* (L.) Cav., *Courrantia chamomilloides* Sch. Bip., *Matricaria bayeri* Kanitz, *Matricaria capitellata* Batt. & Pit., *Matricaria chamomilla* f. *kochiana* (Sch. Bip.) Fiori & Paol., *Matricaria chamomilla* subsp. *pusilla* (Willd.) Holmboe, *Matricaria chamomilla* var. *recutita* (L.) Grierson, *Matricaria chamomilla* var. *recutita* (L.) Fiori, *Matricaria chamomilla* f. *suaveolens* Fiori & Paol., *Matricaria courrantiana* DC., *Matricaria exigua* Tuntas, *Matricaria kochiana* Sch.Bip., *Matricaria pusilla* Willd., *Matricaria recutita* L., *Matricaria recutita* var. *coronata* (Boiss.) Halácsy, *Matricaria recutita* var. *kochiana* (Sch.Bip.) Greuter, *Matricaria recutita* var. *recutita* L., *Matricaria salina* (Schur) Schur, *Matricaria suaveolens* L.

Common/English Names

Annual Camomile, Blue Chamomile, Camomile, Chamomile, Chamomille, Common Chamomile, German Chamomile, Hungarian Chamomile, Pin-Heads, Scented Mayweed, Sweet Chamomile, Sweet False Chamomile, Sweet Feverfew, True Chamomile, White Chamomile, Wild Camomile, Wild Chamomile

Vernacular Names

Albanian: Maraqi
Arabic: Baabunaj, Babunej
Argentina: Manzanilla
Bolivia: Manzanilla
Brazil: Camomila, Camomila Comum, Camomila Vulgar, Camomilha-Verdadeira. Maçanilha, Matricária
Chinese: Yang Gan Ju
Colombia: Camomilla, Manzanilla Chiquita, Manzanilla Commun, Manzanilla Dulce
Czech: Heománek Pravý, Heřmánek Lékařský, Heřmánek Pravý
Danish: Ægte Kamille, Kamille, Lægekamille, Moderurt, Pigeurt, Velduftende Kamille, Vellugtende Kamille

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Dutch: Echte Kamille, Roomse Kamille Sort
Eastonian: Chamomile, Teekummel
Egypt: Babounag
Esperanto: Kamomilo, Matrikario Refaldita, Vera Kamomilo
Finnish: Kamomillasaunio, Kamelinsaunio
French: Camomille, Camomille Allemande, Camomille Commune, Camomille Commune Ou d'Allemagne, Camomille Sauvage, Camomille Vraie, Herba De La Mera, Kamille, Matricaire, Matricaire Fausse Camomile, Matricaire Odorante, Matricaire Tronquée
Gaelic: Fíogadán Cumhra
German: Apfelblümlein, Apfelkraut, Echte Kamille, Feldkamille, Frauenblume, Ganille, Garnille, German Chamomile, Germeine Kamille, Gramillen, Haugenblume, Helmergen, Helmriegen, Hermel, Hermelin, Herminzel, Johannisköpfchen, Kamelle, Kamille, Kammerblume, Kummerblume, Kühmelle, Laugenblume, Mariamagdalenakraut, Muskatblume, Mutterkraut, Mägdeblume, Ramerian, Remi, Romerei
Guatemala: Manzanilla
Honduras: Manzanilla
Hungarian: Orvosi Székfű, Kamilla
Icelandic: Kryddbaldursbrá
India: Baboanh, Gul-Babunah, Roghan Babunah (Urdu)
Italian: Camomirra, Camomilla, Camomilla Commune, Capomilla
Japanese: Kamitsure, Kamiture
Mexico: Chamomille, Manzanilla
Nicaragua: Chamomille
Norwegian: Ettårig Kamille, Kamille, Kamilleblom, Kamomilleblom, Kannelblom, Kvitblom, Moderurt
Papiamento: Kanelublum
Persian: Baabunah
Polish: Rumianek, Rumianek Pospolity
Portuguese: Camomila, Camomila-Alemã, Camomila-Da-Alemanha, Camomila-Dos-Alemães, Camomila-Vulgar, Camomilla Legítima, Chamomilla, Macela, Macella, Mançanila, Margaça-Das-Boticas, Matricária
Russian: Romaška Aptečnaja
Slovašcina: Kamilica Prava, Prava Kamilica
Slovencina: Rumanček Kamilkový, Rumanček Pravý
Spanish: Amargaza, Bastardilla, Bonina, Camamila, Camamila Del Comercio, Camamilda, Camomilla, Chamomilla, Larrambillo, Magarza, Magarza Común, Magarza Montesina, Magarzuela Manzanilla, Manzanilla Alemana, Manzanilla Basta, Manzanilla Bastarda, Manzallina Blanca, Manzanilla Común, Manzanilla De Alemania, Manzanilla De Aragón, Manzanilla De Castilla, Manzanilla De Los Corrales, Manzanilla De Urgel, Manzanilla Del Huerto, Manzanilla Fina, Manzanilla Hedionda, Manzanilla Loca, Manzanilla Olorosa, Manzanilla Ordinaria, Manzanilla Real, Manzanilla Silvestre, Manzanilla Vera, Mazanilla Vulgar
Swedish: Äkta Kamomill, Kamomill, Sötblomster, Sötblomster Kamomill
Tunisia: Babunj, Matricaire
Turkish: Papatya

Origin/Distribution

Matricaria chamomilla is native to southern and eastern Europe and northern and western Asia. It has been introduced elsewhere and has naturalized in North America and Australia.

Agroecology

German chamomile is a cool climate species, growing in areas with temperatures of 7–26 °C and mean annual rainfall of 400–1,400 mm per season. It is frost tolerant down to −12 °C. It grows best in full sun and requires long summer days and high heat units for optimum essential oil yield (Alberts 2009). Optimum oil yields were found in temperature range of 20–26 °C, but increasing temperature had a negative impact on individual flower-head weight and days from buds to full-opened flowers (Bettray and Vömel 1992). Chamomile is not fastidious of soil types but thrives best on a well-drained, sandy or sandy-loam soils and

tolerates pH from 4.8 to 8.5. It will also grow on clayey lime soils as it has a great tolerance to soil alkalinity.

Edible Plant Parts and Uses

German chamomile is cultivated for its essential oil and dried flowers. The oils are used as agents in alcoholic beverages, confections, desserts, perfumes, aromatherapy and cosmetics. Dried flowers are used for aromatic and soothing herbal teas and blend with other teas, in syrups and fruit jelly (Roberts 2000).

Botany

Chamomile is an erect, aromatic, herbaceous annual, 15–80 cm high with a much branched, light green stem. The leaves are alternate, bipinnate or tripinnate with long and linear pinna, mildy pubescent to glabrous (Plate 1). Flowers are borne in solitary terminal capitula, 10–20 mm across, on 15–25 cm grooved peduncle (Plate 1). The receptacle is 6–10 mm wide; is hollow, swollen and obovoid to subglobose; and lacks involucral scales and paleae. The ray florets are ligulate, white 6–10 mm by 2.5–3.5 mm. The central disc florets are bisexual, tubular with 5-teeth, 1.5–2.5 mm long, yellow. The fruit is a yellowish brown cypsela with 3–5 faint ribs.

Nutritive/Medicinal Properties

Proximate nutrient composition per 100 g of brewed chamomile herbal tea was reported as follows: water 99.70 g, energy 1 kcal (4 kJ), carbohydrate 0.2 g, Ca 2 mg, Fe 0.08 mg, Mg 1 mg, K 9 mg, Na 1 mg, Zn 0.04 mg, Cu 0.015 mg, Mn 0.044 mg, F 13 µg, thiamine 0.010 mg, riboflavin 0.004 mg, pantothenic acid 0.011 mg, total folate 1 µg, total choline 0.4 mg, β-carotene 12 µg, vitamin A 1 µg RAE, vitamin A 20 IU, total saturated fatty acids 0.002 g, total monounsaturated fatty acids 0.001 g and total polyunsaturated fatty acids 0.005 g (USDA 2012).

Plate 1 Chamomile flowers and foliage

Other Flower Phytochemicals

Five organic acids were isolated from chamomile flowers: tartaric acid, citric acid, malic acid, malonic acid and succinic acid (Olennikov and Tankhaeva 2005). Mann and Staba (1986) had listed an extensive range of phytochemicals found in chamomile. The main constituents of chamomile flowers included several phenolic compounds, primarily the flavonoids apigenin, quercetin, patuletin, luteolin and their glucosides (McKay and Blumberg 2006). The principal components of the essential oil extracted from the flowers were the terpenoids α-bisabolol and its oxides and azulenes, including chamazulene.

The following chemicals were reported in chamomile flower heads: ascorbic acid, thiamine, niacin, polyphenols (quercetin, rutin, geraniol, gallic acid, tannin, catechin tannic, caprylic acid, kaempferol, thujone) and fatty acids (oleic, linoleic, palmitic, sinapic) (Mann and Staba 1986).

The terpenoids (−)-α-bisabolol oxides A, B and C were isolated from chamomile extract (Schilcher et al. 1976). Two spirocyclic polyines, the isomeric *cis* (*Z*)-enyne dicycloether *cis*-2-[hexadiyne)-(2,4)-ylidene]-1,6-dioxaspiro-[4,4]-nonene) and *trans* (*Z*)-enyne dicycloether *cis*-2-[hexadiyne)-(2,4)-ylidene]-1,6-dioxaspiro-[4,4]-nonene), were found in chamomile flowers (Bohlmann et al. 1961). The following phenyl carboxylic acids, synergic, vanillic, anisic and caffeic acids, were found in both ligulate and tubular chamomile florets (Reichling et al. 1979). Chamomile flower heads were also reported to contain *cis/trans*-en-in-dicycloethers (polyines) (Gasic et al. 1983), anthecotulid (37–120 mg/g) (Hausen et al. 1984) and up to 0.3 % choline (Bayer et al. 1958). In chamomile flowers from different origins, a range of 37.4–98.5 mg/100 g of herniarin and 6–17.8 mg/100 g of umbelliferone were determined (Schilcher and Kamille 1987). The average content in ligulate florets was significantly higher than in the tubular florets. The following coumarins, herniarin, umbelliferone, esculetin, isoscopoletin and scopoletin, were isolated from chamomile flowers (Kotov et al. 1991). A flavone 7-*O*-glucoside-specific glucosidase was purified and characterized from ligulate florets of *Chamomilla recutita*, and salicin, arbutin, naringenin 7-*O*-glucoside, luteolin 5-*O*-glucoside, and various *p*-nitrophenol compounds (-β-D-glucoside, -β-D-galactoside, -β-fucoside and a nitrophenyl-β-D-glucoside) were also isolated from the florets (Maier et al. 1993). The enzyme was confirmed to have a high affinity towards flavone 7-*O*-glucosides. Aqueous alcohol extracts of chamomile flowers were found to contain the following fat soluble compounds: β-farnesene (0.04–0.28 %), bisabolone oxide (<0.01–0.05 %), bisabolol oxide-A (0.15–0.59 %), spiroether (0.3–1.03 %) and pentacosane (0.08–0.11 %) (Kanamori et al. 1992). Two phenylpropanoids and one flavonoid glycosides were isolated from a 1-butanol-soluble portion of chamomile flowers (Kanamori et al. 1993). Their structures were elucidated as *cis*-2-β-D-glucopyranosyloxy-4-methoxy cinnamic acid (1) and *trans*-2-β-D-glucopyranosyloxy-4-methoxy cinnamic acid (2) and cosmosiin (apigenin-7-*O*-β-D-glucopyranoside) (3), respectively. All 3 compounds were found in higher concentration in ligulate flowers (compound (1) 4.32 %, compound (2) 1.32 %, cosmosiin 5.20 %) than tubular flowers (compound (1) 1.07 %, compound (2) 0.52 %, cosmosiin 0.02 %) or involucral scale (compound (1) 2.56 %, compound (2) 1.05 %, cosmosiin 0.17 %). Ahmad and Misra (1997) isolated oleonolic acid, β-sitosterol and β-sitosterol glucoside from the flowers by organic solvent extraction of chamomile flower oil. All three were also found in the capitulum receptacle (compound (1) 0.16 %, compound (2) 0.08 %, cosmosiin <0.01 %), stem (compound (1) 2.45 %, compound (2) 0.69 %, compound (3) 0.02 %) and leaf (compound (1) 1.75 %, compound (2) 0.67 %, cosmosiin 0.02 %). Two polyacylated spermines N1,N5,N10,N14-tetrakis[3-(4-hydroxyphenyl)-2-propenoyl]-1,5,10,14-tetraazatetradecane (tetracoumaroyl spermine) and N1,N5,N10-tris[3-(4-hydroxyphenyl)-2-propenoyl]-1,5,10,|14-tetraazatetradecane were found on chamomile flower extract (Yamamoto et al. 2002). Eleven bioactive phenolic compounds, namely, coumarins, herniarin and umbelliferone; phenylpropanoids, chlorogenic acid and caffeic acid; flavones, apigenin, apigenin-7-*O*-glucoside, luteolin and luteolin-7-*O*-glucoside; flavonols, quercetin and rutin; and flavanone, naringenin, were determined in chamomile extracts (Fonseca et al. 2007). The limits of detection and quantification for apigenin were 35.0 and 150.0 µg/ml, respectively.

The flavonoids quercetin-7-glucoside (quercimeritrin) and apigenin-7-glucoside (apigetrin) were isolated form chamomile florets (Hörhammer et al. 1963). Lipophilic flavonoids isolated from chamomile flowers included eupatoletin, eupalitin, chrysosplenol and chrysosplenitin (3,6,7,3′-tetramethyl-quercetagetin) (Hänsel et al. 1966). A new chamomile flavone apigenin 7-6″-*O*-(acetyl-)-glucoside was isolated from chamomile flowers and florets and the aglyca apigenin, luteolin, patulin, quercetin and isorhamnetin and the glycoside apigenin-7-glucoside, luteolin-7-glucoside, patulitrin and quercimeritrin were identified (Kunde and Isaac 1979). They further reported the presence of flavonoid and postulated a diacetylated apigenin-7-glucoside. They classified

chamomile flavonoids according their polarity into (a) lipophlic aglyca (e.g., methoxylated compounds), (b) hydroxylated flavones aglyca, (c) acetylated flavones monoglycosides and (d) flavones diglycosides. Methylated flavonoid aglycones, eupatoletin, eupalitin and chrysosplenol, were found in the flowers (Exner et al. 1981). From ligulate flowers of *Matricaria chamomilla* were isolated a mixture of apigenin 7-*O*-β-glucoside diacetates, which was shown to be based on (2″, 3″)- and (3″, 4″)-diacetates (Redaelli et al. 1982). The flavones apigenin and its glucosides, apigenin-7-glucoside and apigenin-7-acetylglucoside, were found in ligulate florets but not in the tubular florets of *Matricaria chamomilla* (Redaelli et al. 1981b). Dried ligulate chamomile flowers contained 7–9 % glucosides of apigenin and 0.3–0.5 % free apigenin. Glucosides were identified as apigenin 7-glucoside and a 1:3 mixture of the 2″- and 6″-acetates (Redaelli et al. 1980). The most abundant flavonoid derivatives in chamomile flowers were apigenin 7-glucoside and its acetylated derivatives, as well as luteolin, quercetin and their glycosides (Carle and Isaac 1985). Beside hydroxylated aglyca, methoxylated flavonoids like chrysosplenol, jaceidin, chrysoeriol, patuletin, spinacetin, 6-methoxykaempferol, axillarin, chrysosplenetin, eupatoletin and eupalitin were identified in chamomile flowers (Carle and Isaac 1985).

Accumulation of two phenylpropanoid glycosides, (1) *cis*-2-β-D-glucophyranosyloxy-4-methoxy cinnamic acid and (2) *trans*-2-β-D-glucophyranosyloxy-4-methoxy cinnamic acid and one flavonoid glycoside, (3) cosmosiin (apigenin-7-*O*-β-D-glucopyranoside) glycosides in chamomile flower head, reach a maximum during flowering (Ohe et al. 1995). The content of (1) and (2) reached 2 % and 0.5 % in the head respectively during harvesting, and their content was higher in the ligulate flowers than tubular flowers. Coumarin, umbelliferone and its methoxy analogue herniarin were also found in *M. chamomilla* flowers (Redaelli et al. 1981a). The polyphenolic compounds identified in the methanolic flower-head extract by Mulinacci et al. (2000) included 5-caffeoylquinic acid, 3-caffeoylquinic acid, 4-caffeoylquinic acid, quinic acid, ferulic acid-L-*O*-glycoside, caffeoylquinic acid derivative, ferulic acid-7-*O*-glycoside, quercetin-3-*O*-galactoside, quercetin-7-*O*-galactoside, patuletin-7-*O*-glucoside, dicaffeoylquinic acid derivative, 1,3-dicaffeoylquinic acid, apigenin-7-*O*-glucoside, quercetin derivative, luteolin-4′-*O*-glucoside, quinic acid derivative, apigenin-7-*O*-glucosyl-2″-acetate, apigenin-7-*O*-glucosyl-6″-acetate, apigenin-7-*O*-glucosyl-diacetate, apigenin, luteolin-7-*O*-rutinose and ferulic acid derivative.

Free and total apigenin contents in chamomile extracts were, respectively, determined as 106 and 903 μg/g (methanolic extract), 77 and 817 μg/g (ethanolic extract) and 11.0 and 247 μg/g (glycolic extract) (Fonseca and Tavares 2004). The major flavonoids (apigenin glucosides) identified in the white florets of chamomile were apigenin 7-*O*-glucoside, apigenin-7-(6″-malonyl-glucoside), apigenin-7-(6″-acetyl-glucoside), apigenin-7-(6″-caffeoyl-glucoside), apigenin-7-(4″-acetyl-glucoside), apigenin-7-(4″-acetyl,6″-malonyl-glucoside) and a partially characterized apigenin-7-(mono-acetyl/mono-malonylglucoside) isomer (Svehlikova et al. 2004). The bioactive principles in the ethanol/water extract of chamomile flowers were determined as *cis*-2-β-D-glucopyranosyloxy-4-methoxy-cinnamic acid, *trans*-2-β-D-glucopyranosyloxy-4-methoxy-cinnamic acid, apigenin-7-*O*-β-D-(6″-*O*-rhamnosyl)glucopyranoside (isorhoifolin), apigenin-7-*O*-β-D-glucopyranoside (cosmosiin), apigenin-7-*O*-β-D-(6″-*O*-acetyl) glucopyranoside, 7-Methoxycoumarin (herniarin) and 4′,5,7-trihydroxyflavone (apigenin) (Weber et al. 2008). The following flavonoids, kaempferol, quercetin, myricetin and isorhamnetin, were isolated from the ethanol chamomile flower extract (Mohamed 2010).

The main secondary metabolites of *Matricaria chamomilla* ligulate flowers were apigenin-7-*O*-glucoside derivatives and (*Z*)-2-β-D-glucopyranosyloxy-4-methoxy cinnamic acid and (*E*)-2-β-D-glucopyranosyloxy-4-methoxy cinnamic acid (GMCAs), the precursors of herniarin (Repčák and Krausová 2009). The flavonoids detected were apigenin7-*O*-glucoside,apigenin7-*O*-(6″-malonyl)-glucoside, apigenin 7-*O*-(4″-acetyl)-glucoside,

apigenin 7-*O*-(6″-caffeoyl)-glucoside, apigenin 7-*O*-(6″-acetyl)-glucoside, apigenin 7-*O*-(4″-acetyl, 6″-malonyl)-glucoside, and apigenin. The content of the apigenin glucoside and its main acylated derivatives in ligulate flowers of diploid plants were found to be significantly higher before the start of flowering in comparison with tetraploid plants. During the flowering and post-flowering phase, their content decreased and no difference between diploid and tetraploid plants was observed. The (*E*)-isomer was the dominant form of 2-β-D-glucopyranosyloxy-4-methoxy cinnamic acid. These secondary stress metabolite precursors were accumulated in higher concentrations in young growing ligulate flowers, but during flowering and post-flowering phases, their content decreased. Significantly higher content was found in tetraploid plants in comparison with diploid plants. Aglycones of glycosides were found in low concentrations.

Two new flavonoids quercetin and isorhamnetin besides myricetin and kaempferol were detected in the ethanolic extract of the flower head of *Matricaria chamomilla* growing in Iraq (Mohamed 2010). The most abundant phenolic compounds in both chamomile flowers and chamomile tea extracts were chlorogenic acid, umbelliferone, apigenin and apigenin-7-glucoside (Nováková et al. 2010). In chamomile tea extracts, there was greater abundance of flavonoid glycosides such as rutin or quercitrin, while the aglycone apigenin and its glycoside were present in lower amounts. The total content of polyphenols (in chlorogenic acid equivalents) in chamomile teas showed a significant variability as well as content of total flavonols (0.29–1.21 %) or total phenolic acids (7.7–91.4 mg/200 ml). (Raal et al. 2012). The major phenolic compounds in chamomile tea infusions were chlorogenic acids, ferulic acid glycosides, dicaffeoyl quinic acids and apigenin glycosides. Based on the amounts of essential oil, terpenoids, total flavonols and major phenolic compounds, the quality of the commercial chamomile teas was very variable, and the chamomile teas available in pharmacies should be preferred for the medical purposes. The major polyphenols detected were neochlorogenic acid; chlorogenic acid; cryptochlorogenic acid; ferulic acid glucoside 1; ferulic acid glucoside 2; quercetin galactoside; quercetin glucoside; luteolin glucoside; 3,4-dicaffeoyl quinic acid; 3,5-dicaffeoyl quinic acid; 4,5-dicaffeoyl quinic acid; apigenin glucoside; and apigenin acetylglucoside.

Farnesene, bisabolol, azulene (chamazulene), bisabolol oxide and terpene alcohol (farnesol) were the major constituents of the essential oil from dried chamomile flowers (Mishra et al. 1999). Oil from fresh flowers contained a high amount of terpene alcohol which decreased in shade-dried flowers and was the lowest in sun-dried flowers. The bisabolol content was the highest in sun-dried and minimum in fresh flowers. Farnesene content was higher in shade-dried flowers; bisabolol and azulene were higher in sun-dried flowers. The bisabolol oxide content was comparatively higher in fresh flowers (10.4 %) and was the least (8.4 %) in shade-dried flowers. The essential oil of chamomile inflorescence developed from callus cultures was found to contain chamomillol, gossonorol, cubenol, α-cadinol, (−)-α-bisabolol, 1-azulenethanol acetate and (−)-α-bisabolol acetate (Magiatis et al. 2001).

The Brazilian chamomile flower essential oil contained the following major components: bisabolol oxide B (23 %), bisabolol oxide A (17 %), (*Z*)-β-farnesene (16 %), α-bisabolol (13 %), chamazulene (8 %) and chamo-spiroether (5 %) (Matos et al. 1993). Studies in Yugoslavia found the chamomile essential oil content ranged from 0.24 to 0.50 % (Mimica-Dukic et al. 1993). The main compound in all samples was bisabolol oxide A (33.46–48.48 %); other major compounds were (−)-α-bisabolol, bisabolol oxide B, bisabolon oxide, farnesene, spathulenol, chamazulene, as well as en-in-dicycloether. Thirty-four compounds were identified in chamomile flower essential oil from Cuba, of which α-bisabolol oxide A (23.3 %), chamazulene (14.1 %), α-bisabolone oxide A (13.4 %) and β-caryophyllene (10.4 %) were the main constituents (Pino et al. 2000). Eighty compounds were identified in chamomile essential oil from Iran, of which α-bisabolol oxide A (43.8 %), α-bisabolone oxide A (13.6 %) and β-bisabolene (19.6 %) were predominant (Pino et al. 2002). Thirty-seven

components were found in the essential oil distilled from the flower heads in Eastonia (Orav et al. 2001). Oxygenated sesquiterpenes were the most characteristic chamomile essential oil components comprising 50–70 % of the total oil, among which bisabol oxide A accounted for 20.2 %–33.1 %, bisabolon oxide A 6.7–13.6 %, bisabolol oxide B for 7.9–12.4 % and α-bisabolol 2.9–7.8 %. Chamazulene represented 5.3–7.2 % and en-yn-dicycloether contributed 17.1–21.7 % of the total oil. Sesquiterpenes (5–16 %) mainly comprised (*E*)-β-farnesene (4.3–12.6 %). Monoterpenes and oxygenated monoterpenoid compounds contributed very little (<1 %) to the chamomile oil composition. The minor components included α-pinene trace (tr), sabinene tr 0.1 %,6-methyl-5-hepten-2-one 0.1 %, myrcene tr 0.1 %, 1,2,4-trimethylbenzene tr 0.1 %, 3-octanol 0.1–0.2 %, *p*-cymene tr 0.1 %, 1,8-cineole 0.1 %, limonene 0.1 %, (*E*)-β-ocimene tr 0.1 %, Artemisia ketone 0.2–0.4 %, γ-terpinene tr 0.1 %, terpinolene tr-0.1 %, terpinen-4-ol tr 0.1 %, α-terpineol tr 0.1 %, carvone tr 0.1 %, γ-elemene 0.1–0.3 %, decanoic acid 1.1–2.1 %, β-caryophyllene 0.1 %, germacrene 0.5–1.7 %, γ-muurolene 0.5–1.7 %, α-farnesene 0.3–0.9 %, β-bisabolene tr 0.7 %, γ-cadinene tr 0.1 %, σ-cadinene tr 0.1 %, (*E*)-nerolidol 0.1 %, spathylenol 2.3–3.6 %, caryophyllene oxide tr 0.2 %, T-cadinol 0.2 %, unidentified 0.1 %, and unidentified 0.5–0.9 %. Total oil yield was 1.88–2.09 mg/g. Forty-one components were identified in chamomile grown in the lower region of the Himalayas, representing 97.5 % of the oil (Sashidhara et al. 2006). The main constituents were α-bisabolol oxide A (36.5 %) and B (8.6 %), (*E*)-β-farnesene (14.0 %), α-bisabolol (16 %) and chamazulene (5.6 %). The main constituents, except for α-bisabolol oxide B, were found in higher concentration in oil from the foothills of the Himalayas than in the oil from the northern Indian plain. Eighteen volatile components were identified in the Iranian chamomile flower essential oil (Owlia et al. 2007). The major components were guaiazulene 25.6 %, (*E*)-β-farnesene 20.1 %, chamazulene 12.4 %, α-bisabolol oxide B 7.3 %, α-bisabolol 7.3 %, hexadecanol 5.6 % and germacrene D 3.15 %. Other components included *Z*-γ-bisabolene 2.6 %, -bisabolol oxide A 1.9 %, spathulenol 1.7 %, *n*-nonadecane 1.4 %, caryophyllene oxide 1.2 %, α-muurolene 0.8 %, limonene 0.5 %, γ-terpinene 0.5 %, *n*-pentacosane 0.5 % and sclarene 0.4 %. The main compounds identified in chamomile flower essential oil were α-bisabolol (56.86 %), *trans-trans*-farnesol (15.64 %), *cis*-β-farnesene (7.12 %), guaiazulene (4.24 %), α-cubebene (2.69 %), α-bisabolol oxide A (2.19 %) and chamazulene (2.18 %) (Tolouee et al. 2010). Chamomile essential oil was found to contain 13 compounds, mainly bisabolol and its oxides, chamazulene, farnesene, germacrene and other sesquiterpenes (Hernández-Ceruelos et al. 2002). A total of 39 components were identified, representing over 92 % of the total oil yield of chamomile oils from European countries (Orav et al. 2010). The principal biologically active compounds in chamomile oils were bisabolol oxide A (3.1–56.0 %), α-bisabolol (0.1–44.2 %), bisabolol oxide B (3.9–27.2 %), *cis*-enyne-bicycloether (8.8–26.1 %), bisabolon oxide A (0.5–24.8 %), chamazulene (0.7–15.3 %), spathulenol (1.7–4.8 %) and (*E*)-β-farnesene (2.3–6.6 %). In 8 chamomile samples from 13, bisabolol oxide A (27.5–56.0 %) was predominant (among them in three Estonian samples). α-Bisabolol (23.9–44.2 %) was predominant in the samples from Moldova, Russia and the Czech Republic. The sample from Armenia was rich in bisabolol oxide B (27.2 %) and chamazulene (15.3 %). The oils were obtained in yields of 0.7–6.7 ml/kg and the minimum limit of 4 ml/kg stated by the European Pharmacopoeia was exceeded only in 13 samples from 13 analyzed drugs.

Both aqueous and methanolic chamomile flower extracts demonstrated the presence of mixture of several apigenin glucosides and parent glycone, apigenin (Srivastava and Gupta 2009). Other apigenin glucosides identified in chamomile extracts were mono-caffeoyl glucoside, mono-acetyl glucoside and mono-malonyl glucoside as well as mono-acetyl/mono-malonyl glucosides. The methanolic chamomile extract had high concentration of apigenin-7-*O*-gluco-

side along with several polyphenolic constituents which include caffeic acid, luteolin and luteolin-7-*O*-glucoside, among common flavonoids. The aqueous chamomile extract was found to contain a small fraction (5–7 % of total essential oil) content of the flower. The essential oil content in the methanolic extract consists of chamazulene, α-bisabolol, bisabolol oxides A and B, a cyclic ether and different hydrocarbons which were insoluble in the aqueous phase. Aqueous extracts obtained from both Lebanese and Egyptian chamomile varieties showed the abundance of apigenin-7-*O*-glucoside. Methanolic chamomile extract prepared from ray florets of Lebanese and Egyptian chamomile showed the presence of apigenin-7-*O*-glucoside (39 %) and the aglycone, apigenin, 6.7 % in the Egyptian and 2.3 % in the Lebanese variety. Disc florets of chamomile from Lebanese origin showed higher content of apigenin-7-*O*-glucoside (38.5 %) compared to Egyptian variety (36.1 %) but had no aglycone. Salamon et al. (2010) characterized Egyptian and Iranian chamomile landraces into 4 basic chemotypes based on the main components (%) in the essential oil:

Type A (South American collection): α-bisabolol oxide B (22.43–58.85 %) > α-bisabolol oxide A (4.74–15.68 %) > α-bisabolol (4.37–15.41 %), (en-yn-dicyloethers 2.61–11.27 %, chamazulene 2.70–17.69 %).

Type B (Egypt and central Europe): α-bisabolol oxide A (31.07–52.25 %) > α-bisabolol oxide B (5.27–18.79 %) > α-bisabolol (8.81–12.92 %), (en-yn-dicyloethers 4.08–9.90 %, chamazulene 5.40–7.95 %).

Type C (Spain/Catalonia, Malta, Crimea): α-bisabolol (24.18–77.21 %) > α-bisabolol oxide B (3.17–34.46 %) > α-bisabolol oxide A(2.13–18.50 %) (en-yn-dicyloethers 1.92–12.00 %, chamazulene 1.91–7.89 %).

Type D (southeast Europe, Turkey): α-bisabolol oxide B (10.43–24.20 %) > α-bisabolol oxide A (9.62–25.83 %) > α-bisabolol (8.49–19.58 %), (en-yn-dicyloethers 5.51–10.68 %, chamazulene 1.91–7.89 %). The highest contents of α-bisabolol oxide A and α-bisabolol oxide B in the flower anthodia were found in the Egyptian chamomile.

The total extract yield of chamomile oil obtained by solvent extraction (4.98 %) was much higher than the oil yield obtained by steam distillation even after 6 hours (0.31 %) (Falzari and Menary 2003). The oil yield increased with increasing duration of steam distillation but after 6 hours distillation the yield of solvent extract is still 16 times greater than the yield of steam distilled oil. The main volatile components of chamomile essential oil were *E*-β-farnesene(42.59 %), germacrene D (2.93 %), bicyclogermacrene (1.99 %), (*E*,*E*)-α-farnesene (8.32 %), α-bisabolol oxide B (4.43 %), α-bisabolone oxide A (4.53 %), chamazulene (1.18 %), α-bisabolol oxide A (21.16 %) and *cis*-ene-yne-dicycloether (5.94 %) (Heuskin et al. 2009). Other minor components included *trans*-ene-yne-dicycloether (0.99), (*E*)-phytol (0.23 %), globulol (0.23 %), spathulenol (0.63 %), dendrolasin (0.21 %), dehydronerolidol (0.09 %), *trans*-nerolidol (0.17 %), unidentified sesquiterpene (0.33 %), sesquirosefuran (0.18 %), δ-cadinene (0.18 %), (*Z*,*E*)-α-farnesene (0,83 %), β-selinene (0.22 %), unidentified sesquiterpene (0.10 %), aromadendrene (0.07 %), β-caryophyllene (0.17 %), α-gurjunene (0.04 %), sativene (0.04 %), β-elemene (0.7 %), α-isocomene (0.26 %), β-maaliene (0.07 %), α-copaene (0.04 %), 4,8-dimethylnona-3,8-dien-2-one (0.04 %), isoborneol (0.03 %), artemesia alcohol (0.06 %), artemisia ketone (0.32 %), γ-terpinene (0.17 %), *cis*-β-ocimene (0.69 %), *trans*-β-ocimene (0.11 %), limonene (0.10 %), *p*-cymene (0.11 %), 2-pentylfuran (0.05 %), 6-methyl-5-hepten-2-one (0.03 %), sabinene (0.04 %) and α-pinene (0.03 %). Precocenes and piperitone (Yaguchi et al. 2006) and (*E*)- and (*Z*)-spiroethers (Yoshinari et al. 2008) were isolated from chamomile essential oil.

The constituents of chamomile flower oil comprised oxides (59.42 %), hydrocarbons (5.88 %), ethers (11.98 %), acids/esters (3.87 %), aldehydes/ketones (0.79 %), sesquiterpene lactones (6.18 %), alcohols (2.57 %), coumarins/miscellaneous compounds (0.35 %) and unknowns (5.62 %) (Tschiggerl and Bucar 2012). The major constituents were α-bisabolol oxide A (29.92 %), α-bisabolol oxide B (21.13 %), α-bisabolone oxide A (7.87 %), β-farnesene (3.90 %), *cis*-spiroether

(11.67 %) and chamazulene (6.18 %). The major constituents of the flower infusion extract obtained by hydrodistillation were α-bisabolol oxide A (28.26 %), α-bisabolol oxide B (25.92 %), α-bisabolone oxide A (5.83 %), β-farnesene (1.10 %), *cis*-spiroether (4.69 %), chamazulene (19.11 %) and decanoic acid (1.56 %). The major constituents of the flower infusion extract obtained by solid phase extraction were α-bisabolol oxide A (22.80 %), α-bisabolol oxide B (8.09 %), α-bisabolone oxide A (1.59 %), *cis*-spiroether (25.62 %), *trans*-spiroether (6.40 %), chamazulene (1.77 %), achillin (2.88 %), matricarin/acetoxyachillin (5.20 %) and methylumbelliferone (5.55 %). Two sesquiterpene lactones leucodin (0.53 %) and acetoxyachillin were newly indentified together with achillin and matricarin in the chamomile infusion extract. They found that high amounts of spiroethers (ca. 30% in the infusion as compared to ca. 12 % in the genuine oil) and coumarins (ca. 7 %) and reduced amounts of bisabolol oxides (ca. 32 % in the infusion vs. ca. 60 % in the genuine oil) can be regarded as markers of the volatile fraction of chamomile tea. Their results demonstrated that solid phase extraction or other liquid extraction methods should be preferred over hydrodistillation when characterizing the aromatic composition of infusions.

The highest essential oil content was found in fully developed flowers approximately 1 week after beginning of flowering (Franz 1980). The composition of the essential oil depended on the stage of development. Flower buds contained more hydrocarbons and (−)-α-bisabolol, whereas with development of the flowers, chamazulene and the (−)-α-bisabolol oxides increased. The content of enin-dicycloethers increased in the receptacle. In another study, the quantity of α-bisabolol, α-bisabolol oxides A and B and α-bisabolon oxide A in chamomile flower reached a maximum at full bloom and then declined (Arak et al. 1980). The farnesene content of the flower decreased gradually with flower growth and development. The qualitative composition of essential oil remained stable at all stages of flower development. Accumulation of essential oil in chamomile flowers continued during drying, and its quantitative composition depended on the drying method. Harvesting at the early flowering phase and drying in a shaded place were recommended.

Among 30 compounds detected in dried chamomile flowers at two development stages, (*E*)-β-farnesene (49 %), artemisia ketone (10 %) and germacrene D (9 %) were the predominant volatile components in the HS-SPME (headspace solid-phase microextraction) extract, while α-bisabolol oxide A (42 %), chamazulene (21 %) and (*Z*)-spiroether (8 %) were the main essential oil constituents among the 13 compounds obtained by SDSE (steam distillation-solvent extraction) (Rafieiolhossaini et al. 2012). (*E*)-β-farnesene was the only compound which showed significant differences between the development stages of two flowers: stage I, when ligulate flowers start to develop and tubular flowers were still closed, and stage II, when tubular flowers were partially to completely opened. Eliasová et al. (2012) found that polyamine conjugate 1*N*,5*N*,10*N*,14*N*-tetracoumaroyl spermine (tetracoumaroyl spermine) was present mainly in tubular flowers, reaching its maximal content during the 3rd phase of flowering when the corollae of tubular flowers start to open. The later observed decrease could result from a release of pollen that also contained a considerable amount of tetracoumaroyl spermine. They postulated that tetracoumaroyl spermine may play an important role in pollen development. This polyamine from chamomile flower heads could be used for the treatment of several human disorders such as depression and anxiety.

The purified mucilage from chamomile flowers yielded xylose (21 %), arabinose (10 %), galactose (15 %), glucose (7 %), rhamnose (2 %) and glucuronic acid (45 %) (Janecke and Weisser 1964, 1965). The mucilage had a degree of polymerization of approximately 27 (molecular weight 3,500–4,200) and the linkages of sugars in the mucilage were suggested to be predominantly β-glycosidic. Carle and Isaac (1985) reported that chamomile mucilage consists of fructose, arabinose, xylose, glucose, galactose, rhamnose, galacturonic acid and glucosamine and the main chain the polysaccharide tp consists of α-1→4

connected D-galacturone acids. The polysaccharide was later confirmed to be methyl-glucurone oxylane (Füller et al. 1991, 1993). They also identified a neutral fructane of medium molecular mass 3,600 containing 74.3 % fructose, 3.4 % glucose (similar to inulin) and a strongly branched rhamnogalacturonane of medium molecular mass 9,300 consisting of 28 % uronic acid and 3.2 % protein (similar to pectin). These were found to have arabino-3,6-galactane glycoproteins as side chains. In an aqueous alcoholic chamomile extract, only fructanes were found.

Root Phytochemicals

The essential oil of *Matricaria chamomilla* roots contained the sesquiterpenes chamomillol, caryophyllene, caryophyllenepoxide and the polyenes Chamomillaester I and II (Reichling et al. 1984). The essential oil accumulated in schizogenous oil passages and oil cells restricted to the roots. Callus surface cultures of *Matricaria chamomilla* initiated from stems and flower heads produced an essential oil similar to that of the root. It exclusively accumulated in oil cells typical of the roots.

Plant Aerial Parts/Leaf/Cell Culture Phytochemicals

Sesquiterpenes, flavonoids, coumarins and polyacetylenes are considered the most important constituents of the chamomile drug (Schilcher and Kamille 1987). Secondary metabolites found in *M. chamomilla* included isobutyl angelate, 2-methylbutyl angelate, farnesene, β-farnesene, farnesol, (−)-α-bisabolol, bisabolol oxide A, bisabolol oxide B, matricin, chamazulene, guaiazulene, umbelliferone, herniarin, caffeic acid, chlorogenic acid, apigenin, luteolin, apigenin-7-*O*-glucoside, luteolin 7-*O*-glucoside, quercetin and *Z*-enyne dicycloether.

Flavonoids found in chamomile leaves included 7-glucosides of quercetin, isorhamnetin and luteolin together with small amounts of chrysoeriol and apigenin 7-glucoside and their aglyca (Greger 1975).

Polyphenolic compounds (g/kg dry matter) in the aerial chamomile plant parts were determined as follows: chlorogenic acid 1.16 g, 3,5-DCQA (dicaffeoylquinic acid) 2.92 g, 4,5, DCQA 1.61 g, total caffeoyl derivatives 5.69 g, total dihydroxycinnamic acid derivatives 15.89 g, total flavonoids 9.48 g, total dihydroxycinnamic acid derivatives + flavonoids 25.37 g and total polyphenolic compounds 36.79 g (Fraisse et al. 2011). The highest amount of phenolic and flavonoid was detected in the methanol extract of chamomile aerial parts with a mean value of 50.7 and 36.7 % and the lowest in the aqueous extract with a mean value of 3.94 and 1.36 %, respectively (Haghi et al. 2013). The apigenin 7-glucoside (0.21–1.23 g/100 g dry samples) in the crude extracts was much higher than the free apigenin (0.04–0.74 23 g/100 g dry samples). The compounds detected were chlorogenic acid, caffeic acid, *p*-coumaric acid, salicylic acid and flavonoids, rutin, apigenin-7-glucoside, quercetin, luteolin, apigenin, kaempferol and isorhamnetin.

Matricaria chamomilla cell suspensions cultured in a two phase system consisting of an aqueous nutrient medium and a nontoxic lipophilic phase (triglyceride) accumulated (Bisson et al. 1983) a great number of lipophilic substances in the triglyceride phase during the first week of culture period. One of these substances was identified as α-bisabolol. The composition of the essential oil of chamomile hairy root cultures on different media, namely, Murashige-Skoog (MS) medium and Gamborg (B5) media, was found to be similar, but differing in proportion (Máday et al. 1999). The main component of the essential oil was *trans*-β-farnesene, as in the intact roots. Chamomile essential oil was found to contain primarily chamazulene, (−)-α-bisabolol, bisabolol oxides, bisabolon oxide A, *trans*-β-farnesene, α-farnesene, spathulenol, β-eudesmol and *cis*/*trans*-en-in-dicycloethers. Formaldehyde was found in intact plants, micropropagated plants and hairy root cultures of chamomile (Máday et al. 2000). HCHO should not be considered as a side product, but a basic and indispensable component, required for various biological processes in chamomile.

Flavonoids, Coumarins, Mucilages, Mono- and Oligosaccharides Also Had Pharmacological Effects

Among the cultivated and wild chamomile species examined, the wild species from the areas of Szeghalom were found to contain the highest quantity of β-eudesmol (9.25 % in the total essential oil) in intact and organized roots of chamomile cultures (Szöke et al. 2004a). A new component α-selinene (Szöke et al. 2004c) and germacrene D, berkheyaradulene, 4-(2′, 4′, 4′-trimethyl-bicyclo[4.1.0]hept-2′-en-3′-yl)-3-buten-2-one, geranyl-isovalerate and cedrol, were found in the hairy roots of sterile chamomile cultures (Szöke et al. 2004d). These cultures generated the most important terpenoid and polyin compounds characteristics of the intact plant. Among wild chamomile populations in Hungary, a population was found in the area of Szabadkigyós containing significant amounts, on average 48 %-of (−)-α-bisabolol in its inflorescence oil. The intact roots of in vitro cultures contained no (−)-α-bisabolol but contained the sesquiterpene alcohol β-eudesmol. The main components of hairy root cultures derived from wild chamomile rich in (−)-α-bisabolol in the inflorescence oil were *trans*-β-farnesene, α-farnesene, geranyl isovalerate and cedrol. β-Selinene was identified as a new component of the genetically transformed cultures (Szöke et al. 2004b).

Effect of Abiotic Factors on Chamomile Oil and Chemical Composition

Optimum chamomile oil yield was found to be strongly influenced by genotype and optimum ecological conditions (Bettray and Vömel 1992). Herb quantity, individual flower-head weight and days from buds to full-opened flowers of genotypes were reduced with increasing temperature, but content of apigenin, (−)-α-bisabolol and essential oil but not chamazulene rose with increasing temperature, optimal yields were obtained from 20 to 26 °C. The content of apigenin-7-glucoside was influenced by genotype and not temperature. The increased content of the coumarin, umbelliferone, was observed in leaves 12 hours after abiotic stress elicitation by $CuCl_2$ (Repcák et al. 2001). In 48 hours, this amount rose approximately ten times. In the same period of time, a decrease of (*Z*)- and (*E*)-2-β-D-glucopyranosyloxy-4-methoxy cinnamic acid and an increase of herniarin were found. The content of herniarin in the $CuCl_2$-treated chamomile plants rose approximately three times, simultaneously with a decline of its precursor (*Z*)- and (*E*)-2-β-D-glucopyranosyloxy-4-methoxycinnamic acid (Eliasová et al. 2004). The highest amounts of umbelliferone in stressed plants exceeded 9 and 20 times those observed in control plants of the tetraploid and diploid cultivar, respectively. Due to stress, the concentration of ene-yne-dicycloether in leaves decreased by more than 40 %. The pattern of quantity changes of the examined compounds in tetraploid and diploid plants was similar. The aerial parts of chamomile were found to synthesize and accumulate(*Z*)- and (*E*)-2-β-D: -glucopyranosyloxy-4-methoxy cinnamic acids (GMCA), the precursors of phytoanticipin herniarin (7-methoxycoumarin), a compound with anticoagulant properties (Repcák et al. 2009).

Studies found that the yield of dry flower and essential oil per pot, essential oil percent and its composition in *Matricaria chamomilla* varied with irrigation regimes (Pirzad et al. 2006). Highest amount of essential oil percent, yield of dry flower and essential oil per pot were obtained from irrigation at 85 % of the field capacity. However, it was not significantly different from irrigation at 70 % of field capacity. Lowest amount of essential oil percent were obtained when the plants irrigated with 100 and 55 % of field capacity. Minimum yield of dry flower and essential oil per pot were observed when the plants irrigated with 55 % of field capacity, but it was not significantly different from irrigation at 100 % of field capacity. Major constituents of the essential oil for all irrigation treatments were azulene-7-ethyl-1,4-dimethyl, limonene, bisabolol oxides A and B, bisabolone oxide, *trans*-β-farnesene and isobornyl isobutyrate <8-isobutyryloxy>.

Nitrogen deficiency was found to induce changes of free amino acids and coumarin contents

in chamomile leaves (Kovacik et al. 2006). Among secondary metabolites, the sum of 2-β-D-glucopyranosyloxy-4-methoxycinnamic acids increased sharply, herniarin increased slowly and the content of umbelliferone was low in N-deficient plants. A decrease in levels of all detected amino acids, besides histidine, was found. Within aromatic amino acids, tyrosine was the most abundant. The content of free phenylalanine was significantly lower in both control and N-deficient plants when compared to the content of tyrosine. The increase of herniarin glucosidic precursors was attributed to enhancing phenylalanine ammonia-lyase activity under nitrogen deficiency and nitrogen-free carbon skeletons were shunted in to the phenylpropanoid metabolism, including biosynthesis of (*Z*)-and (*E*)-2-β-D-glucopyranosyloxy-4-methoxycinnamic acids.

In the 3 years' experiment (2005–2007), Gosztola et al. (2010) found the moderately warm and relatively wet year of 2006 produced the highest contents of essential oil and also that of its alpha-bisabolol component in 28 wild populations of chamomile and 4 registered cultivars. Although bisabolol oxide A also showed a high variability through the years, its direct connection with weather conditions could not be proven. A moderate variability was established for the proportions of chamazulene and the lowest one for bisabolol-oxide B. Considerable genotype–weather interaction was suggested, especially for the essential oil content and for the ratio of bisabolol oxide A. The results of studies suggested that the hexaconazole-induced tolerance to water deficit stress in chamomile was related to the changes in growth variables, antioxidants and the apigenin-7-glucoside content (Hojati et al. 2011). The exogenous application of 15 mg/l provided better protection when compared to the other concentration.

Chamomile had been reported to have antioxidant, antimicrobial antiplatelet activities in vitro and antiinflammatory, antimutagenic, cholesterol-lowering antispasmodic and anxiolytic activities in vivo (McKay and Blumberg 2006). However, human studies had been limited, and clinical trials examining the purported sedative properties of chamomile tea were lacking.

Antioxidant Activity

Chamomile flower essential oil exhibited good antioxidant when evaluated using the β-carotene bleaching assay (Owlia et al. 2007). Total antioxidant capacity (%) (DPPH scavenging activity) of chamomile aerial plant parts was 2.78 % and contribution from the main caffeoyl derivatives was as follows: chlorogenic acid 4.31 %, 3,5-DCQA (dicaffeoylquinic acid) 13.66 %, 4,5-DCQA 7.53 % and total caffeoyl derivatives 25.50 % (Fraisse et al. 2011).

It was found that chamazulene, a bioactive compound of chamomile, inhibited lipid peroxidation in a concentration and time-dependent manner presenting an IC_{50} of 18 μM after 45 minutes incubation (Rekka et al. 1996). It also inhibited the autoxidation of dimethyl sulfoxide (33 mM) by 76 % at 25 mM and had a weak capacity to interact with DPPH radical.

Anticancer Activity

Exposure of chamomile aqueous and methanolic extracts caused minimal growth inhibitory responses in normal cells, whereas a significant decrease in cell viability was observed in various human cancer cell lines (Srivastava and Gupta 2007, 2009). Chamomile exposure resulted in differential apoptosis in cancer cells but not in normal cells at similar doses. The aqueous and methanolic chamomile flower extracts exhibited antiproliferative and apoptosis inducing effects on human prostate cancer PC-3 cells (Srivastava and Gupta 2009). Exposure of PC-3 cells with aqueous chamomile extract for 24 hours resulted in dose-dependent increase in cell growth inhibition varying from 3 to 25 % at concentration ranging from 25 to 800 μg/ml. Similarly, 4–74 % cell growth inhibition was observed after exposure of PC-3 cells to methanolic chamomile extract ranging from 25 to 800 μg/ml. Exposure of PC-3 cells to both aqueous and methanolic chamomile extract at 200 μg/ml concentration for 24 hours caused induction of apoptosis. Similar cell growth inhibitory and apoptotic effects were noted in other human cancer cell lines including breast, colon, fibrosarcoma and cervical

adenocarcinoma. Apigenin glucosides inhibited cancer cell growth but to a lesser extent than the parent aglycone, apigenin. Ex-vivo experiments suggested that deconjugation of glycosides occurred in vivo to produce aglycone, especially in the small intestine. The cytotoxicity of 10 essential oils including chamomile oil on human prostate carcinoma cell (PC-3) was significantly stronger than on human lung carcinoma (A549) and human breast cancer (MCF-7) cell lines (Zu et al. 2010). Studies showed the combination of 5-fluorouracil, an anticancer agent and bisabololoxide A, one of main constituents in German chamomile, inhibited the growth of human leukaemia K562 cells although the additive inhibition of growth by bisabololoxide A became smaller as the concentration of 5-fluorouracil increased (Ogata-Ikeda et al. 2011). The authors suggested that the simultaneous application of German chamomile containing bisabololoxide A may reduce the dose of 5-fluorouracil.

Studies demonstrated that chamomile and Marigold (*Calendula officinalis*) tea exerted selective dose-dependent cytotoxic action against target cancer cells; cytotoxicity of marigold tea was higher than chamomile (Matić et al. 2012). However, the cytotoxic effect of chamomile tea was very weak to healthy peripheral blood mononuclear cells (PBMC), while the effect of marigold tea on PBMC was more pronounced. Chemical analyses showed that dominant phenolic compounds in examined infusions and decoctions were flavonoid glycosides and hydroxycinnamic acid derivatives.

Antigenotoxic Activity

Three phenols (apigenin, bisabolol and protocatechuic acid) from two medicinal plants, *Matricaria chamomilla* and *Uncaria tomentosa*, showed an antigenotoxic effect against the hydrogen peroxide effect in the wing spot test of *Drosophila melanogaster* and also exhibited tumoricidal activity (Anter et al. 2011). Apigenin (2.24–35.96 mM) showed a lower 50 % inhibitory concentration than bisabolol and protocatechuic acid. They did not exhibit any genotoxic effect. These phenolics also induced apoptosis in HL-60 leukaemia cells. The authors suggested that the antioxidant activity of *Chamomilla* and *Uncaria* could be partially responsible of their beneficial activity.

Antiinflammatory Activity

In Vitro Studies

Chamomile treatment inhibited LPS-induced NO production and significantly blocked interleukin IL-1β, IL-6 and TNFα-induced NO levels in RAW 264.7 macrophages (Bhaskaran et al. 2010). Chamomile caused reduction in LPS-induced iNOS mRNA and protein expression. The study found that chamomile inhibited NO production and iNOS gene expression by inhibiting RelA/p65 activation and supported the utilization of chamomile as an effective antiinflammatory agent. Chamomile infusions from both the capitula and sifted flowers exhibited antiinflammatory activity when tested on phorbol 12-myristate 13-acetate-stimulated human adenocarcinoma gastric cells and human neutrophil elastase (Bulgari et al. 2012) This antiinflammatory activity was postulated due to the inhibition of neutrophil elastase and gastric metalloproteinase-9 activity and secretion, the inhibition occurring in a concentration-dependent manner. The promoter activity was also inhibited and the decrease of metalloproteinase-9 expression was found to be associated with the inhibition of NF-kB driven transcription. The results suggested that the flavonoid-7-glycosides, major constituents of chamomile flowers, may be responsible for the antiinflammatory action of the chamomile infusion observed.

Studies showed that matricine, chamazulene, (−)-α-bisabolol and guaiazulene, components of chamomile exhibited varying degree of antiinflammatory activity in rat paw carrageenan oedema (Jakovlev et al. 1983). Two to four hours after administration, matricine on a molar basis was equally effective as (−)-α-bisabolol. In contrast, chamazulene and guaiazulene showed significantly less activity than (−)-α-bisabolol and matricine. After 4 hours, the pharmacological

effects of guaiazulene decreased significantly, whereas chamazulene showed nearly constant activities over the entire testing period. Safayhi et al. (1994) found that chamazulene inhibited the formation of leukotriene B4 in intact neutrophilic granulocytes, while matricine showed no effect up to 200 μM. Chamazulene (IC_{50}: 2 μM), but not matricine, suppressed the chemical peroxidation of arachidonic acid. Further, matricine (up to 200 μM) had no effects on the cyclooxygenase and 12-lipoxygenase activities in human platelets. Therefore, they concluded that chamazulene, but not matricine, may contribute to the antiinflammatory activity of chamomile extracts by inhibiting the leukotriene synthesis and additional antioxidative effects.

Matricine and chamazulene and (−)-α-bisabolol, components of chamomile essential oil, had no distinct effects on protamine sulphate-provoked degranulation of mast cells from Lewis-1a rats (Miller et al. 1996). The *trans*-enyne-dicycloether partly inhibited the degranulation of rat mast cells in concentrations above 10^{-4} M. Studies in lipopolysaccharide (LPS)-activated RAW 264.7 mouse macrophages suggested that modulation of inducible cyclooxygenase (COX-2) and inducible nitric oxide synthase (iNOS) by apigenin and related flavonoids (genistein, kaempferol) may be important in inflammation and carcinogenesis (Liang et al. 1999). Suppression of transcriptional activation of COX-2 and iNOS by apigenin might mainly be mediated through inhibition of IkB kinase activity induced by LPS or interferon gamma. Chamazulene carboxylic acid, a natural profen and matricin, a degradation product of proazulenic sesquiterpene lactones, both found in chamomile and yarrow, were found to have antiinflammatory activity (Ramadan et al. 2006). Matricin and the yarrow proazulenes were proposed to be antiinflammatory through conversion to chamazulene carboxylic acid.

Aqueous herbal extracts of chamomile (*Matricaria chamomilla*), meadowsweet (*Filipendula ulmaria*) and willow bark (*Salix alba*) and isolated polyphenolic compounds (apigenin, quercetin and salicylic acid, 0–100 μM) were found to have antiinflammatory activity in THP1 macrophages (Drummond et al. 2012). At concentrations of 10 μM, both apigenin and quercetin reduced interleukin IL-6 significantly. Apigenin at 10 μM and quercetin at 25 μM reduced tumour necrosis factor-alpha (TNF-α) significantly. Among the herbal extracts, willow bark had the greatest antiinflammatory activity at reducing IL-6 and TNF-α production. This was followed by meadowsweet and then chamomile.

Animal Studies

Alpha-bisabolol, a component of chamomile oil, suppressed carrageenan-induced paw oedema in rats (Jakolev and Schlichtegroll 1969). In mice, hydroalcoholic extracts of chamomile induced a reduction of oedema similar to the nonsteroidal antiinflammatory agent benzydamine used as reference (Tubaro et al. 1984). Three polysaccharides isolated from chamomile flower heads exhibited remarkable antiinflammatory activity against mouse ear oedema induced by croton oil (Füller et al. 1991, 1993, 2000). Animal studies showed that (−)-α-bisabolol, a bioactive sesquiterpene alcohol obtained from chamomile plant, was found to have peripheral antiinflammatory and antinociceptive activities (Rocha et al. 2011b). In the inflammatory models of paw oedema induced by carrageenan and dextran, the mice treated with (−)-α-bisabolol showed smaller oedemas compared to animals treated only with the vehicle. (−)-α-Bisabolol was capable of reducing paw oedemas induced by 5-HT but not oedemas induced by histamine. (−)-α-Bisabolol exhibited antinociceptive activity in the models of visceral nociception induced by acetic acid and in the second phase of the nociception test induced by the intraplantar administration of formalin. (−)-α-Bisabolol did not have any effect in a thermal nociception model using a hot plate but was able to reduce mechanical inflammatory hypernociception induced by carrageenan. These findings suggested the antinociceptive action of (−)-α-bisabolol was not linked to a central mechanism but instead was related to the inflammatory process. (−)-α-Bisabolol also decreased leukocyte migration, protein extravasations and the amount of TNF-α to the peritoneal cavity in response to carrageenan. Further, (−)-α-bisabolol diminished neutrophil degranulation in response to phorbol myristate acetate.

Clinical Studies

In a phase III double-blind, placebo-controlled study involving 164 patients (men and women), mouthwash containing chamomile flower extract did not decrease 5-fluorouracil-induced stomatitis (Fidler et al. 1996). Mazokopakis et al. (2005) reported a case of methotrexate-induced oral mucositis in a patient with rheumatoid arthritis, who was successfully treated with wild chamomile mouthwashes. Studies showed that hamsters with oral mucositis induced by 5-fluoracil treated with chamomile had a 12-fold greater chance of scoring zero (absence of mucositis) than the control group (Pavesi et al. 2011). Also animals treated with chamomile or the corticoid agent (betamethasone elixir—Celestone®) weighed significantly less than those in the control group. The group treated with the corticoid agent exhibited a more severe clinical condition, whereas the group treated with chamomile exhibited mild mucositis throughout the experiment. Analysis of the histopathological results demonstrated that the group treated with chamomile exhibited a lesser degree of mucositis throughout the evaluation period in comparison to the control and corticoid groups.

In a clinical dose response curve study of 25 patients with phlebitis, peripheral intravenous infusion of chamomile extract elicited an antiinflammatory effect (Reis et al. 2011). The time regression of phlebitis was shorter for groups with 2.5 % concentration (mean = 29.2 hours) and 5 % concentration (mean = 38.8 hours). Local toxicity was almost not observed.

Wound Healing Activity

Studies showed that rats with dead space wounds from excision and incision, treated with chamomile, exhibited a greater reduction in the wound area when compared with the controls (61 % versus 48 %), faster epithelialization and a significantly higher wound-breaking strength after 15 days (Nayak et al. 2007). Additionally, wet and dry granulation tissue weight and hydroxyproline content were significantly higher. In separate studies, male albino rats with induced secondary degree cutaneous burns, treated by rubbing with chamomile extract dissolved in olive oil twice a day, exhibited accelerated wound healing compared to control (Jarrahi 2008). In a subsequent study Jarrahi et al. (2010) demonstrated that chamomile extract dissolved in olive oil administered topically exhibited wound healing potential in linear incisional wound model in male Wistar rats. Studies by Martins et al. (2009) showed that male rats treated with chamomile presented significantly faster wound healing of experimental ulcers in comparison to those treated with corticosteroids, triamcinolone acetonide and clobetasol propionate. Other animal studies showed chamomile to have wound healing effect (Duarte et al. 2011). Rats with inflicted tongue ulcer treated with chamomile showed the best results regarding epithelialization and percentage of collagen fibers after 10 days. As expected, time had a statistically significant effect on fibroblast count, epithelialization, inflammation and wound size; animals sacrificed at 3 days showed the worst results.

In a double-blind trial of 14 patients with weeping wound area after dermabrasion of tattoos, the therapeutic efficacy of chamomile extract was shown by the significant decrease of the weeping wound area as well as the drying tendency (Glowania et al. 1987). In a controlled clinical study of colostomy patients with peristomal skin lesions, the lesions healed significantly faster in the chamomile than in the hydrocortisone group (Charousaei et al. 2011). Stoma patient symptoms (pain and itching) were also resolved more expediently in the chamomile than in the hydrocortisone group. The results suggested that German chamomile could be recommended to relieve itching and inflammation and that twice-daily application facilitated healing of peristomal skin lesions.

Antiviral Activity

Matricaria chamomilla was one of four plants found to inhibit the growth of human herpesvirus 1 and poliovirus 2 in cell culture (Suganda et al. 1983). The hydroalcoholic extract of *Matricaria chamomilla* was found to inhibit poliovirus cellular development and viral RNA synthesis

(Vilaginès et al. 1985). The essential oils anise oil, dwarf-pine oil and chamomile oil exhibited high levels of antiviral activity against acyclovir-sensitive herpes simplex virus type 1 (HSV-1) strain KOS and acyclovir-resistant clinical HSV isolates as well as acyclovir-resistant strain Angelotti (Koch et al. 2008a). At maximum non-cytotoxic concentrations of these plant oils, plaque formation was significantly reduced by 96.6–99.9 %, when herpes viruses were preincubated with drugs before attachment to host cells. No significant effect on viral infectivity could be achieved by adding these compounds during the replication phase. These results indicated that anise oil, dwarf-pine oil and chamomile oil affected the virus by interrupting adsorption of herpes viruses and in a different manner than acyclovir, which was effective after attachment inside the infected cells. Thus, the investigated essential oils were capable of exerting a direct effect on HSV and might be useful in the treatment of drug-resistant viruses. Additionally chamomile oil did not reveal any irritating potential on hen's egg chorioallantoic membrane, demonstrated the highest selectivity index among the oils tested and was highly active against clinically relevant acyclovir-resistant HSV-1 strains. They further found that chamomile oil exhibited a high selectivity index and appeared to be a promising candidate for topical therapeutic application as virucidal agents for treatment of herpes genitalis (Koch et al. 2008b). The inhibitory concentrations (IC_{50}) of chamomile oil against herpes simplex virus type 2 (HSV-2) in-vitro on RC-37 cells was 0.003 %. The results confirmed that essential oils like chamomile affected HSV-2 mainly before adsorption probably by interacting with the viral envelope.

Antimicrobial Activity

Of six matricaria esters (MEs) and two matricaria lactones (MLs), (2*Z*,8*Z*)-ME and (2*E*-8*Z*)-ME gave minimum inhibitory concentrations (MICs) of 50 µg/ml against *Mycobacterium tuberculosis* and respective MICs of 25 and 50 µg/ml against *Mycobacterium avium* (Lu et al. 1998). The (4*Z*,8*Z*)-ML, (2*Z*)-8-dehydro-ME and (2*Z*,8*Z*)-10-angeloyloxy-(2*Z*,8*Z*)-ME showed respective MICs of 12.5, 25, 25 µg/ml against *M. tuberculosis* and MICs of 50, 25, 25 µg/ml against *M. avium*, respectively. The MICs of (2*Z*,8*Z*)-10-tigloyloxy-ME and (2*E*,8*Z*)-10-angeloyloxy-ME and (4*E*,8*Z*)-ML ranged from 50 to >100 µg/ml 1 against both pathogenic mycobacteria.

Chamomile flower essential oil was found to be strongly antimicrobial against *Streptococcus* pathogens in-vitro: *Streptococcus pyogenes*, *S. mutans*, *S. salivarius*, *S. faecalis* and *S. sanguis* with MICs/MBCs values (µg/ml) of 0.1/0.2, 0.5/1.5,0.5/0.8, 4/7 and 0.5/11 respectively (Owlia et al. 2007). Chamomile essential oil was active against three strains of *Staphylococcus aureus*, *Candida albicans* and *Candida krusei* causal agents of acute otitis externa (Nogueira et al. 2008). Gram-positive bacteria were found to be more sensitive to the action of chamomile oil than Gram-negative bacteria (Aggag and Yousef 2009). The oil also showed marked fungicidal activity against *Candida albicans*. The incorporation of the volatile oil in topical preparations for staphylococcal infections was suggested. Chamomile flower oil exhibited antibacterial activity in-vitro against *Helicobacter pylori* (Shikov et al. 2008). The MIC_{90} (minimal inhibitory concentration) and MIC_{50} were 125 and 62.5 mg/ml, respectively. Chamomile oil extract inhibited the production of urease *by H. pylori* and affected the morphological and fermentative properties of *H. pylori.* Studies by Cwikla et al. (2010) found that the herbal extracts showing the highest growth inhibition of *Campylobacter jejuni* were *Calendula officinalis*, *Matricaria recutita*, *Zingiber officinale*, *Salvia officinalis*, *Foeniculum vulgare* and *Silybum marianum*. *C. jejuni* is the most common cause of enteric infections, particularly among children, resulting in severe diarrhoea.

German chamomile essential oil exhibited specific inhibition towards aflatoxin G(1) (AFG(1)) production, and (*E*)- and (*Z*)-spiroethers were isolated as the active compounds from the oil (Yoshinari et al. 2008). The (*E*)- and (*Z*)-spiroethers inhibited AFG(1) production of *Aspergillus parasiticus* with inhibitory concentration 50 %

(IC_{50}) values of 2.8 and 20.8 μM, respectively, without inhibiting fungal growth. The spiroethers were found to inhibit *O*-methylsterigmatocystin conversion to AFG(1) pathway. The (*E*)- and (*Z*)-spiroethers inhibited the enzymatic activity of TRI4 dose-dependently and interfered with 3-ADON (trichothecene 3-acetyldeoxynivalenol) production by *Fusarium graminearum*, with IC_{50} values of 27.1 and 103 μM, respectively. Their results suggested that the spiroethers inhibited AFG(1) and 3-ADON production by inhibiting cytochrome CYPA and TRI4, respectively.

Matricaria chamomilla extract and *Eugenia uniflora* were highly inhibitory against 16 *Staphylococcus aureus* strains (Silva et al. 2012). Studies showed that the antibacterial effect of 50 % aqueous ethanol extract of chamomile flower was attributable to *cis*-spiroether, *trans*-spiroether and the coumarins like herniarin and umbelliferone (Móricz et al. 2012).

In-vitro studies showed that *Aspergillus niger* growth was inhibited dose-dependently with a maximum of approximately 92.50 % at the highest chamomile flower essential oil concentration (Tolouee et al. 2010). A marked retardation in conidial production by the fungus was noticed in relation to the inhibition of hyphal growth. The main changes of hyphae observed by transmission electron microscopy were disruption of cytoplasmic membranes and intracellular organelles, detachment of plasma membrane from the cell wall, cytoplasm depletion and complete disorganization of hyphal compartments. The findings indicated the potential of chamomile essential oil in preventing fungal contamination and subsequent deterioration of stored food and other susceptible materials.

Antidiabetic Activity

In streptozotocin-induced diabetic rats, treatment with different doses of chamomile ethanol extract significantly reduced postprandial hyperglycaemia and oxidative stress, and augmented the antioxidant system (Cemek et al. 2008). In histological investigations, chamomile treatment protected the majority of the pancreatic islet cells, with respect to the control group. As a result, chamomile exhibited significant antihyperglycemic effect and protected beta cells in streptozotocin-induced diabetic rats, in a dose-dependent manner, and diminished the hyperglycaemia-related oxidative stress. In another study, hot water chamomile extract and its major components esculetin (3) and quercetin (7) exhibited moderate inhibition of sucrase with IC_{50} values of 0.9 mg/ml and 72 and 71 μM, respectively (Kato et al. 2008). In a sucrose-loading test, the administration of esculetin (50 mg/kg body weight) fully suppressed hyperglycaemia after 15 and 30 minutes, but the extract (500 mg/kg body weight) and quercetin (50 mg/kg body weight) were less effective. In contrast, a long-term feed test (21 days) using a streptozotocin-induced rat diabetes model revealed that the same doses of chamomile extract and quercetin showed significant suppression of blood glucose levels. It was also found that these samples increased the liver glycogen levels. Further, chamomile extract exhibited potent inhibition against aldose reductase (ALR2), with an IC_{50} value of 16.9 μg/ml, and its components, umbelliferone (1), esculetin (3), luteolin (6) and quercetin (7), could significantly inhibit the accumulation of sorbitol in human erythrocytes. These results clearly suggested that daily consumption of chamomile tea with meals could contribute to the prevention of the progress of hyperglycaemia and diabetic complications. Chamomile extract exhibited antidiabetic potential in alloxan-induced diabetic rats (Estakhr and Javdan 2011). The extract significantly reduced the level of glucose, total cholesterol and triglycerides with an increase in insulin and glycogen concentration to near normal levels in a dose-dependent manner. In another study, administration of chamomile leaf extract 200 mg/kg body weight once daily for 21 days reduced the elevated fasted blood glucose (FBG) by 62.2 %, and the levels of urea, creatinine, uric acid, aspartate transaminase, alanine transaminase, alkaline phosphatase, total cholesterol, triglyceride and LDL-cholesterol were also reduced in streptozotocin-induced diabetic rats (Najla et al. 2012). There was also improvement in the histological changes in the liver. The results

demonstrated that the water extract of *Matricaria chamomilla* possessed a strong hypoglycemic effect in streptozotocin-induced diabetic rats.

Nephroprotective Activity

M. chamomilla injection of rats corrected the hypocalcaemia that resulted from cisplatin nephrotoxicity, normalized the kidney functions, improved the apoptotic markers, reduced the oxidative stress markers and significantly increased the body weight (Salama 2012). Its nephroprotective activity was probably attributed to its antioxidant activities and inhibition of gamma glutamyl transferase activity.

Neuroprotective Activity

Studies showed that the methanolic chamomile extract elicited potent dose-dependent neuroprotective activity against global cerebral ischaemia/reperfusion injury-induced oxidative stress in rats (Chandrashekhar et al. 2010). The extract decreased in lipid peroxidation and increase in the superoxide dismutase, catalase, glutathione and total thiol levels in extract treated groups as compared to ischaemia/reperfusion group. Cerebral infarction area was significantly reduced in extract treated groups as compared to ischaemia/reperfusion group. Another study showed that the methanol extract of German chamomile elicited potent neuroprotective activity against aluminium fluoride-induced oxidative stress in rats (Ranpariya et al. 2011). Chamomile significantly decreased lipid peroxidation and increased superoxide dismutase (SOD), catalase (CAT), glutathione (GSH) and total thiol levels in extract-treated animals as compared with negative control group. The histopathological studies also revealed the potent neuroprotective action of German chamomile against oxidative brain damage.

Immunomodulatory Activity

The heteroglycan polysaccharide was chamomile flower was found to enhance phagocytosis in mice in the chemoluminescence model (Wagner et al. 1985). Maximum activity of 64 % was observed at a concentration of 10–3 mg/ml. Intragastric and parenteral administration of chamomile heteropolysaccharides chamomile was found to normalize the immune response upon air cooling and enhanced (but do not normalize) this process upon immersion cooling (Uteshev et al. 1999). The immunomodulating effect of the heteropolysaccharides upon cooling was attributed to initiation of immunostimulating properties of heavy erythrocytes (macrocytes), activation of immunoregulation cells of peripheral blood, and increased sensitivity of effector cells to helper signals.

Analgesic Activity

Administration of chamomile hydroalcoholic extract before formalin injection showed significant decrease of pain responses in vincristine-induced neuropathy in both phases in mice (Nouri and Abad 2012). Administration of vincristine produced significant increase in pain response in the second phase of the formalin test. Injection of chamomile and vincristine together showed that chamomile was able to decrease the vincristine induced pain significantly.

Anxiolytic/Antidepressant/Sedative Activities

Animal Studies

Lyophilized infusion of chamomile flower administered intraperitoneally in mice displayed a depressive effect on the central nervous system (Della Loggia et al. 1981, 1982). A sedative effect of chamomile flower extract was demonstrated via prolongation of hexobarbital-induced sleep, reduction of spontaneous mobility and reduction of explorative activity in mice. In contrast to diazepam, chrysin and apigenin do not cause reductions in memory. Restriction stress-induced increases in plasma ACTH (adrenocorticotropic hormone) levels in normal and ovariectomized rats were decreased by inhalation of chamomile flower oil vapour and administration

of diazepam (Yamada et al. 1996). Inhaling chamomile vapour induced greater decreases in plasma ACTH levels in ovariectomized rats then treatment with diazepam; this difference was not observed in normal rats. The plasma ACTH level decreased further when diazepam was administered along with inhaling chamomile oil vapour. Flumazenil was found to block the decrease in plasma ACTH level induced by inhaled chamomile oil vapour.

Apigenin, from chamomile flower head, exhibited clear anxiolytic activity in mice in the elevated plus maze without evidencing sedation or muscle relaxant effects at doses similar to those used for classical benzodiazepines, and no anticonvulsant action was detected (Viola et al. 1995). Apigenin competitively inhibited the binding of flunitrazepam and had no effect on muscarinic receptors, alpha 1-adrenoceptors and on the binding of muscimol to GABAA receptors. However, a tenfold increase in dosage produced a mild sedative effect since a 26 % reduction in ambulatory locomotor activity and a 35 % decrement in hole-board parameters were evident. The results indicated apigenin to be a ligand for the central benzodiazepine receptors exerting anxiolytic and slight sedative effects but not being anticonvulsant or myorelaxant. Electrophysiological studies performed on cultured cerebellar granule cells showed that apigenin, from methanol chamomile flower extract, reduced GABA (gamma-aminobutyric acid)-activated Cl^- currents in a dose-dependent fashion (Avallone et al. 2000). Apigenin reduced the latency in the onset of picrotoxin-induced convulsions. Further, apigenin injected i.p. in rats reduced locomotor activity, but did not demonstrate anxiolytic, myorelaxant or anticonvulsant activities. The results suggested that the inhibitory activity of apigenin on locomotor behaviour in rats could not be ascribed to an interaction with GABA(A)-benzodiazepine receptor but to other neurotransmission systems, since it was not blocked by Ro 15-1788. Of two flavonoids, apigenin and chrysin, contained in *Matricaria chamomilla*, chrysin exhibited a clear anxiolytic effect when injected at the dose of 1 mg/kg in rats, apigenin failed to exert this activity (Zanoli et al. 2000). The anxiolytic effect of chrysin, which was blocked by the injection of Flumazenil, could be linked to an activation of the GABA(A) receptor unit.

Studies suggest that treatment with Chamomilla 6cH was found to be related to the recovery of basal behavioural conditions in mice subjected to stressful conditions (Pinto et al. 2008). Mice who cohabitated with a sick cagemate showed a decrease in their general activity, but those treated with Chamomilla 6cH were less severely affected. In the open field area model, only the amitriptyline and ethanol treated mice showed significant excitatory behaviour; chamomilla 6cH-treated animals scored intermediate between water control and ethanol or amitriptyline.

Studies found that *M. recutita* exhibited benzodiazepine-like effects of *Matricaria recutita* on morphine withdrawal syndrome in adult male Wistar rats (Kesmati et al. 2008). Chamomile decreased significantly the number of climbing in comparison to control group, but it had no significant effect on other signs. Flumazenil increased significantly the signs of jumping and face washing in comparison to control group. Chamomile in the presence of flumazenil exhibited no sedative effect and the climbing behaviour increased significantly. The sedative effect of *M. recutita* on morphine withdrawal syndrome was suggested to be related to its benzodiazepine-like components that acted on benzodiazepine receptors. Studies showed that pretreatment of male mice with different doses of chamomile hydro-methanolic extract increased the latency of the beginning time of seizure induced by picrotoxin (Heidari et al. 2009). The most effective dose was 200 mg/kg. In addition, this dose delayed the time of death in mice but had no effect on the death rate.

Matricaria recutita essential oil at 50 and 100 mg/kg significantly increased the numbers of spontaneous locomotor activities, exhibited anxiogenic effect in the open field, elevated plus-maze and social interaction tests and decreased the immobility times of mice in tail suspension tests (Can et al. 2012). The falling latencies in rotarod tests did not change. This activity profile of the essential oil was similar to the typical psychostimulant caffeine.

Clinical Studies

In a small observation study of three 14–16-year-old male psychiatric outpatients, diagnosed with attention-deficit disorder (ADHD), administration of chamomile was found to improve patients' mean score for Conners's hyperactivity, inattention and immaturity factors (Niederhofer 2009). The small study indicated that chamomile might be a slightly effective treatment also for ADHD.

In a randomized, double-blind, placebo-controlled efficacy trial involving 57 patients with mild to moderate generalized anxiety disorder (GAD) Amsterdam et al. (2009) observed a significantly greater reduction in mean total Hamilton Anxiety Rating (HAM-A) score during chamomile versus placebo therapy. They found that chamomile may have modest anxiolytic activity in patients with mild to moderate GAD. They conducted another randomized, double-blind, placebo-controlled study, to examine the antianxiety and antidepressant action of oral chamomile extract in participants with symptoms of comorbid anxiety and depression (Amsterdam et al. 2012). Of the 57 participants in the 2009 trial, 19 had anxiety with comorbid depression; 16 had anxiety with a past history of depression; and 22 had anxiety with no current or past depression. They observed a significantly greater reduction over time in total Hamilton Depression Rating (HAM-D) scores for chamomile versus placebo in all participants. They also observed a clinically meaningful but nonsignificant trend for a greater reduction in total HAM-D scores for chamomile versus placebo in participants with current comorbid depression. They found a significantly greater reduction over time for chamomile versus placebo in all participants in the HAM-D core mood item scores and a clinically meaningful but nonsignificant trend for a greater reduction over time for chamomile versus placebo in participants without current or past depression. Their findings suggested that chamomile may provide clinically meaningful antidepressant activity that occurs in addition to its previously observed anxiolytic activity. In a double-blind, randomized, placebo-controlled of subjects suffering generalized anxiety disorder, chamomile showed potential for use in treating such disorder (Faustino et al. 2010).

Inhibition of Morphine Dependence

Animal studies showed that the withdrawal behavioural manifestations and weight loss were inhibited significantly by chronic co-administration of *M. chamomilla* extract with morphine (Gomaa et al. 2003). Administration of a single dose of *M. chamomilla* before the naloxone challenge in morphine-dependent rats abolished the withdrawal behavioural manifestations. The dramatic increase of plasma cAMP induced by naloxone-precipitated abstinence was prevented by chronic co-administration of *M. chamomilla* extract with morphine. The results suggested that *M. chamomilla* extract inhibited the development of morphine dependence and expression of abstinence syndrome.

Sleep Enhancing Activity

A significant decrease in sleep latency in rats was observed with chamomile extract at a dose of 300 mg/kg, but no significant effects were observed on total times of wakefulness, non-rapid eye movement (non-REM) sleep, REM sleep and delta activity during non-REM sleep (Shinomiya et al. 2005). Chamomile extract was found to have benzodiazepine-like hypnotic activity.

In a randomized, double-blind, placebo-controlled pilot trial in 34 patients aged 18–65 years with DSM-IV (*D*iagnostic and Statistical Manual of Mental Disorders) primary insomnia for ≥6-months, chamomile, 270 mg twice daily for 28 days, was found to provide modest benefits of daytime functioning and mixed benefits on sleep diary measures relative to placebo (Zick et al. 2011).

Oral Hygiene Activity

Chamomile hydroalcoholic extract was found to be significantly more effective than distilled water and tea tree oil (*Melaleuca alternifolia*) as an intracanal irrigant for the removal of the smear layer (Sadr Lahijani et al. 2006). The most effective removal of smear layer occurred with the use

of NaOCl with a final rinse of 17 % ethylenediaminetetraacetic acid (EDTA) (negative control) followed by the use of a chamomile extract. The use of a 2.5 % NaOCl solution alone, without EDTA and that of tea tree oil, was found to have only minor effects.

Gastroprotective/Antiulcerogenic Activities

Torrado et al. (1995) reported significant protective effect against gastric toxicity induced by 200 mg/kg acetylsalicylic acid was achieved after oral administration of chamomile oil to rats at doses ranging from 0.8 to 80 mg/kg (−)-α-bisabolol. Earlier, studies found that oral administration of chamomile flower extract and (−)-α-bisabolol inhibited the development of ulcers induced in rats by indomethacin, stress or ethanol (Szelenyi et al. 1979). They also reduced healing time for ulcers induced by chemical stress (acetic acid) or heat coagulation.

Extracts from the plants *Iberis amara*, *Melissa officinalis*, *Matricaria recutita*, *Carum carvi*, *Mentha x piperita*, *Glycyrrhiza glabra*, *Angelica archangelica*, *Silybum marianum* and *Chelidonium majus*, singly and combined in the form of a commercial preparation, STW 5 (Iberogast) and a modified formulation, STW 5-II, lacking the last 3 constituents, were found to have antiulcerogenic activity against indomethacin-induced gastric ulcers of rats (Khayyal et al. 2001). All extracts produced a dose-dependent antiulcerogenic activity associated with a reduced acid output and an increased mucin secretion, an increase in prostaglandin E2 release and a decrease in leukotrienes. The most beneficial effects were observed with the combined formulations STW 5 and STW 5-II in a dose of 10 ml/kg b.w., comparable with cimetidine in a dose of 100 mg/kg b.w. The antiulcerogenic activity of the extracts was also confirmed histologically. The cytoprotective effect of the extracts could be partly due to their flavonoid content and to their free radical scavenging properties.

Oral administration of chamomile extract at 400 mg/kg was found to be effective in preventing HCl-ethanol-induced gastric ulceration in mice and did not produce toxic effects in doses up to 5,000 mg/kg (Karbalay-Doust and Noorafshan 2009). In another study, chamomile extract was found to reduce gastric damage in rats at all doses tested (Bezerra et al. 2009). α-bisabolol and its bioactive component at oral doses of 50 and 100 mg/kg markedly attenuated the gastric lesions induced by ethanol by 87 and 96 %, respectively. Further, the α-bisabolol effect was significantly reduced in rats pretreated with glibenclamide, an inhibitor of K^+ATP^- channel activation. The results suggested that α-bisabolol reduced the gastric damage induced by ethanol, at least in part, by the mechanism of activation of K^+ATP^- channels. In another study, oral administration of (−)-α-bisabolol (bioactive sesquiterpene from chamomile) 100 and 200 mg/kg was able to protect the gastric mucosa from ethanol (0.2 ml/animal p.o.) and indomethacin-induced ulcer (20 mg/kg p.o.) in mice (Moura Rocha et al. 2010). Administration of L-NAME (10 mg/kg i.p.), glibenclamide (10 mg/kg i.p.) or indomethacin (10 mg/kg p.o.) was not able to revert the gastroprotection promoted by (−)-α-bisabolol 200 mg/kg on the ethanol-induced ulcer. Dosage of gastric reduced glutathione (GSH) levels showed that ethanol and indomethacin reduced the content of nonprotein sulfhydryl (NP-SH) groups, while (−)-α-bisabolol significantly decreased the reduction of these levels on ulcer-induced mice, but not in mice without ulcer. The data indicated that the gastroprotective effect on ethanol and indomethacin-induced ulcer promoted by (−)-α-bisabolol may be associated with an increase of gastric sulfhydryl groups bioavailability leading to a reduction of gastric oxidative injury induced by ethanol and indomethacin. Using ethanol-induced gastric lesions model, Rocha et al. (2011a) found that (−)-α-bisabolol-induced gastroprotection was associated with reduction in oxidative stress caused by lipid peroxidation, increase in superoxide dismutase activity and reduction in inflammatory neutrophil migration in the gastric mucosa.

Pretreatment with chamomile hydroalcoholic extract significantly reduced ethanol-induced gastric lesions in rats (Cemek et al. 2010).

Chamomile significantly reduced malonaldehyde, and significantly increased GSH (reduced glutathione) levels in gastric tissue or whole blood. Serum beta-carotene and retinol levels were significantly higher in the 200 mg/kg chamomile-administered group with respect to control. The gastroprotective effect of chamomile was attributed, at least in part, upon the reduction in lipid peroxidation and augmentation in antioxidant activity. Studies showed that treatment with aqueous chamomile extract significantly and dose-dependently reduced gastric ulcer index induced by ethanol in albino rats (Al-Hashem 2010). Chamomile treatment prevented the fall in glutathione (GSH) level induced by ethanol and increased GSH level. Chamomile treatment alleviated, or completely resolved ethanol-induced degenerative alterations, including disorganization of cell nuclei and gland morphology with erosion in the gastric mucosa and interrupted muscularis mucosa.

Chamomile flowers have been traditionally used in the treatment of gastrointestinal disorders such as dyspepsia, gastritis and peptic ulcer disease. In a study of in-vitro susceptibility of 15 *Helicobacter pylori* strains to botanical extracts, Mahady et al. (2005) found that the methanol extracts of *Myristica fragrans* (seed) had a MIC of 12.5 µg/ml; *Zingiber officinale* (ginger rhizome/root) and *Rosmarinus officinalis* (rosemary leaf) had an MIC of 25 µg/ml. In comparison methanol extracts of *Matricaria recutita* (flowers) and *Ginkgo biloba* (leaves) were less potent with a MIC >100 µg/ml.

In double-blind, randomized, placebo-controlled, multicenter trial of 120 patients with functional dyspepsia, the herbal preparation (bitter candy tuft, matricaria flower, peppermint leaves, caraway, licorice root and lemon balm) tested improved dyspeptic symptoms significantly better than placebo after 8 weeks treatment (Madisch et al. 2004).

Hepatoprotective Activity

The methanol extract of chamomile capitula (300 mg/kg) exhibited significant antioxidant activity against CCl4 induced liver injury in rats (Gupta et al. 2006). The extract exhibited significant antioxidant activity by showing increased levels of glutathione peroxidase, glutathione-s-transferase, glutathione reductase, superoxide dismutase, catalase and glutathione. It decreased lipid peroxidation and halted hepatic damage. The aqueous ethanolic extract of chamomile capitula exhibited hepatoprotective activity against paracetamol-induced hepatic damage in albino rats (Gupta and Misra 2006). Chamomile extract protected against decreases in the levels of GSH, blood glutathione, serum marker enzymes, liver Na^+K^+-ATPase activity, abnormal high level of serum alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) bilirubin and increased liver thiobarbutiric acid-reactive substance resulting from hepatocellular damage and hepatic dysfunction induced by paracetamol.

Antipruritic/Antiallergic Activity

In a study 161 patients suffering from inflammatory dermatoses on hands, forearms and lower legs, 3–4 weeks application of Kamillosan cream (containing chamomile extracts) was found to be as effective as hydrocortisone for eczema and more effective than 0.75 % fluocortin butyl ester and 5 % bufexamac (Aertgeerts et al. 1985). A controlled and physician-blind randomized trial found no major differences in skin reactions after acute radiation between areas treated with Kamillosan cream (chamomile) and almond ointment (Maiche et al. 1991). None of these agents could prevent the skin reaction and all patients got grade 1 erythema. A lesser number and a later appearance of grade 2 reactions suggested an advantage for Kamillosan cream, although the difference between the results achieved was not statistically significant. The patients, however, preferred Kamillosan cream because of its rapid absorption and stainlessness. In a partially double-blind, randomized study carried out as a half-side comparison, 2 weeks application of Kamillosan(R) cream showed a mild superiority towards 0.5 % hydrocortisone and a marginal difference as compared to placebo in atopic eczema (Patzelt-Wenczler and Ponce-Pöschl 2000).

Intradermal application of liposomal apigenin-7-glucoside inhibited in a dose-dependent manner skin inflammation caused by xanthine oxidase and cumene hydroperoxide in rats (Fuchs and Milbradt 1993). Glucose-oxidase (hydrogen peroxide)-induced dermatitis was not significantly inhibited. The results are in good agreement with the in-vitro superoxide anion radical and peroxyl radical scavenging properties of apigenin and indicated that its antioxidant properties may have contributed to the antiinflammatory effect in this model system. The ethyl acetate extract of German chamomile dose-dependently suppressed compound 48/80-induced scratching without affecting body weight increase in ddY mice (Kobayashi et al. 2003). The ethyl acetate fraction of the ethanol extract and the ethanol extract of hot water extraction residue of German chamomile flower also showed strong inhibition on the compound 48/80-induced scratching. The inhibitory effects of the dietary intake of the German chamomile extracts on compound 48/80-induced itch-scratch response were comparable to oxatomide (10 mg/kg, p.o.), an antiallergic agent. The combined administration of the ethyl acetate extract of German chamomile (300 mg/kg) and antihistamine H1 antagonists, oxatomide (10 mg/kg) and fexofenadine (10 mg/kg), remarkably enhanced the antipruritic effects of these agents mice (Kobayashi et al. 2005). They found that the co-medication with the ethyl acetate extract or essential oil of German chamomile and antihistamines might be effective for the pruritus which could not be perfectly resolved alone by conventional antihistamines.

The methanol chamomile extract exhibited inhibitory effects on anaphylaxis induced by compound 48/80 and significant dose-dependent antipruritic property by inhibiting mast cell degranulation in rats (Chandrashekhar et al. 2011). Dose-dependent reduction in the histamine release, along with decreased release of serum, rat peritoneal and bronchoalveolar lavage fluid nitric oxide (NO) levels was observed. The results suggested the methanol chamomile extract exhibited potent antiallergic activity by inhibition of histamine release from mast cells.

Spasmolytic Activity

Alcoholic chamomile extracts obtained from ligulate flowers appeared to exert stronger spasmolytic activity than from tubular florets (Achterrath-Tuckermann et al. 1980; Carle and Gomaa 1992). Beside flavonoids, components of the essential oil were assumed to contribute to the spasmolytic effects. (−)-α-bisabolol, (+)-α-bisabolol and, to a lower extent their oxides, the chamomile oil itself, *cis*-spiroether, a standardized hydroalcoholic extract (Kamillosan®) and the coumarin derivatives umbelliferone and herniarin, exhibited spasmolytic activity in isolated guinea pig ileum. The hydrophilic (flavonoids) and the lipophilic components (essential oil) of chamomile were found to contribute to the musculotropic antispasmodic effect.

The extract of dried chamomile flowers was found to contain a potent tachykinin the extract of dried. The structure of the antagonist was identifiedasN1,N5,N10,N14-tetrakis[3-(4-hydroxyphenyl)-2-propenoyl]-1,5,10,14-tetraazatetradecane (tetracoumaroyl spermine, 1a) (Yamamoto et al. 2002). The Ki values of 1a, estimated from the inhibitory action on the substance P (SP)-induced contraction of the guinea pig ileum and the inhibition of the binding of [3H][Sar9, Met(O2)11] SP to human NK1 receptors, were 21.9 and 3.3 nM, respectively. The antagonist was concentrated in chamomile pollen. Another new compound found in the flower, N1,N5,N10-tris[3-(4-hydroxyphenyl)-2-propenoyl]-1,5,10,14-tetraazatetradecane, exhibited no tachykinin antagonist activity.

Inhibition of human cAMP-phosphodiesterase was found to be a mechanism for the spasmolytic effect of *Matricaria recutita* (Maschi et al. 2008). Chamomile flower/capitula infusion inhibited human platelet cAMP- and cGMP-phosphodiesterases (PDE) activity (IC_{50} = 17.9–40.5 µg/ml), while cGMP-PDE5 was less affected (−15 % at 50 µg/ml). Among the individual compounds tested, only flavonoids showed an inhibitory effect (IC_{50} = 1.3–14.9 µM), contributing to around 39 % of the infusion inhibition; other compounds responsible for cAMP-PDE inhibition still remain unknown.

Antidiarrhoeal Activity

The results obtained in the study by Calzada et al. (2010) provided some scientific support to the popular use of 23 of the plants including *M. recutita*, tested for the treatment of gastrointestinal disorders such as diarrhoea in Mexican traditional medicine. These plants showed moderate inhibitory activity (30–100 %) against charcoal-gum acacia-induced hyperperistalsis in rats. Their activities were greater than that of or equal to loperamide (34 % of inhibition at doses of 10 mg/kg) drug used as control.

Antimutagenic Activity

Studies found chamomile essential oil exhibited a dose-dependent inhibitory effect on the sister chromatid exchanges formed by both mutagens, daunorubicin and methyl methanesulfonate (Hernández-Ceruelos et al. 2002). In the case of daunorubicin, a statistically significant result was observed in the three tested doses: from the lowest to the highest dose, the inhibitory values corresponded to 25.7, 63.1 and 75.5 %. No alterations were found with respect to the cellular proliferation kinetics, but a reduction in the mitotic index was detected. In the case of methanesulfonate, the inhibitory values were 24.8, 45.8 and 60.6 %; no alterations were found in either the cellular proliferation kinetics or in the mitotic indices. Their results suggested chamomile oil may be an effective antimutagen. Alpha-bisabolol (BISA), a sesquiterpene alcohol found in chamomile oil, markedly and dose-dependently reduced the mutagenic effects of aflatoxin B1, 2-aminoanthracene and 2-aminofluorene, cyclophosphamide and benzo[a]pyrene, B[a]P mutgens using TA100, TA98, TA97a and TA1535 *Salmonella typhimurium* strains, without and with addition of S9 mixture microsome assay (Gomes-Carneiro et al. 2005). Gomes-Carneiro showed weak inhibitory effect on 4-nitroquinoline-*N*-oxide and 2-nitrofluorene and did not alter the mutagenicity of sodium azide and 4-nitroquinoline-*N*-oxide mutagens. It was also found that BISA inhibited pentoxyresorufin-o-depentylase and ethoxyresorufin-*o*-deethylase, markers for cytochromes CYP2B1 and 1A1 in rat liver microsomes. The results suggested that BISA-induced antimutagenicity could be mediated by an inhibitory effect on the metabolic activation of these promutagens.

Antiarthritic Activity

In a placebo-controlled double-blind crossover trial of 42 patients (40–76 years old) with painful knee osteoarthritis, administration of the herbal pomade Marhame-Mafasel (comprising a mixture of medicinal herbs including *Arnebia euchroma* and *Matricaria chamomilla*) elicited positive analgesic (pain reduction) effect in primary knee osteoarthritis (Soltanian et al. 2010) The herbal joint pomade Marhame-Mafasel had a significantly greater mean change in score compared to the placebo group for osteoarthritis severity.

Cardiovascular Activity

Haemodynamic measurements were obtained prior to and 30 minutes after the oral ingestion of chamomile tea on 12 patients with cardiac disease who underwent cardiac catheterization (Gould et al. 1973). With chamomile tea, the patients demonstrated a small but significant increase in the mean brachial artery pressure. No other significant haemodynamic changes were observed.

All the test beverages containing different polyphenol structures and being rich in either phenolic acids (chlorogenic acid in coffee), monomeric flavonoids (herb teas), chamomile (*Matricaria recutita*), vervain (*Verbena officinalis*), lime flower (*Tilia cordata*), pennyroyal (*Mentha pulegium*) and peppermint (*Mentha piperita*) or complex polyphenol polymerization products (black tea and cocoa) were found to be potent inhibitors of Fe absorption and reduced absorption in a dose-dependent fashion depending on the content of total polyphenols (Hurrell et al. 1999). Compared with a water control meal, beverages containing 20–50 mg total polyphenols/serving

reduced Fe absorption from the bread meal by 50–70 %, whereas beverages containing 100–400 mg total polyphenols/serving reduced Fe absorption by 60–90 %. Inhibition by black tea was 79–94 %, peppermint tea 84 %, pennyroyal 73 %, cocoa 71 %, vervain 59 %, lime flower 52 % and chamomile 47 %. At an identical concentration of total polyphenols, black tea was more inhibitory than cocoa, and more inhibitory than herb teas chamomile, vervain, lime flower and pennyroyal, but was of equal inhibition to peppermint tea.

Menopause Treatment Activity

In a placebo-controlled experiment on 55 postmenopausal women who complained of hot flushes and refused hormonal therapy, 12-week treatment with Climex (*Angelica sinensis* and *Matricaria chamomilla* plant extracts) appeared to be effective for menopausal symptoms without apparent major adverse effects (Kupfersztain et al. 2003). This hormone-free preparation may be used as an important modality for menopausal women with contraindications for hormone replacement therapy.

Antiosteoporotic Activity

Studies demonstrated that all the plant extracts (*Sideritis euboea*, *Sideritis clandestina*, *Matricaria chamomilla* and *Pimpinella anisum*) studied at a concentration range 10–100 μg/ml stimulated osteoblastic cell differentiation and exhibited antiestrogenic effect on breast cancer cells without proliferative effects on cervical adenocarcinoma (HeLa) ells (Kassi et al. 2004). The presence of estradiol inhibited the antiestrogenic effect induced by the extracts on MCF-7 breast cancer cells, suggesting an estrogen receptor-related mechanism. The authors concluded that the aqueous extracts derived from *Sideritis euboea*, *Sideritis clandestina*, *Matricaria chamomilla* and *Pimpinella anisum* may form the basis to design 'functional foods' for the prevention of osteoporosis.

Antifertility Activity

Chamomile hydroalcoholic extract was found to decrease spermatozoa count and motility, spermatozoon tail length and serum testosterone level and increase serum estradiol level in male adult rat (Karbalay-Doust et al. 2010). The body weight and weight and volume of the testis in the control and treated rats did not change significantly.

Antileishmanial Activity

Chamomile essential oil was found to be active against *Leishmania infantum* promastigotes, the main species responsible for human leishmaniasis in Spain (Morales-Yuste et al. 2010). At the two highest concentrations tested (1,000 and 500 μg/ml), (−)α-bisabolol (a principal chamomile oil component) and pentamidine (control agent) achieved 100 % inhibition of *L. infantum* promastigote. 80 % ethanol chamomile extract inhibited *Leishmania mexicana* growth by 100 % at protein concentration of 0.8 mg/ml (Shnitzler et al. 1996). Chamomile also inhibited human cell lines HeLa growth by 78 % and T_4 growth 100 %.

Anthelminthic Activity

Studies found *Matricaria chamomilla* essential oil and two of its main components (chamazulene and α-bisabolol) to have larvicidal activity against the L(3) larvae of the nematode Anisakis type I in in vitro and in vivo assays (Romero et al. 2012). The essential oil (125 μg/ml) caused the death of all nematodes, which showed cuticle changes and intestinal wall rupture. In the in-vivo assays, only 2.2 % of infected rats treated with the essential oil showed gastric wall lesions in comparison to 93.3 % of control. Chamazulene was ineffective, while α-bisabolol showed high activity to that of the essential oil in in vitro tests but proved less active in vivo. These findings suggested that the larvicidal activity may result from the synergistic action of different compounds of

M. chamomilla essential oil. Neither of the tested products induced irritative damage in the intestinal tissues.

Herb/Drug Interaction Activity

The crude chamomile essential oil demonstrated inhibition of four selected human cytochrome P450 enzymes (CYP1A2, CYP2C9, CYP2D6 and CYP3A4), with CYP1A2 being more sensitive than the other isoforms (Ganzera et al. 2006). Three constituents of the oil, namely, chamazulene (IC_{50} = 4.41 μM), *cis*-spiroether (IC_{50} = 2 μM) and *trans*-spiroether (IC_{50} = 0.47 μM), showed to be potent inhibitors of this enzyme, also being active towards CYP3A4. CYP2C9 and CYP2D6 were less inhibited; only chamazulene (IC_{50} = 1.06 μM) and α-bisabolol (IC_{50} = 2.18 μM) revealed a significant inhibition of the latter. These in-vitro data suggested that chamomile preparations containing constituents that inhibited the activities of major human drug metabolizing enzymes may interact with drugs whose route of elimination is mainly via cytochromes (especially CYP1A2). Sega and Pilote (2006) reported a case of a 70-year-old woman who, while being treated with warfarin, was admitted to hospital with multiple internal haemorrhages after having used chamomile products (tea and body lotion) to soothe upper respiratory tract symptoms. This case highlighted a theoretical risk for potentiation, since chamomile contained coumarins.

Inhibition of Mycotoxin Production

Precocenes and piperitone isolated from chamomile essential oil inhibited deoxynivalenol production by *Fusarium graminearum* and may be useful for protecting crops from deoxynivalenol contamination (Yaguchi et al. 2006). Precocenes I and II and piperitone inhibited the production of 3-acetyldeoxynivalenol, a biosynthetic precursor of deoxynivalenol produced by *F. graminearum* in a liquid and solid cultures. Precocene II and piperitone decreased the mRNA levels of *Tri4*, *Tri5*, *Tri6* and *Tri10* encoding proteins required for deoxynivalenol biosynthesis. The (*E*)-spiroether and (*Z*)-spiroether isolated from chamomile essential oil showed specific inhibition towards aflatoxin G(1)(AFG(1)) production by the fungus *Aspergillus parasiticus* without inhibiting fungal growth (Yoshinari et al. 2008). (*E*)- and (*Z*)-spiroethers inhibited the enzymatic activity of TRI4 dose-dependently and interfered with 3-acetyldeoxynivalenol production by *Fusarium graminearum.*

Insecticidal Activity

Treatment with the volatile oils of chamomile flowers (LD_{50} 76 μg/fly) and *Clerodendron inerme* leaf (LD_{50} 64 μg/fly) induced serious effects on the biology and biotic potential of the adult house fly *Musca domestica* (Shoukry 1997). Treatment significantly increased the acidic and the aromatic amino acids during oogenesis and significantly decreased content of aliphatic amino acids. The concentration of basic and the sulphur amino acids was varied with the two treatments, and the amino acid was completely disappeared in the ovaries of the treated flies.

Pharmacokinetic Studies

After oral ingestion of 40 ml of a hydroethanolic chamomile flower extract (containing 225.5 mg of apigenin 7-glucoside, 22.5 mg of apigenin and 15.1 mg of herniarin per 100 ml), no flavones could be detected in blood plasma nor in 24-hours urine of the female volunteer, while herniarin was found in both (maximum plasma concentration of 35 ng/ml; 0.324 mg in 24-hours-urine) (Tschirsch and Hölzl 1993).

Allergy Problem

Subiza et al. (1990) reported seven hay fever patients that suffered from conjunctivitis, two of them also had lid angioedema after eye washing with chamomile tea. All seven patients had positive

skin prick tests to the chamomile tea extract, *Matricaria chamomilla* pollen and *Artemisia vulgaris* pollen extracts. Positive conjunctival provocations were also observed in all the patients with the chamomile tea extract. They found that chamomile tea eye washing could induce allergic conjunctivitis and attributed this to pollens contained in these infusions as the allergens responsible for these reactions. German chamomile, a common and well-known allergen, had been reported to elicit type-IV allergic reactions such as allergic and systemic contact dermatitis in some people consuming chamomile tea (Pereira et al. 1997; Rodríguez-Serna et al. 1998).

In a clinical study conducted between 1991 and 2009, 36 selected patients with known or suspected Compositae contact allergy were patch tested with herniarin (from chamomile) 1 % petrolatum (Paulsen et al. 2010). Among 36 patients tested, there was 1 positive and 3 doubtful positive reactions to herniarin. All 4 patients had a relevant contact allergy to German chamomile, whereas the majority of the remaining 32 patients had chamomile allergy of unknown relevance. Sensitization may occur through, for example, external use of chamomile tea or use of chamomile-containing topical herbal remedies. Andres et al. (2009) reported a case of a 38-year-old Caucasian man who developed an episode of severe anaphylaxis with generalized urticaria, angioedema and severe dyspnoea 1 hour after consuming chamomile tea. Laboratory examination demonstrated a total serum IgE of 123 kU/l with specific IgE against chamomile (4.94 kU/l, class 3). Skin prick test and labial provocation test with chamomile elicited a strong positive reaction. Their case confirmed the presence of a type-I allergy to orally ingested chamomile. Contact dermatitis from bisabolol, a primary component in German chamomile, had been reported in Europe and in the United States (Russell and Jacob 2010). Patch testing with bisabolol-containing products or bisabolol may be useful in the work-up of patients with presumptive allergic contact dermatitis or potentially worsening atopic dermatitis. Patients sensitized to bisabolol should be counselled to avoid any bisabolol-containing products.

Toxicity/Safety Studies

Bisabololoxide A (BSBO), a principal constituent in German chamomile, was found to induce apoptosis and cellular changes of rat thymocytes when incubated with BSBO at concentrations of 30 μM for 24 hours (Ogata et al. 2010). The significant changes in cellular parameters of rat thymocytes by BSBO were not observed when the concentration was 10 μM or less. Furthermore, the short incubation (3 hours) of cells even with 30–100 μM BSBO did not significantly affect the cells. Therefore, the authors suggested BSBO to be practically safe when German chamomile is conventionally used.

Traditional Medicinal Uses

Chamomile has been used as herbal folk medicine since antiquity in ancient Egypt, Greece and Rome (Mann and Staba 1986). The herb is considered antispasmodic, carminative, diaphoretic, sedative, stomachic and emmenagogue (Grieve 1971; Mann and Staba 1986; Martens 1995; Alberts 2009). The herb has been used as bitter, tonic, insect repellent, antiseptic, antispasmodic, sudorific and anthelminthic and as a folk remedies against asthma, colic, fevers, inflammations and cancer. It is used as a digestive aid to treat gastrointestinal disturbances including flatulence, motion sickness, indigestion, nausea and vomiting and as a liver stimulant (Mann and Staba 1986). It is used to treat hysteria, nightmares and other sleep problems (Martens 1995). Eye washing with chamomile tea is a folk remedy used by the general public to treat conjunctivitis and other ocular reactions (Subiza et al. 1990). Chamomile has long been used in traditional medicine for the treatment of inflammation-related disorders (Bhaskaran et al. 2010). In a 3-year study of ethnopharmacology and folk-medicine use among the population of the Atlantic Coast of Colombia, 39 plant species were identified to be of traditional medical importance, among which was *M. chamomilla* for colic ailments (Gómez-Estrada et al. 2011).

Other Uses

Chamomile (dried flower heads and extracts) is used in medicine, tinting hair and in cosmetics. Dried chamomile leaves are used in potpourri and herb pillows for their aromatic apple-like smell. The leaves are burnt in aromatherapy for their soothing scent to relax the mind and body. In Egypt, chamomile is steep in religion as the plant was consecrated to the god of the sun.

Chamomile flowers also have insecticidal properties. Studies showed that chamomile flower-head extracts elicited highly significant acaricidal activity against the mite *Psoroptes cuniculi*, responsible for otoacariasis in domestic animals (Macchioni et al. 2004). The decoction of 10 % was the only formulation which gave 100 % activity at all the three observations times of 24, 48 or 72 hours. Chamomile flower extract was found to have acaricidal activity against engorged *Rhipicephalus annulatus* tick in-vitro (Pirali-Kheirabadi and Razzaghi-Abyaneh 2007). The mortality rate caused by different dilutions of chamomile flower extract ranged from 6.67 to 26.7 %, whereas no mortality was recorded for non-treated control group. The mass of produced eggs varied form 0.23 g (in 8.0 % solutions) to 0.58 g (in control), with no statistical differences between the treatments and control. In the highest concentration used (8.0 %) chamomile extract caused 46.67 % failure in egg laying in engorged females while non-failure was observed for non-treated control group. Macroscopic observations indicated that in effective concentrations of the extract (4.0 and 8.0 %), patchy haemorrhagic swelling appeared on the skin of treated ticks.

Comments

Chamomile is cultivated commercially in Europe, Belarus, Ukraine, Moldova, North Caucasus to South Siberia, North Africa (Egypt, Ethiopia), Middle Asia (Turkey, Afghanistan), Asia (Pakistan, North India and Japan), North and South America (Eastern USA, Cuba, Argentina and Brazil), and New Zealand (Alberts 2009).

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Tagetes erecta

Scientific Name

***Tagetes erecta* L.**

Synonyms

Tagetes ernstii H. Rob. & Nicolson, *Tagetes excelsa* Soule, *Tagetes heterocarpha* Rydb., *Tagetes major* Gaertn. (illeg.), *Tagetes remotiflora* Kunze, *Tagetes tenuifolia* Millsp.

Family

Asteraceae

Common/English Names

African Marigold, American Marigold, Aztec Marigold, Big Marigold, Marigold, Mexican Marigold, Saffron Marigold

Vernacular Names

Chinese: Wan Shou Ju, Wan Shou Ju Ye
Czech: Aksamitník Vzpřímený
Danish: Opret Fløjlsblomst
Dutch: Afrikaantje
Eastonian: Kõrge Peiulill
Esperanto: Tageto, Taĝeto
Finnish: Isosamettikukka
French: Rose D'inde, Tagète Rose D'inde
German: Hohe Studentenblume, Studentenblume
India: Narji Phool (Assamese), Genda (Bengali), Genda, Hajara, Hajari, Hajri, Jhandu (Hindi), Chandu Hoo, Chandu Mallige, Chendu Mallige, Seeme Shavantige, Seemeshyaavanthige, Shraavanashyaavanthige (Kannada), Gondephool (Konkani), Bowdu (Lahaul), Sanarei (Manipuri), Makh Mal, Makhamala, Rajiachaphul, Rajjachaphool, Roji, Thurukasaamanthi, Vedipu Naaripoo, Zendu, Zendu Malli (Marathi), D-Erhken, Derhken (Mizoram), D-Erhken, Derhken, Mandyaphul (Oriya), Jhandu, Sthulapushpa, Zandu, Zanduga (Sanskrit), Banti, Kancappucceti, Totika, Totikavantippa, Tulukkaccevvanti, Tulukkamallikai, Tulukkuccevvanti, Turiyotacamanti (Tamil), Banti (Telugu)
Japanese: Senju-Giku
Korean: Cheonsugug
Mexico: Flor De Muertos
Philippines: Ahito (Iloko), Amarillo (Spanish), Amarillo (Tagalog)
Polish: Aksamitka Wyniosła, Aksamitka Wzniesiona
Portuguese: Cravo De Defuntos, Cravo Da Índia, Cravo De Tune, Maravilha, Rosa De Oiro
Russian: Barchatcy Prjamostojaščie
Slovašcina: Rumena Žametnica, Žametnica Rumena
Slovencina: Aksamietnica Vzpriamená
Spanish: Cempasúchil, Flor De Muerto, Zempoalxochitl
Swahili: Tururu
Swedish: Stor Tagetes
Thai: Dao Ruang

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Origin/Distribution

Tagetes erecta is native to Central America—Mexico and Guatemala—and most probably naturalized in the rest of Central America and the western Andes of South America. In Mexico, it is found in the wild in the states of San Luis Potosí, Chiapas, State of México, Puebla, Sinaloa, Tlaxcala and Veracruz. It became naturalized also elsewhere in the tropics and subtropics and is widely cultivated globally as a popular garden ornamental. It is cultivated commercially for its dye mainly in Latin America, in Africa on a small scale in Zambia and South Africa.

Agroecology

Tagetes erecta is found wild in the pine–oak forest zone of Mexico in a warm, low-humidity climate. In the tropics, it grows well up to 2,000 m altitude as in the Andes. It thrives best in sunny locations, in well-drained loamy and clay soils of varying pH. Besides being grown as a garden ornamental, it is often found as an escape, e.g. in the United States, where it occurs along roadsides.

Edible Plant Parts and Uses

The flowers are eaten in Thailand (Kaisoon et al. 2011, 2012). *T. erecta* is grown commercially for the extraction of a food colourant (Tanaka 1976; Facciola 1990; Green 1995). The food colourant lutein is a purified extract obtained from marigold oleoresin, which is extracted from the petals of marigold flowers with organic solvents (Cantrill 2004). The food colourant is used in baked goods and baking mixes (cereal and energy bars, crackers and crispbreads), beverages and beverage bases (bottled water, carbonated beverages, meal replacements and ready-to-drink tea), breakfast cereals (instant and regular hot cereals), chewing gum, dairy product analogues (imitation milks, soy milk), egg products (liquid, frozen or dried egg substitutes), fats and oils (margarine-like spreads, butter, cheese, salad dressings), frozen dairy desserts and mixes (frozen yogurt), gravies and sauces (tomato-based sauces), hard candy, infant and toddler foods (junior-, strained- and toddler-type baby foods), milk products (dry milk, fermented milk beverages, flavoured milk and milk drinks, milk-based meal replacements, yogurt), processed fruits and fruit juices (energy, sport and isotonic drinks; fruit juices; nectars; vegetable juice), soft candy (chewy and nougat candy), fruit snacks, and soups and soup mixes (canned soups) (Green 1995; Cantrill 2004).

Marigold (*Tagetes erecta*) inflorescences have been utilized as lutein pigment source for food colouring, mainly of poultry skin and eggs (Del Villar-Martínez et al. 2010). Marigold flowers are also a good source of carotenoids. There are many reports on carotenoids and their effect on the prevention of certain ocular diseases, ischaemic heart disease, strokes, photoprotection, immune response, aging and cancer.

Botany

An erect branched, coarse, glabrous herbaceous annual herb 3–180 cm tall with angular to rounded stems and a tap root. Leaves deeply pinnatifid with 6–17 linear-lanceolate segments, each segment 1–4 cm × 0.5–2 cm, glandular, acute at both ends and margin serrate (Plates 1 and 2). Inflorescence a solitary terminal capitulum, (3–)5–12 cm across; peduncle 3–12 cm long. Involucre campanulate with 4–10 acute or obtuse lobes each bearing 2 rows of linear glands. Ray florets, female, ligulate, broadly obovate, 5–9 in 1-seriate in wild types, numerous in cultivars, yellow in wild types, lemon-yellow, orange to deep brown-red in cultivars (Plates 1 and 2). Disc florets, tubular, numerous, 8–10 mm long; stamens 5, anthers united into a tube around the style; ovary inferior, 1-loculed, style bifid. Fruit an angular achene 7–10 mm long, black, glabrous to finely hispid, with pappus of basally connate scales.

Plate 1 Yellow flowers and pinnate leaves

Plate 2 Orange flowers and pinnate leaves

Nutritive/Medicinal Properties

Flower Phytochemicals

Marigold flower (*Tagetes erecta*) is one of the richest and purest sources of xanthophylls (Tsao et al. 2004; Sowbhagya et al. 2013). The main carotenoid found in *Tagetes erecta* petals was *trans* lutein ($C_{40}H_{56}O_2$), occurring in either free or esterified to one or two fatty acids (Gómez et al. 1978). About 95 % of lutein present in the flowers was reported to be in the form of esters out of with lutein palmitate as the major pigment (Gau et al. 1983). Dimyristate, myristate, palmitate, stearate and distearate were the other esters of lutein present in marigold flowers. Lutein ester concentrations in fresh marigold flowers vary from 4.0 mg/g in greenish yellow flowers to 800 mg/g in orange brown flowers. Gregory et al. (1986) found that lutein ester concentrations in fresh marigold (*T. erecta*) flowers varied from 4 pg/g in greenish yellow flowers to 800 pg/g in orange brown flowers. Lutein and eight lutein esters are (2) lutein monomyristate, (3) lutein monopalmitate, (4) lutein monostearate, (5) unknown, (6) lutein dimyristate, (7) lutein myristate–palmitate, (8) lutein dipalmitate, (9) lutein palmitate–stearate, (10) lutein distearate content in two different parts (petals and calyces) of flower heads from different types of marigold belonging to the species *Tagetes patula* and *T. erecta* were evaluated (Piccaglia et al. 1998). Relevant quantitative differences were found among the marigold types which had a total content of pigments ranging from 17 to 570 mg/100 g in the petals and from 0.4 to 18.6 mg/100 g in the calyces. The following geometric isomers of native lutein diesters were separated by high-performance liquid chromatography–mass spectrometry (Tsao et al. 2004): *cis*-lutein isomeric dimyristate, myristate–palmitate, dipalmitate and palmitate–stearate diesters, as well as the rare combinations of both *trans*- and *cis*-lutein laurate–palmitate and *trans*- and *cis*-lutein myristate–stearate. The presence of the all-*trans*-lutein laurate–myristate, dimyristate, myristate–palmitate, palmitate–stearate and distearate diesters, reported by others, was also confirmed.

The following carotenoids were found in the flowers: lutein, lutein palmitate, lutein dimyristate, lutein myristate, lutein stearate and lutein distearate (Gau et al. 1983; Sowbhagya et al. 2013); lutein and lutein dipalmitate diesters, lutein myristate palmitate diesters, lutein lauristate myristate diesters, lutein dimyristate diesters, lutein palmitate stearistate diesters, lutein violaxanthin monoesters, lutein neoxanthin violaxanthin diesters and β-carotene and zeaxanthin (Breithaupt et al. 2001; Scalia and Francis 1989). The saponified extract of commercially prepared marigold flower (*Tagetes erecta*) extract was found to contain 93 % utilizable pigments consisting of all-*trans* and *cis* isomers of zeaxanthin (5 %), all-*trans* and *cis* isomers of lutein and lutein esters (88 %) (Hadden et al. 1999). Insignificant levels (<0.3 %) of lutein oxidation products were detected in the saponified extract.

This compositional determination is important for the application of marigold extract in nutritional supplements and increases its value as a poultry feed colourant because it contains more biologically useful lutein compounds than previously believed. The flowers of *T. erecta* cultivars were found to be rich in carotenoids (Kishimoto et al. 2007). Carotenoids in orange *Tagetes erecta* flowers were predominantly lutein and smaller quantities of violaxanthin and (9′Z)-neoxanthin. Total carotenoids in *T. erecta* cv. Orange Isis was 2,130 μg/g FW and in cv. Yellow Isis flowers was 48.4 μg/g FW (Kishimoto et al. 2007). Enzyme-mediated solvent extraction of carotenoids from marigold flower (*Tagetes erecta*) under optimal conditions afforded a carotenoid recovery yield of 97 % (Barzana et al. 2002). Erstwhile, extraction gave almost 50 % losses of the carotenoids depending on conditions for silaging, drying and solvent extraction.

The maximum amount of xanthophylls accumulated in the flowers with orange (or orange with claret spots) petals, where the content of carotenoids (recalculated for lutein) exceeded 5 mg/g of fresh petals against 1 mg/g for yellow and 0.2 mg/g for lemon-yellow flowers (Deineka et al. 2007). The marigold flowers of orange colour with claret spots were characterized by a high content of anthocyanins. The main component was cyanidin-3-glucoside; some samples also contained a significant amount (10–50 %) of another cyanidin derivative identical to that of cyanidin-3-glucoside acylated with malonic acid. The main acids of isolated lutein diester esters were myristic and palmitic acids (accounting for 85–90 % of the total sum of acid radicals); smaller fractions represented stearic and lauric acid radicals.

Total carotenoids in the fresh orange flowers of *T. erecta* was 1,304 mg/kg comprising 619 mg/kg carotenes and 685 mg/kg xanthophylls, whereas total carotenoids in the dried flowers were 4,397 mg/kg made up of flowers, 1,954 mg/kg carotenes and 2,443 mg/kg xanthophylls (Tinoi et al. 2006). The quantitative composition (mg/kg) of the carotenoids in the fresh petals was 85.5 mg b-carotene, 31.6 mg cryptoxanthin, 1,062 mg lutein, 43.7 mg violaxanthin, 53.7 mg zeaxanthin and 34 mg unidentified. The quantitative composition (mg/kg) of the carotenoids in the dried petals was 65 mg b-carotene, 78.2 mg cryptoxanthin, 3,869 mg lutein, 92.8 mg violaxanthin, 166 mg zeaxanthin and 126 mg unidentified. The concentrations of lutein and zeaxanthin in 20 marigold (*T. erecta*) samples were assessed by saponification using traditional heater and microwave-assisted hydrolysis; the regression coefficient of lutein obtained by two methods was 0.9688 and that of zeaxanthin was 0.9527 (Liu et al. 2011). The limit of detection for lutein and zeaxanthin was 0.05 and 0.1 μg/ml, respectively, and the limit of quantification for lutein and zeaxanthin was 0.05 mg/100 g and 0.1 mg/100g, respectively. Pretreatment of marigold flowers with an aqueous enzyme solution (0.2 %), sodium hydroxide and citric acid solution resulted in improved resin, pigment yield and retention of carotenoid pigment during storage (Sowbhagya et al. 2013).

Vanegas-Espinoza et al. (2011) found that green callus from *T. erecta* leaf explants produced violaxanthin, lutein, zeaxanthin, β-carotene and esterified carotenoids, while yellow callus generated mainly lutein and esterified carotenoids, and brown callus produced lutein.

The carotenoid (3*R*,3′*R*,6′*R*)-lutein isolated from extracts of marigold flowers (*Tagetes erecta*) can be efficiently converted to (3*R*,3′*S*,6′*R*)-lutein (3′-epilutein) and (3*R*,3′*R*)-zeaxanthin (Khachik 2003). The two dietary carotenoid, (3*R*,3′*R*,6′*R*)-lutein and (3*R*,3′*R*)-zeaxanthin, and their metabolite (3*R*,3′*S*,6′*R*)-lutein (3′-epilutein) (3) accumulate in human serum, milk and ocular tissues and had been reported to play an important role in the prevention of age-related macular degeneration. Marigold (*Tagetes erecta*) flowers were found to show different levels of pigmentation caused by lutein, and several genes in the carotenoid biosynthetic pathway were identified: phytoene synthase (Psy), phytoene desaturase (Pds), lycopene β-cyclase (Lcy-b) and lycopene ε-cyclase (Lcy-e) (Del Villar-Martínez et al. 2010).

The dominant fatty acids of marigold (*T. erecta*) flower oleoresin were linoleic acid (>26.41 %), palmitic acid (>24.22 %) and oleic

acid (>20.12 %). Lutein esters, α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol were the dominant antioxidant compounds in the flower extracts (Gong et al. 2011).

Phenolic acids detected in the ethanol extract of *Tagetes erecta* flowers (mg/100 g DW) included: gallic acid, 14.74 mg; protocatechuic acid, 10.09 mg; *p*-hydroxybenzoic acid, 3.44 mg; chlorogenic acid, 13.64 mg; vanillic acid, 47.81; caffeic acid, 3.65 mg; syringic acid, 15.83 mg; *p*-coumaric acid, 253.05 mg; ferulic acid, 48.61 mg; sinapic acid, 531.39 mg; and total, 942.25 mg (Kaisoon et al. 2012). Flavonoid compounds found in the lyophilized hydrophilic extracts of *T. erecta* flowers (mg/100 g DW) included the following: rutin, 5.09 mg; myricetin, 54.81 mg; quercetin, 13.57 mg; apigenin, 8.41 mg; kaempferol 25.683.42 mg; and total, 165.3 mg.

Six oleanane-type triterpenoid esters were isolated from the golden flowers of *Tagetes erecta*, and their structures characterized as 3-*O*-[(9*Z*)-hexadec-9-enoyl]erythrodiol (1), 11α,12α:13*β*,28-diepoxyoleanan-3*β*-yl (9*Z*)-hexadec-9-enoate (2), 13*β*,28-epoxyolean-11-en-3*β*-yl (9*Z*)-hexadec-9-enoate (3), 28-hydroxy-11-oxoolean-12-en-3*β*-yl (9*Z*)-hexadec-9-enoate (4), 3-*O*-[(9*Z*)-hexadec-9-enoyl]-*β*-amyrin (5) and 11-oxoolean-12-en-3*β*-yl (9*Z*)-hexadec-9-enoate (6) (Faizi and Naz 2004). Aerial oxidation (autoxidation) converted amyrin 1 into 2–4 and transformed amyrin 5 into 6. Also isolated were β-amyrin (7), erythrodiol (8) and ursolic acid. From *T. erecta* flowers, the following compounds were isolated: phenolic derivatives (syringic acid, gallic acid, 3,4-dihydroxybenzonic acid and 3,4-dihydroxy-5-methoxy-benzoicacid), terpenoid β-amyrin, steroids β-sitosterol and stigmasterol, and flavonoids (quercetagetin, quercetagetin-7-methyl ether and quercetagetin-5-methyl ether) (Huang et al. 2006). Also isolated from the flowers were the terpenoid dammarenediol 3-*O*-*n*-palmitate; flavonoid quercetagetin 3-*O*-glucoside; miscellaneous compounds 16*Z*,19*Z*-pentacosadienoic acid; and monolinoleoyl glycerol and vitamin E (Huang et al. 2007). Two new optical isomeric compounds named 3-α-galactosyl disyringic acid 15-a and 3-β-galact-osyl disyringic acid 15-b were isolated from the flowers together with 22 other compounds, and 20 of them were identified as tetratriacontane; dammarenediol II 3-*O*-*n*-palmitate; β-amyrin; 16*Z*,*19Z*-pentacosadienoic acid; uvaol; β-sitosterol; stigmasterol; vitamin E (α-tocopherol); 9*Z*,12*Z*,15*Z*-octadecatrienl-ol; monolinoleoyl glycerol; syringic acid; 11, 3,4-dihydroxybenzonic acid; quercetagetin 7-methyl ether; quercetagetin; *n*-hexadecane; quercetagetin 5-methyl ether; 5,7-dimethoxy quercetin; gallic acid; 3,4-dihydroxy-5-methoxybenzoic acid; and quercetagetin 3-*O*-glucoside (Huang 2007). Xu et al. (2011) isolated 22 compounds from the flowers: β-sitosterol, β-daucosterol, 7β-hydroxysitosterol, lupeol, erythrodiol, erythrodiol-3-palmitate, 1-[5′-(1-propyn-1-yl)-[2,2′-bithiophen]-5-yl]-ethanone, α-terthienyl, quercetagetin, quercetagetin-7-methyl ether, quercetagetin-7-*O*-glucoside, kaempferol, syringic acid, gallic acid, 3-α-galactosyl disyringic acid, 3-β-galactosyl disyringic acid, 6-ethoxy-2,4-dimethylquinoline, oplodiol, (3*S*,6*R*,7*E*)-hydroxy-4,7-megastigmadien-9-one, palmitin, ethylene glycol linoleate and *n*-hexadecane.

Twenty compounds were identified in the flower essential oil of *T. erecta*, and the major constituents were γ-cadinene, δ-cadinene and *cis*-caryophyllene and other sesquiterpenes (Shi et al. 1988). Analysis of composition of volatile flower oil of yellow *T. erecta* in Yanbian region by GC/MS showed *trans*-caryophyllene (33.18 %), β-cubebene (11.22 %), limonene (4.81 %), α-terpinolene (4.44 %), 1,3,6-octatriene, 3.7-dimethyl(*E*)- (3.36 %) and 2-cyclohexen-1-one,3 methyl-6-(1-methylethyl) (3.10 %) to be the main components (Leng et al. 1999). Forty-five constituents of the flower oil accounting for 94.0 % were identified, and the major constituents were limonene (6.9 %), terpinolene (4.7 %), (*Z*)-myroxide (7.9 %), piperitone (28.5 %), piperitenone (10.9 %), piperitenone oxide (7.2 %) and β-caryophyllene (7.0 %) (Krishna et al. 2004). Eighteen components were identified in the *T. erecta* flower essential oil: β-caryophyllene (15.2 %), limonene (11.7 %), methyl eugenol (12.3 %), (*E*)-ocimene (13.7 %), piperitone (91.2 %), piperitenone (8.1 %) and α-terpinolene (11.9 %) were the main components (Gutiérrez et al. 2006). Other compounds included linalool

(4.6 %), umbellulone (4.3 %), camphor (3.8 %), caryophyllene oxide (2.3 %), indole (1.8 %), *n*-undecane (1.7 %), citronellol (1.0 %), geraniol (0.9 %), and verbenone (traces). Twenty-five compounds were identified in the flower essential oil of *T. erecta* grown in Venezuela, of which linalool (22.5 %), 2-hexyl-l-decanol (18.3 %), piperitone (13.4 %), 4-terpinyl acetate (7.8 %) and caryophyllene (6.6 %) are the main components (Martínez et al. 2009). The volatile compounds identified in marigold (*Tagetes erecta* L.) flower oil were α-sesquiphellandrene, β-sesquiphellandrene, 2-methyl-6-(4-methyl cyclohexadienyl) hept-4-en-2-ol, myristoleic acid), and trieicosane (Prasad et al. 2012).

Thirty-three components in *T. erecta* leaf and stem oil and 34 components in flower oil were identified (Sefidkon et al. 2004). The main characterized constituents were β-caryophyllene (8.5 and 35.2 %), terpinolene (18.4 and 6.3 %), (*E*)-ocimenone (12.6 and 9.8 %), (*Z*)-β-ocimene (10.4 and 13.7 %), piperitenone (10.4 and 2.6 %), (*Z*)-ocimenone (5.5 and 7.7 %), limonene (6.2 and 2.5 %), germacrene D (3.0 and 4.1 %), piperitone (4.2 and 0.6 %), (*Z*)-tagetone (3.7 and 1.5 %), fenchol (2.6 and 1.9 %), (*E*)-tagetone (2.2 and 1.3 %) and bicyclogermacrene (1.6 and 2.1 %) in leaf and stem oil and flower oil, respectively. Some components like *p*-cymene-8-ol, terpinen-4-ol, α-terpineole and verbenone were found only in stem and leaf oil, and some components like β-bourbonene, α-humulene, δ-cadinene, spathulenol and T-muurolol were found only in flower oil.

A mixture of two tannin-related anomers 3,4-di-*O*-[syringate]-α-D-glucopyranose and 3,4-di-*O*-[syringate]-β-D-glucopyranose, together with syringic acid, was isolated from the alcohol extract of *Tagetes erecta* (Zhou et al. 2012). *T. erecta* flowers were found to have good amounts of syringic acid and β-amyrin (2.30 %, w/w and 0.06 %) (Maity et al. 2011).

Seven electrophysiologically active floral volatile compounds benzaldehyde, (*S*)-(−)-limonene, (*R,S*)-(+/−)-linalool, (*E*)-myroxide, (*Z*)-β-ocimene, phenylacetaldehyde and (*R*)-(−)-piperitone were detected in the air-entrained headspace samples of live flowers of *Tagetes erecta* linked to a female *Helicoverpa armigera* (Bruce and Cork 2001).

Flavonoids found in the flowers and leaves included quercetagetin and kaempferitrin (Vasudevan et al. 1997).

Leaf/Plant Callus Phytochemicals

Twenty-seven compounds were found in *T. erecta* leaf oil (Machado et al. 1994). The major compounds were terpinolene (12.4 %), (*E*)-B-ocimene (13.1 %), piperitone (20 %) and limonene (11.0 %) (Machado et al. 1994). Indole was also found as a minor component. Forty-four constituents representing 94.1 % of the leaf oil were identified, and the major constituents of the leaf oil were limonene (7.6 %), terpinolene (11.2 %), (*Z*)-myroxide (4.2 %), piperitone (52.4 %) and piperitenone (5.0 %) (Krishna et al. 2004). Twenty-six components, accounting for 89 % of the total oil, were found in *T. erecta* leaf essential oil (Singh et al. 2003). The major constituents were (*Z*)-β-ocimene (42.2 %), dihydrotagetone (14.3 %), (*Z*)-tagetone (8.3 %), limonene (7.3 %), (*E*)-ocimenone (6.1 %) and (*Z*)-ocimenone (5.3 %). The essential oil of *T. erecta* leaves and inflorescences was found to contain mainly piperitone (35.9 %) and terpinolene (22.2 %) (Armas et al. 2012).

The essential oil from *T. erecta* differed largely from *T. minuta*, *T. tenuifolia* and *T. patula*, containing mainly limonene, β-caryophyllene and piperitone (Héthélyi et al. 1986).

Pyrethrins were isolated from the callus tissues of *T. erecta* (Sarin 2004).

Root Phytochemicals

Two mutants of *Tagetes erecta* were found to contain high amounts in the root extracts of the C13 monothiophene 2-(but-3-en-1-ynyl)-5-(penta-1,3-diynyl)-thiophene that was previously not found in *T. erecta* and also high amounts of two C13 bithienyls that were absent or present at low concentrations in the wild type (Jacobs et al. 1995). The mutant phenotype was also expressed

in 21 *Agrobacterium rhizogenes* transformed root clones derived from both mutants. Monothiophene found accumulating in the mutant was the common precursor for all bithienyl thiophenes in wild-type and mutant *Tagetes erecta*. Thiopene derivatives α-terthienyl and 5-butyl-2,2′-bithienyl were found in the roots (Vasudevan et al. 1997). A new bithienyl compound, 2-hydroxymethyl-non-3-ynoic acid 2-[2,2′]-bithiophenyl-5-ethyl ester from the roots of *T. erecta* (Gupta and Vasudeva 2010). Wang et al. (2002) isolated thiopene derivatives: 5,5′-dimethyl-2,2′-bithienyl; 5-vinyl-2,2′-bithiophene and 5-(3-butene-1-ynyl)-2,2′-bithiophene; and flavonoids: quercetagetin 3-*O*-glucoside and kaempferol. Liu et al. (2007) detected bacteriostatic alkaloids from the roots. Roots of *Tagetes* species (*T. erecta*, *T. filifolia*, *T. lucida*, *T. minuta*, *T. patula* and *T. tenuifolia*) had the highest diversity and contents of thiophenes (from 64 to 100 % of the total thiophene amount), with 5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT) as the main component followed by 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc), 2,2′:5′,2″-terthienyl (alpha-T) and 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH) (Marotti et al. 2010).

Antioxidant Activity

T. erecta flower essential oil was found to have antioxidant activity (Gutiérrez et al. 2006). However, the scavenging effects of *T. erecta* flower essential oil (100 mg/ml) on diphenyl-1-picrylhydrazyl (DPPH) radical were lower (71.5 %) than that of α-tocopherol (95.1 %) at 100 mg/ml. In the ABTS (2,2′-azino-bis-(3-ethylbenztiazoline-6-sulphonic acid) model reaction, the essential oil exhibited inhibitory activity on the ABTS radical at 100 mg (57.3 %) less than α-tocopherol (70.5 %). The inhibitory effect of the essential oil (73.6 %) on 2-deoxy-2-ribose oxidation induced by Fe^{3+}/H_2O_2 was also lower than that for α-tocopherol (94.2 %). Significant differences in peroxide value were found between the control and the linoleic acid containing oil or antioxidant (α-tocopherol). The antioxidative activity of the oil increased with concentration up to 12.5 μg/ml and decreased at higher concentrations of oil, 200 mg/ml. The thiocyanate test showed that at a concentration of 50 mg/ml, the inhibition of oxidation of linoleic acid produced by oil was 71.1 %, respectively, as compared to the blank control and was less efficient than α-tocopherol (92.1 %). Ethanol flower extract of *Tagetes erecta* demonstrated antioxidant property in all the in-vitro models like 1,1-diphenyl-2-picrylhydrazyl (DPPH), reducing power and superoxide radical scavenging activity at different concentrations (Chivde et al. 2011b). It exhibited higher reducing power than the ascorbic acid standard but lower DPPH and superoxide scavenging activities.

Studies showed that the yield of oleoresin and total antioxidant activity of the marigold (*T. erecta*) extracts were affected by the pressure and temperature of SC-CO(2) (Gong et al. 2011). Lutein esters, α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol were the dominant antioxidant compounds in the extracts. In a comparative study of four edible flowers, the phenolics (mg GAE (gallic acid equivalent)/g DW) of the flowers were determined as follows: *Tagetes erecta* (212.9) > *Antigonon leptopus* (177.2) > *Bougainvillea glabra* (138.2) > *Cosmos sulphureus* (102.5) (Kaisoon et al. 2012). *Tagetes erecta* was found to have the highest antioxidant activity of the four edible flowers tested. Total reducing capacity (FRAP) (μmol Fe^{2+}/g DW) was ranked as *Tagetes erecta* (329.4) > *Bougainvillea glabra* (307.1) > *Antigonon leptopus* (281.9) > *Cosmos sulphureus* (99.9). The ORAC (oxygen radical absorbance capacity) (μmol T Eq (trolox equivalent)/g DW) ranks were *Antigonon leptopus* (491.9) > *Tagetes erecta* (394.2) > *Bougainvillea glabra* (276) > *Cosmos sulphureus* (*214.8*). Cellular antioxidant activity (CAA) (μM QE (quercetin equivalent)/g DW) ranks were *Tagetes erecta* (413, most effective) > *Bougainvillea glabra* (859.6) > *Cosmos sulphureus* (966.1) > *Antigonon leptopus* (967.4).

The content of total phenolics and flavonoids in defatted marigold (*T. erecta*) extracts varied significantly with different solvents, and the extract by

ethyl alcohol (EtOH)/water afforded the highest content of total phenolics and flavonoids, 62.33 mg gallic acid equivalents (GAE)/g and 97.00 mg rutin equivalent (RE)/g, respectively (Gong et al. 2012). The results of the correlation analysis showed that the antioxidant activity as evaluated by ABTS, DPPH radical scavenging and FRAP assays was well correlated with the content of total phenolics and flavonoids ($R^2 > 0.900$). Gallic acid, gallicin, quercetagetin, 6-hydroxykaempferol-*O*-hexoside, patuletin-*O*-hexoside and quercetin were the dominant antioxidant compounds in the extracts, and quercetagetin was identified as the strongest antioxidant capacity

Lutein extracted and purified from marigold *Tagetes erecta* flower showed a greater antioxidant activity than the other two common carotenoids, β-carotene and lycopene as examined by the photochemiluminescence (PCL) assay and the β-carotene-linoleic acid model system (beta-CLAMS) (Wang et al. 2006).

Antidiabetic Activity

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against α-glucosidase enzyme was found as: *Tagetes erecta* (98.51 % inhibition, IC_{50} 0.06 mg/ml) > *Antigonon leptopus* (58.24 % inhibition, IC_{50} 3.26 mg/ml) > *Bougainvillea glabra* (37.30 % inhibition, IC_{50} 5.21 mg/ml) > *Cosmos sulphureus* (32.32 % inhibition, IC_{50} 5.62 mg/ml) (Kaisoon et al. 2012).

Hypolipidemic Activity

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against lipase activity was determined as *Cosmos sulphureus* (43.39 % inhibition, IC_{50} 4.60 mg/ml) > *Tagetes erecta* (41.61 % inhibition, IC_{50} 4.82 mg/ml) > *Bougainvillea glabra* (40.05 % inhibition, IC_{50} 5.14 mg/ml) > *Antigonon leptopus* (26.70 % inhibition, IC_{50} 7.87 mg/ml) (Kaisoon et al. 2012).

Antiproliferative/Cytotoxicity Activity

Tagetes erecta had highest antiproliferative activity among four edible flowers against one cancer cell line tested (Kaisoon et al. 2012). Antiproliferative activity (IC_{50} mg/ml) of polyphenolic extract against HC-29 (colorectal adenocarcinoma) cells was *Tagetes erecta* > (1.5) > *Bougainvillea glabra* (1.7) > *Antigonon leptopus* (2.4) > *Cosmos sulphureus* (5.2). Antiproliferative activity (IC_{50} mg/ml) of polyphenolic extract against AGS (gastric adenocarcinoma) cells was *Antigonon leptopus* (0.2) > *Bougainvillea glabra* (2.1) > *Tagetes erecta* (2.2) > *Cosmos sulphureus* (44.8). Antiproliferative activity (IC_{50} mg/ml) of polyphenolic extract against Bl-13 (bladder cancer) cells was *Antigonon leptopus* (0.9) > *Bougainvillea glabra* (2.3) > *Tagetes erecta* (3.0) > *Cosmos sulphureus* (56.5).

The ethanol extract of *T. erecta* roots scavenged DPPH free radicals thereby exhibiting antioxidant activity with an IC_{50} of 35.9 μg/ml and conferred marked cytotoxicity against the HeLa (LD_{50} of 164.28 μg/ml) and PC-3 cell lines (LD_{50} of 407.3 μg/ml) (Gupta et al. 2012). Among the 21 isolates obtained, T_3 showed antioxidant activity with IC_{50} of 11.56 μg/ml and cytotoxicity with LD_{50} of 12.5 μg/ml against HeLa and 30.25 μg/ml against prostate PC-3 cell lines and was characterized as 2-ethynyl-5-(thiophen-2-yl) thiophene.

Antimicrobial Activity

T. erecta essential leaf oil completely inhibited the growth of *Fusarium oxysporum* and *Trichophyton mentagrophytes* (Rai and Acharya 1999). *T. erecta* root extracts (petroleum ether, chloroform, ethyl acetate, methanol and aqueous) exhibited significant antimicrobial activity against three Gram-positive and two Gram-negative bacterial and two fungal strains with MIC values ranging between 12.5 and 100 μg/ml (Gupta and Vasudeva 2010). Methanol extract of *Tagetes erecta* at 40 mg/ml concentration was

found to have better inhibitory activity when compared to cold and hot aqueous extracts (Jain et al. 2012). The methanol extract exerted highest inhibition against *Aeromonas sobria*, *Aeromonas hydrophila*, *Staphylococcus aureus* (MTCC7405) and *Staphylococcus aureus* (clinical isolate) and was weakly inhibitory against *Bacillus subtilis.* Minimal inhibitory concentrations (MICs) were between concentrations of 20–160 mg/ml with both aqueous or methanol extracts.

T. erecta leaf extract exhibited high in vitro antibacterial activity against *Propionibacterium acnes and Acinetobacter baumannii* (mean activity index > 0.9); moderate activity against *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus cereus*, *Erysipelothrix rhusiopathiae*, *Alcaligenes faecalis*, *Escherichia coli and Pseudomonas aeruginosa* (mean activity index 0.7–0.89); low activity against *Klebsiella pneumoniae* and *Salmonella enteritidis* (mean activity index < 0.5); and negligible activity against (mean activity index < 0.1) *Streptococcus pneumoniae*, *Streptococcus agalactiae and Staphylococcus saprophyticus* (Dasgupta et al. 2012).

Anti-wrinkle/Wound Healing Activity

The methanol extract of *T. erecta* flowers showed significant hyaluronidase and elastase inhibition with IC_{50} of 11.70 and 4.13 μg/ml, respectively, and better MMP-1 inhibition compared to standard oleanolic acid (Maity et al. 2011). The isolated compounds syringic acid and β-amyrin were found to inhibit the enzymes comparable to oleanolic acid. The results suggested that the plant may be useful as an anti-wrinkle agent.

In both excision and burn wound models, a significant increase in the wound healing activity was observed in the adult albino mice treated with hydroalcoholic leaf extract of *Gymnema sylvestere* and *Tagetes erecta* and their combined extract (Hussain et al. 2011).

Hepatoprotective Activity

Ethyl acetate fraction of *T. erecta* ethanol flower extract administered orally to albino Wistar rats at the dose of 400 mg/kg orally significantly decreased the elevated serum marker enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), and total bilirubin almost to the normal level compared to CCl_4-intoxicated group (Giri et al. 2011). Histological changes in the liver of rats treated with 400 mg/kg of the flower extract and CCl_4 showed a significant recovery except for cytoplasmic vascular degenerations around portal tracts, mild inflammation and foci of lobular inflammation. In another study, pretreatment of male rats with ethanol flower extract of *Tagetes erecta* (200 and 400 mg/kg) before CCl_4 injection reduced the biochemical markers of hepatic injury like SGPT, SGOT, ALP and bilirubin levels which were also confirmed by histopathological examination (Chivde et al. 2011a). The results indicated *T. erecta* flower extract to possess hepatoprotective which may be attributed to the quercetin-related flavonoids present in the flowers.

Antimutagenic Activity

Lutein and xanthophylls from Aztec Marigold (*T. erecta*) inhibited mutagenicity of 1-nitropyrene (1-NP) in a dose-dependent manner (González de Mejía et al. 1997a). In a dose–response curve of 1-nitropyrene (1-NP), the mutagenic potency was 4,317 revertants/nmol, and the dose of 0.06 μg of 1-NP/plate was chosen for the antimutagenicity studies. Lutein and the pigments were not toxic to *Salmonella typhimurium* tester strain YG1024 at the concentrations tested (0.002, 0.02, 0.2, 2.0 and 10 μg/plate). The percentages of inhibition of 1-NP mutagenicity were 72, 92 and 66.2 % for lutein (10 μg/plate), pigment for poultry use (10 μg/plate) and pigment for human use (2 μg/plate), respectively. Lutein had no effect on the DNA-repair system of strain YG1024. Pure lutein and xanthophylls from Aztec Marigold

flower (oleoresin and xanthophyll plus) inhibited the mutagenicity of aflatoxin B1 (AFB1) in a dose-dependent manner (González de Mejía et al. 1997b). The pigments were more efficient at inhibiting the AFB1 mutagenicity than pure lutein. The percentages of inhibition on AFB1 mutagenicity were 37, 66 and 76 % for lutein, oleoresin and xanthophyll plus at the dose of 2 micrograms/plate, respectively. Lutein had a modest effect on the DNA-repair system of YG1024. The results suggested that the inhibitory mechanism of lutein against AFB1 mutagenicity was most probably the result of a combination of the following events, formation of a complex between lutein and AFB1 and direct interaction between lutein and AFB1 metabolites, and finally that the lutein may also affect the metabolic activation of AFB1 by S9 and the expression of AFB1-modified *Salmonella typhimurium* DNA.

Larvicidal Activity

The larvicidal effects of essential oil from the leaves of *T. erecta* and some other plants were evaluated against *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti* (Namrata et al. 2000). *T. erecta* oil was found to be the most effective at lower concentration. Among the tested samples, the chloroform soluble fractions of *T. erecta* flowers showed the highest toxicity and consequently, the lowest LC_{50} values (14.14, 17.06, 36.88 and 75.48 µg/ml) against all the instar larvae of *Culex quinquefasciatus* (Nikkon et al. 2011). *T. erecta* essential oil was active against third instar larvae of *Aedes aegypti*, with LC_{50} of 79.78 µg/ml and LC_{90} of 100.84 µg/ml (Marques et al. 2011). The main larvicidal compounds were piperitone (45.72 %), D-limonene (9.67 %) and piperitenone (5.89 %). The larvicidal thiophene contents were higher in the roots and flowers as demonstrated by high-performance liquid chromatography analysis.

No hatchability *Anopheles subpictus* was observed with hexane leaf extract of *T. erecta* at 1,000 ppm (Elango et al. 2010a). The percentages of effective oviposition repellency of hexane and chloroform extracts were 81.53 and 72.77 % at 500 ppm. The methanol extract of *T. erecta* showed complete protection (repellency) against *Culex tritaeniorhynchus* in 90 minutes at 250 ppm (Elango et al. 2010b). The methanol leaf extract of *T. erecta* leaves showed good oviposition-deterrent, ovicidal and repellent activities against the malaria vector, *Anopheles subpictus* (Elango et al. 2011b). Mortality (no egg hatchability) was 100 % with the extract at 998.85 mg/l and maximum adult repellent activity was observed at 499.42 mg/l. After 24 hours of exposure, the highest adulticidal activity against *Anopheles subpictus* was observed in the methanol leaf extract of *T. erecta* (LD_{50} = 89.83 ppm; LD_{90} = 607.85 ppm); and effective EI (adult emergence inhibition) was EI_{50} = 92.82 ppm and EI_{90} = 582.59 ppm (Elango et al. 2011a). The results suggested that the leaf methanol extract of *T. erecta* had the potential to be used as an ideal eco-friendly approach for the control of *A. subpictus*.

Antiaging Activity

Studies showed that the administration of *Tagetes erecta* extract could effectively enhance the antioxidant capacity and delay D-galactose-induced aging in Wistar rats (Pei et al. 2007). The marigold extract significantly decreased MDA (malonaldehyde) content in the liver, kidney, heart, brain and prostate and other organs of the rats and significantly increased the activity of SOD (superoxide dismutase) and GSH-Px (glutathione peroxidise) compared to non-extract treated D-galactose-induced aged rats.

Keratolytic Activity

In a double-blind, placebo-controlled, 4-week study of 30 patients with painful plantar hyperkeratotic lesions, patients treated with an active paste pad of fresh marigold (*T. erecta*) plant combined with isopropyl alcohol (poultice dressing) showed a significant decrease in hyperkeratotic lesion width, length and pain when compared to the placebo group (Khan et al. 1996). The keratolytic

property of *Tagetes* was further confirmed in several published case studies (Khan and Evans 1996; Khan and Khan 2000). Patients receiving a similar therapy as previously described reported pain relief after 48 hours of the first dressing application. Further, patients who used the home therapy and orthotic control after the initial 8-week period had no recurrence of the lesions after 1 year.

Anticataract Activity

Quercetagetin extracted from *Tagetes erecta* inhibited aldose reductase of Wistar rat lens by 93.9 % at 10^{-4} M, 76.0 % at 10^{-5} M and 13.3 % at 10^{-6} M (Li et al. 1991).

Anthelminthic Activity

Studies showed that after 96 hours exposure, *T. erecta* acetonic plant extract produced 99.7 % lethal activity on the fourth larval stage of *Haemonchus contortus*, followed by *Castela tortuosa* hexane extract (85.8 %) and *T. erecta* methanol extract (58.3 %) (Aguilar et al. 2008).

Commercially available Aztec Marigold (*Tagetes erecta*) flower extract exhibited in vitro antioxidant activity and in vivo dose-dependent analgesic effect on acetic-acid-induced abdominal writhing (Bashir and Gilani 2008). The results supported the medicinal uses of Aztec Marigold as an antiinflammatory and analgesic.

Antiplasmodial Activity

Among *T. erecta* root extracts tested, ethyl acetate extract exhibited significant antiplasmodial efficacy with the 50 % inhibitory concentrations (IC_{50}) of 0.02 and 0.07 mg/ml against the chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*, respectively (Gupta and Vasudeva 2010). The new bithienyl compound, 2-hydroxymethyl-non-3-ynoic acid 2-[2,2′]-bithiophenyl-5-ethyl ester, also showed significant schizonticidal activity against both chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum* with the IC_{50} values of 0.01 and 0.02 mg/ml.

Toxicity/Genotoxicity Studies

In the subacute toxicity, treatment of chloroform fraction of *T. erecta* flowers at 200 and 400 mg/kg doses to Long Evan's rats did not make any significant alterations on the haematological and biochemical parameters of rats compared with that of untreated controls (Nikkon et al. 2009b). Histopathological examination also showed no detectable changes in the liver, kidney, heart and lungs of chloroform fraction-treated rats. The study revealed that the chloroform fraction of *Tagetes erecta* had no toxic effects.

Lutein and its ester form isolated from marigold flowers (*Tagetes erecta*), administered orally to Wistar rats at doses of 4, 40 and 400 mg/kg body weight for 4 weeks for short-term toxicity study and 13 weeks for a subchronic toxicity study, did not produced any mortality, change in body weight, food consumption pattern, organ weight and other adverse side reactions (Harikumar et al. 2008). Administration of lutein and ester form did not alter the hepatic and renal function and did not produce any change in the haematological parameters and lipid profile. Histopathological analysis of the organs supported the nontoxicity of lutein and its ester form.

Using the standard Ames test in the presence and absence of S9 mix, lutein extracted and purified from marigold *Tagetes erecta* flower was not only found to be non-mutagenic at all doses (at 334, 668 and 1,335 μg/plate), but it showed an anti-mutagenic effect in a dose-dependent manner (Wang et al. 2006). Similar results were found in a chromosome aberration test using Chinese hamster ovary cells for the evaluation of clastogenicity and anticlastogenicity of lutein at 66.8, 133.5 and 267.0 mg/l. The findings provided scientific evidence for the safe use and health beneficial effects of lutein.

The essential oils of *Tagetes* flowers were tested for their toxicological potential on mice; the results showed that the oils had a low toxicity

with a TD_{50} 99.6 mg/kg for *T. erecta* and 112 mg/kg for *T. patula* (Martínez et al. 2009).

Acute and subchronic toxicity and mutagenicity studies in Wistar rats were carried out on Lutemax 2020, a lutein and zeaxanthin (including meso-isomer)-enriched product obtained from marigold (*Tagetes erecta*) flowers (Ravikrishnan et al. 2011). Lutein and zeaxanthin, naturally occurring carotenoids, had been shown to reduce the risk of cataracts and age-related macular degeneration. The results of mutagenicity testing in *Salmonella typhimurium* did not reveal any genotoxicity. The no-observed-adverse-effect level (NOAEL) for lutein/zeaxanthin concentrate was determined as 400 mg/kg bw/day, the highest dose tested.

Traditional Medicinal Uses

The flowers of *T. erecta* are officially listed in the Mexican Pharmacopoeia (Neher 1968). In Mexico, an infusion or decoction of the whole plant is taken internally for colds and respiratory ailments and as a stimulant. In Mexico, juice and leaves ground in water, are taken as an appetizer, aphrodisiac, diaphoretic, emetic, antipyretic, muscle relaxant, for liver problems, irregular menstrual flow, and dropsy (oedema). The flower and leaf decoction is taken as a carminative to relieve colic and intestinal gas and as a diuretic. An ointment is made from the leaves and juice and applied externally for malarial treatment. In Brazil, a whole plant infusion is taken for bronchitis and rheumatism, leaf infusion as vermifuge and a root infusion taken internally as a laxative (Neher 1968). In India, flower juice is taken internally as blood purifier and for piles, plant juice is used as ear drop and for eye infections, and a hot leaf poultice is used for boils and carbuncles (Neher 1968). *Tagetes erecta* flower is claimed to treat skin diseases like sores, burns, wounds, ulcers, eczema, and several other skin ailments (Maity et al. 2011). *T. erecta* is often used in sedation, depressurization, broadening bronchus, heat clearing and detoxicating, dissipating phlegm and stopping coughing, and spasmolysis and as an antiinflammatory (Huang 2007) It is widely used for upper respiratory tract infection, whooping cough, conjunctivitis, oral cavity inflammation, odontalgia, pharyngitis, vertigo, children infantile convulsion, amenorrhea, blood stasis, stomach ache, ulcerative carbuncle and rheumatism, among others.

Other Uses

The plant is popular as a house and garden ornamental throughout most temperate countries. The flowers are used as a source of yellow fabric dye known as ‘egandai’ or ‘gendia’ (Neher 1968). Fresh flowers are also used as cut flowers. Fresh and dry flowers can be used to dye wool, silk and cellulose fibres into shades of golden-yellow to orange and olive-green to bronze, depending on the mordant used. The plant contains phytochemical with broad biocidal activities against animal parasites, insect pests, fungi and nematodes.

The acetone extract of *T. erecta* exhibited antiparasitic activity against the sheep fluke *Paramphistomum cervi*, with LC_{50} value of 425.73 ppm (Elango and Rahuman 2011). The pyrethrin mixture isolated from callus tissues exerted a ‘knock down’ effect against stored product pests, *Tribolium* spp. (Sarin 2004). Among the crude extracts and its fractions of the flower of *Tagetes erecta*, the chloroform fraction showed highest toxicity against both the larvae and adults of *Tribolium castaneum* followed by petroleum ether fraction and ethanol extract (Nikkon et al. 2009a). The LC_{50} values of chloroform fraction against first, second, third, fourth, fifth and sixth instar larvae were 11.64, 14.23, 19.26, 29.02, 36.66 and 59.51 µg/cm^2 (72 hours), respectively, and for adults, the value was 65.93 µg/cm^2 (72 hours). *T. erecta* leaf essential oil showed 100 % mortality of white termite (*Odontotermes obesus* Rhamb.) at a dose of 6 µl/petri-plate after 24 hours of exposure, while at lower doses and shorter exposures, it showed diminished mortality rates (Singh et al. 2003). The oil only partially affected the mycelial growth of the tested fungi.

The plant was found to contain polyacetylenic thiopenes in their roots that conferred strong biocidal activity, useful for suppressing nematode

populations in the soil, and as sources of safe and natural pesticides (Marotti et al. 2010). *T. erecta* and *T. patula* were employed as a cover crop in Indian tea plantations to suppress nematodes (Neher 1968). Greenhouse studies by Ploeg (1999) demonstrated that preplanting of marigold cultivars of *Tagetes patula*, *T. erecta*, *T. signata* and a *Tagetes* hybrid all reduced galling and numbers of second-stage juveniles of *Meloidogyne incognita*, *M. javanica*, *M. arenaria* and *M. hapla* in subsequent tomato plantings. Natarajan et al. (2006) found that the aqueous extract of the whole plant was more efficacious than the stem extract and both were more efficacious than the root extract in controlling tomato root-knot nematode, *Meloidogyne incognita*. Studies found that population levels of root-lesion nematode (*Pratylenchus penetrans*) were consistently lower under marigolds (*Tagetes tenuifolia* cv. Nemakill and cv. Nemanon, *T. patula* ssp. *nana*, unidentified cv., and *T. erecta* cv. Crackerjack) compared to the other cover crops tested (Kimpinski et al. 2000). Correspondingly, average potato tuber yields were significantly higher (8–14 %) when potato followed marigolds. Results of other studies suggested that *Pratylenchus penetrans* population density may be significantly reduced when marigold (*Tagetes erecta*) were double cropped with potatoes or tomatoes (Alexander and Waldenmaier 2002). During the 3 years of the study, *P. penetrans* soil population density declined by an average of 93 % from the preplant level when marigold was grown in rotation with potato and by 98 % when marigold was grown in rotation with tomato. There was a significant reduction in the number of *P. penetrans* found in both potato and tomato roots when the crops followed marigolds. The ethanol root extract of *T. erecta* exerted >90 % mortality rate of the nematode, *Bursaphelenchus xylophilus* (Ju et al. 2010).

The essential oil of *Tagetes erecta* leaves exhibited complete inhibition of growth of *Pythium aphanidermatum*, the damping-off pathogen, at a concentration of 2,000 ppm (2.0×103 µl/l) dilution (Kishore and Dwivedi 1991). During pot trials, the oil indicated its efficacy for controlling the damping-off of seedlings of tomato up to 50 %.

Comments

The major producers of *Tagetes erecta* are Mexico, Peru, Ecuador, Argentina, and Venezuela; minor producers are India, South Africa, and Zambia. Refer also to notes under other *Tagetes* species.

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Tagetes lucida

Scientific Name

***Tagetes lucida* Cav.**

Synonyms

Tagetes anethina Sessé & Moc., *Tagetes florida* Sweet, *Tagetes gilletii* De Wild., *Tagetes lucida* (Sweet) Voss, *Tagetes lucida* f. *florida* (Sweet) Voss, *Tagetes lucida* subsp. *schiedeana* (Less.) Neher, *Tagetes pineda* La Llave, *Tagetes schiedeana* Less, *Tagetes seleri* Rydb.

Family

Asteraceae

Common/English Names

Cloud Plant, Mexican Mint Marigold, Mexican Tarragon, Mint-Marigold, Spanish Tarragon, Sweet Scent Marigold, Sweet Scent Mexican Marigold, Sweet Mace, Texas Tarragon, Winter Tarragon

Vernacular Names

Chinese: Tian Wan Shou Ju
Czech: Aksamitník Světlý
Danish: Mexikansk Esdragon
Eastonian: Läikiv Peiulill
German: Glänzende Samtblume, Samtblume, Winterestragon, Mexicanischer Estragon
Finnish: Rohtosamettikukka, Tuoksusamettikukka
French: Tagète, Tagète Luisante, Estragon Du Mexique
Mexico: Anis, Anisillo, Curucumin, Hierba Anis, Hierba De Santa Maria, Hierbanis, Pericón, Santa Maria, Tzitziqi, Yerba De Nube, Yahutli (Ancient Aztec)
Polish: Aksamitka Yahutli
Russian: Meksikanski Estragon
Spanish: Anisillo, Hierba Anis, Pericón, Perriquillo, Yauhtli, Yerba Anis
Swedish: Mexikansk Dragon

Origin/Distribution

The plant is native to Central America (Mexico, Honduras and Guatemala) and South America. It thrives in the south of the United States and in México and is grown in many warm temperate areas worldwide. It is cultivated as an ornamental in the highlands in Java.

Agroecology

It is an aromatic herb distributed naturally from Mexico to Honduras, at elevations between 1,000 and 2,000 m. A robust perennial herb grown as an annual. It requires full sun or partial shade and needs well-drained, moderately fertile soil,

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growing well in clayey and sandy soils. It is fairly drought tolerant and frost sensitive; hard freezes will kill it to the ground. It is easily propagated through stem cuttings.

Edible Plant Parts and Uses

Leaves and flowers are edible (Hedrick 1972; Facciola 1990; Brown 2011). Petals are used as condiments. Flowers are used in salads. The anise-scented foliage is used in salads, soups, sauces, stews and poultry and fish dishes. Mexican Marigold is good for bouquet garni for flavoured butter and herbed vinegar. The dried leaves and flowering tops are brewed into a pleasant, soothing, anise-flavoured tea which is a very popular drink in Latin America. The leaves were an important flavouring of 'chocolatl', the foaming cocoa-based drink of the Aztecs. The petals are used as a condiment. The natives in Mexico prepare a tea from the shoots.

It is cultivated commercially in Costa Rica as a spice herb; it contains an oil having an anise-like odour, and the fresh aerial parts of this plant are sold in the supermarket as a substitute of tarragon (*Artemisia dracunculus* L.).

Plate 1 Winter Tarragon flowers and leaves

Botany

A half-hardy semi-woody herb to subshrub that grows 46–76 cm high and 48 cm spread. The plant is bushy with many smooth, upright, unbranched stems. The leaves are opposite, linear to oblong, about 7.6 cm long, and shiny medium green and finely toothed margin, acute and tapering base, sessile and glandular (Plates 1, 2 and 3). Bruised leaves have a sweet tarragon-like smell with overtones of anise. In summer it bears terminal clusters of small yellow to orange flower heads on the ends of the stems. The flowers are about 1.5 cm in diameter, bisexual comprising a single whorl of 3–5 (−7) ray florets with yellow to orange-yellow corollas, and numerous disc florets in the centre of the capitulum (Plates 1 and 2).

Plate 2 Close view of Winter Tarragon flowers

Plate 3 Lanceolate leaves with finely serrated margins

Nutritive/Medicinal Properties

Guzmán and Manjarrez (1962) reported methyl eugenol (80 %) and methyl chavicol (12 %) as the major components of *T. lucida* plant oil. Anethole (23.8 %), eugenol (24.3 %) and methyl chavicol (33.9 %) were reported as major constituents (Bicchi et al. 1994). From a methanol extract of the entire plant collected in Mexico, four coumarins were isolated (Rios and Flores 1976). Also, three bithienyls [5-(3-buten-1-ynyl)-2,2′-bithienyl, 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl, 5-(4-acethoxy-1-butynyl)-2,2′-bithienyl] and α-terthienyl were isolated from roots of the plant (Bohlmann et al. 1973). Bicchi et al. (1997) identified 53 compounds in the essential oil of *T. lucida* aerial plant parts, and anethole (23.8 %), methyl eugenol (24.3 %) and estragole (33.9 %) were the major constituents. Cicció (2004) identified 30 compounds from the oils of *T. lucida* flowers, stems and leaves: methyl chavicol (95–97 %) was the major constituent, with minor quantities of the monoterpenes, β-myrcene (0.6–1.8 %), (*E*)-β-ocimene (0.2 %) and linalool (0.2–0.3 %). The sesquiterpene hydrocarbons amounted to only about 1–2 %: β-caryophyllene (0.2–0.3 %), (*E*)-β-farnesene (0.3–0.9 %), germacrene-D (0.2–0.5 %) and (*E*,*E*)-α-farnesene (0.1–0.3 %). The flower oil also contained two bithienyls, 5′-mehtyl-5-(3-buten-1-ynyl)-2,2′bithienyl (0.1 %) and 5-(3-penten-1-ynyl)-2,2,-bithienyl *n*-heneicosane (0.8 %) and δ-cardinene 0.1 % as minor constituents.

Tagetes lucida was reported to contain the following flavonoids: isorhamnetin and its 7-*O*-glucoside, a quercetagetin 3-*O*-arabinosylgalactoside and patuletin (Abdala 1999). Céspedes et al. (2006) isolated seven coumarins, namely, 7,8-dihydroxycoumarin, umbelliferone (7-hydroxycoumarin), scoparone (6,7-dimethoxycoumarin), esculetin (6,7-dihydroxycoumarin), 6-hydroxy-7-methoxycoumarin,herniarin(7-methoxycoumarin) and scopoletin (6-methoxy-7-hydroxycoumarin), and three flavonoids, patuletin, quercetin and quercetagetin, from CH_2Cl_2 and MeOH extracts from aerial plant parts of *T. lucida*. Additionally, 6,7-diacetoxycoumarin, 6-methoxy-7-acetylcoumarin and 6-acetoxy-7-methoxycoumarin derivatives were synthesized. 8-Methoxypsoralen; 8-acetyl-7-hydroxycoumarin; 7,8-dihydroxy-6-meth-oxy-coumarin; 6,7-dimethoxy-4-methylcoumarin; 5,7-dihydroxy-4-methylcoumarin;4-hydroxycoumarin; 4-hydroxy-6,7-dimethylcoumarin; naringenin; glycoside-7-rhamnonaringin and rutin were commercially obtained. The following phenylpropanoids scopoletin and 7-methoxycoumarin were reported from the plant by Oranday et al. (2008).

Roots of *Tagetes* species (*T. erecta*, *T. filifolia*, *T. lucida*, *T. minuta*, *T. patula* and *T. tenuifolia*) were found to have the highest diversity and contents of thiophenes (from 64 to 100 % of the total thiophene amount), with 5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT) as the main component followed by 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc), 2,2′:5′,2″-terthienyl (alpha-T) and 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH) (Marotti et al. 2010). *Tagetes lucida* and *T. tenuifolia* possessed the highest amounts of total thiophenes (6717.3 and 6452.5 mg/kg dry weight, respectively). Thiophenes are polyacetylenic compounds that possess strong

biocidal activity, useful for suppressing nematode populations in the soil and as sources of safe and natural pesticides.

Antioxidant Activity

Methanol extract of *Tagetes lucida* leaves yielded a new flavonol glycoside, quercetagenin 3,4′-dimethyl ether 7-*O*-β-D-glucopyranoside; two new phenolic acids, 3-(2-*O*-β-D-glucopyranosyl-4-methoxyphenyl)propanoic acid and its methylester; and known flavonols, aromatic acids and 7-methoxycoumarin (Aquino et al. 2002). Using the DPPH test, the extract and some of its constituents showed significant free radical scavenging effect in comparison to α-tocopherol and standard flavonols. The antioxidant activity of the essential oil from *Tagetes lucida* showed a low mean effective concentration (EC_{50}), with value of 37.9 μg/ml (Olivero-Verbel et al. 2010). The main component of the oil was estragole (95.7%).

Antidepressant Activity

Tagetes lucida had been reported to have antidepressant property in rats. Studies reported that the aqueous extract (10, 50, 100 mg/(kg/day)) of *T. lucida* significantly reduced immobility of the rats and increased swimming without affecting climbing behaviour in the forced swimming test (Guadarrama-Cruz et al. 2008). Similar doses were not able to modify neither the motor activity nor the on male sexual behaviour. *T. lucida* has been used in Mexican traditional medicine for the treatment of different central nervous system (CNS) diseases, in particular for depression. Of the different extracts of *T. lucida* (methanol, hexane, dichloromethane and aqueous, 10 and 50 mg/kg), only the aqueous extract of *T. lucida* administered to rats at a dose of 50 mg/kg significantly reduced immobility behaviour and increased swimming in the forced swimming test similar to fluoxetine (Gabriela et al. 2012). An antidepressant effect was observed after 7 days of treatment with the aqueous extract. Pretreatment with PCPA, an inhibitor of serotonin synthesis (100 mg/kg/day for 4 consecutive days), inhibited the antidepressant effect of both *T. lucida* and fluoxetine. Further, the aqueous extract of *T. lucida*, administered p.o., did not produce lethality or any significant changes in behaviour. They concluded that the aqueous extract of *T. lucida* manifested an antidepressant-like effect in the forced swimming test mediated by the serotonergic system, with no adverse effects when administered p.o.

Antimicrobial Activity

Several papers also reported on the antimicrobial activity of the aerial plant parts of *T. lucida*. Caceres et al. (1990) reported that *T. lucida* was one of ten plants that exhibited the best antibacterial activity against five enterobacteria pathogenic to man (enteropathogenic *Escherichia coli*, *Salmonella enteritidis*, *Salmonella typhi*, *Shigella dysenteriae* and *Shigella flexneri*). They also reported that *T. lucida* exhibited antimicrobial activity against three Gram-positive bacteria causing respiratory infections (*Staphylococcus aureus*, *Streptococcus pneumoniae and Streptococcus pyogenes*) (Caceres et al. 1991). The methanol/chloroform extract of *T. lucida* aerial plant parts was active against *Aeromonas hominis* and *Pseudomonas aeruginosa*, while the chloroform extract was active against the same bacteria and also against *Escherichia coli* and *Enterobacter alcalifaciens* (Capunzo et al. 2003). The petroleum ether extract did not show antibacterial activity. The ethyl acetate extract of *T. lucida* showed antibacterial activity against *Shigella boydii*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Sarcina lutea* and four strains of *Vibrio cholerae* (Hernández et al. 2006). The bioactive compound 5,7,4′-trimethoxyflavone was identified.

Céspedes et al. (2006) isolated seven coumarins, namely, 7,8-dihydroxycoumarin (4), umbelliferone (7-hydroxycoumarin) (5), scoparone (6,7-dimethoxycoumarin) (7), esculetin (6,7-dihydroxycoumarin) (11), 6-hydroxy-7-methoxycoumarin (12), herniarin (7-methoxycoumarin)

(13) and scopoletin (6-methoxy-7-hydroxycoumarin) (14), and three flavonoids, patuletin (18), quercetin (19) and quercetagetin (20), from CH_2Cl_2 and MeOH extracts from aerial plant parts of *T. lucida*. In addition, 6,7-diacetoxycoumarin (15), 6-methoxy-7-acetylcoumarin (16) and 6-acetoxy-7-methoxycoumarin (17) derivatives were synthesized. 8-Methoxypsoralen (1), 8-acetyl-7-hydroxycoumarin (2), 7,8-dihydroxy-6-meth-oxycoumarin (3), 6,7-dimethoxy-4-methylcoumarin (6), 5,7-dihydroxy-4-methy lcoumarin (8), 4-hydroxycoumarin (9), 4-hydroxy-6,7-dimethylcoumarin (10), naringenin (21), glycoside-7-rhamnonaringin (22) and rutin (23) were commercially obtained. The most active compounds against Gram-positive and Gram-negative bacteria (*Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella* sp., *Shigella boydii*, *Shigella* sp., *Enterobacter aerogenes*, *Enterobacter agglomerans*, *Sarcina lutea*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Yersinia enterocolitica* and *Vibrio cholerae* (three El Tor strains, CDC-V12, clinic case, and INDRE-206 were obtained from contaminated water), and *V. cholerae* (NO-O1)) were the dihydroxylated coumarins: 7,8-dihydroxy-6-meth-oxycoumarin and 7,8-dihydroxycoumarin. In addition, compounds 2–4, 6, 7 and 11 showed inhibitory activity against *Vibrio cholerae*, a key bacterium in the contaminated water; compounds 2–4 were the most active. Coumarins were the most effective compounds against Gram-negative bacteria. The extract MeOH/CH_2Cl_2 (1: 4) M2 at 0.4 μg/disc inhibited the growth of *Escherichia coli* and *Proteus mirabilis* (40 %), *Klebsiella pneumoniae* (31.1 %), *Salmonella* sp. (35.5 %) and *Shigell*a sp. (0 %) at 72 hours of culture. The dimethoxy compounds 6 and 7 showed potent activity against fungal strains (*Aspergillus niger*, *Penicillium notatum*, *Fusarium moniliforme*, *Fusarium sporotrichum*, *Rhizoctonia solani* and *Trichophyton mentagrophytes*), especially *Trichophyton mentagrophytes* and *R. solani* (100 % of inhibition at 125.0 and 250.0 μg/ml, respectively).

The methanol-chloroform and ethyl acetate extracts of *T. lucida* exhibited pronounced antifungal activity against fungi *Candida albicans*, *Colletotrichum lindemuthianum*, *Mucor circinelloides*, *Saccharomyces cerevisiae* and *Sporothrix schenckii* (Damián-Badillo et al. 2008b).

Forty volatile compounds were identified in the leaf essential oil, of which estragole (96.8 %) was the major constituent (Regalado et al. 2011). The essential oil exhibited significant antioxidant activities as evaluated by two different in-vitro assays (DPPH and TBARS), and significant activities were evidenced. The preliminary screening of its antiplasmodial, antibacterial, antifungal and antiviral activities was carried out against *Plasmodium berghei*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans*, *Acinetobacter lwoffii* and *Enterobacter aerogenes* and against strains HHV 1 and HHV 2. The essential oil showed moderate activity against *P. berghei* and *E. coli.*

Anticancer/Cytotoxic Activity

The hexane leaf extract of *Tagetes lucida* exhibited marked cytotoxic activity (Mejia-Barajas et al. 2010). The bioactive compounds isolated from the leaf extract were 7-methoxycoumarin and 6,7-dimethoxycoumarin; both compounds caused cytotoxicity in *Artemia salina*, with LC_{50} values of 28 and 238 μg/ml, respectively. The ethanol and aqueous extracts of *T. lucida* were found to be cytotoxic ($ED_{50} < 20$ μg/ml) against T47D cell line (human breast cancer) and the aqueous extract from *T. lucida* cytotoxic to HeLa (human cervix cancer) cell line (Vega-Avila et al. 2009). *T. lucida* (aerial parts) essential oil showed cytotoxicity (LC_{50} 24 hours = 22.4 μg/ml, LC_{50} 48 hours = 17.63 μg/ml) on the brine shrimp *Artemia franciscana* assay (Olivero-Verbel et al. 2010).

Larvicidal Activity

Coumarins, scopoletin and 7-methoxycoumarin isolated from the plant exhibited larvicidal activity against the malarial vector, *Aedes aegypti* (Oranday et al. 2008).

Traditional Medicinal Uses

The leaves and whole plant are digestive, diuretic, febrifuge, hypotensive, narcotic, anaesthetic, sedative and stimulant (Bown 1995). It is used internally in the treatment of sore eyes, diarrhoea, nausea, indigestion, colic, hiccups, rheumatism, malaria and feverish illnesses. Externally, it is used to treat scorpion bites and to remove ticks.

T. lucida was one of the most widely used medicinal plants in western Mexico (Neher 1968). The whole plant is dried and made into a tea by Indians for treating scorpion bites, fever, ague, diarrhoea and also as an aphrodisiac. The leaves are macerated in water and taken internally to cure hiccups. In ceremonies, the Huichol Indians from the Sierra Madre Mountains reportedly have visions when smoking the herb in combination with the consumption of fermented Tarragon tea, which is prepared the same way 'Sinicuichi' is prepared (Siegel et al. 1977). People who had been struck by lightning were treated with extracts of *Tagetes lucida*.

T. lucida is one of the plants most used by the Latin American population for the treatment of gastrointestinal disorders (Giron et al. 1991; Damián-Badillo et al. 2008b).

In Mexico, fresh herbage of *Tagetes lucida* is used as a tea for abdominal pains, to calm stomachs, to relax nerves and to alleviate the symptoms of a hangover (Bye and Linares 1983). In Mexico, juice that has been pressed from the herbage or crushed leaves are mixed with water or wine and drunk as an aphrodisiac. A tea of the plant is also used as a stimulant. It has been recognized since Spanish Colonial times that *Tagetes lucida* has aphrodisiac effects. In Mexico, it is believed that the herbage promotes lactation (Jiu 1966). It is also used as a bath additive to treat rheumatism (Siegel et al. 1977).

In India, juice from freshly pressed leaves is administered to treat eczema. In Argentina, a decoction of the leaves is drunk for coughs, and when applied topically on the skin, it is well known as an insect repellent.

Other Uses

Tagetes lucida is an aromatic herb distributed naturally in Central and South America, where it is used as a spice, for medicinal purposes, as insecticide, for religious purposes and as ornamental plant (Olivero-Verbel et al. 2010).

In Mexico and Guatemala, *Tagetes lucida* has played an important role in social, cultural and religious rites since the Aztec era till today (Kaplan 1960; Neher 1968; Diaz et al. 1977). The flowers are prominently used in religious Catholic and indigenous festivities especially in ceremonies for the dead and in the Catholic All Souls Days (Kaplan 1960). *Tagetes* flowers are commonly used for arcs and altar decorations. Even today, many Mexican Indians burn the dried foliage of *Tagetes lucida* as an incense on their home altars and during public ceremonies (Neher 1968). They would sprinkle a powder of the plant into the faces of prisoners of war who were to be burned as sacrifices, so that they would be sedated during their ordeal. The Aztecs referred to *Tagetes lucida* as 'yahutli', 'plant of the clouds' (Siegel et al. 1977). The Huichol Indians of the Sierra Madre of Mexico would smoke dried herbage of *T. lucida* (commonly referred to as *tumutsáli*) alone or mixed with tobacco from *Nicotiana rustica*. This smoking mixture, although sometimes smoked recreationally, does have ceremonial importance and hallucinogenic effects. It is reported to be smoked as a rite of passage in sexual shamanic rituals, most likely due to its aphrodisiac effects. Bundles of the dried herbage are placed as offerings in temples, administrative buildings and sacred sites (Siegel et al. 1977). The dried leaves and flowers are also smoked in cigarettes made from corn husks, often in combination with the ingestion of peyote (*Lophophora williamsii*). The combinations of smoking the herbage of *Tagetes lucida* along with consuming peyote, 'tesquino' or 'nawa' (fermented maize beverage), or homemade 'ci' or 'soter' (cactus liquor) are believed to produce very active, vivid hallucinations.

The plant contains polyacetylenic thiophenes which possess strong biocidal activity, useful for

suppressing nematode populations in the soil and as sources of safe and natural pesticides (Marotti et al. 2010).

Mexican Tarragon is an attractive landscape ornamental often used in perennial borders. Secretions from the roots of growing plants have an insecticidal effect on the soil and are reported to be effective against nematodes, keeled slugs and couch grass weed. The growing plant also has a repellent effect on various insect pests such as the asparagus beetle and bean weevils. The dried plant is burnt as an incense and to repel insects. A yellow dye obtained from the flowers is used for textile.

Epoxidation of dimethyldioxirane with the main constituents of the essential oils obtained from *Tagetes lucida*, *Cymbopogon citratus*, *Lippia alba* and *Eucalyptus citriodora* generated modified epoxides with potential uses in several areas of medicine and industry (Veloza et al. 2011).

Comments

Dried leaves will retain some of their distinctive sweet aroma but are not as good as fresh leaves. It is better to freeze the leaves or store in vinegar.

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Tagetes patula

Scientific Name

***Tagetes patula* L.**

Synonyms

No synonyms recorded

Family

Asteraceae

Common/English Names

Dwarf French Marigold, Dwarf Marigold, French Marigold, Spreading Marigold, Stinkweed, Wild Marigold

Vernacular Names

Asturian: Claveles Turcos
Brazil: Cravo De Defunto, Cravo-Fétido, Roso-Do-Bobo
Catalan: Clavell De Moro, Damasquina
Chinese: Kong Que Cao
Cook Islands: Merīkō, Merīkōro, Mērīkōro, Mērīkōro (Maori)
Croatian: Garofal Žuti, Gromniščica, Fratrići, Kadifica, Konavljanin, Žutjelj Mali
Czech: Aksamitník Rozkladitý
Danish: Fløjlsblomst, Udbredt Fløjlsblomst, Udspærret Fløjlsblomst
Eastonian: Madal Peiulill
Finnish: Ryhmäsamettikukka, Samettikukka
French: Oeillet D'inde
German: Gewöhnliche Samtblume, Studentenblume
Hungarian: Bársonyvirág
India: Genda (Bengali), Guljharo, Makhanala (Gujarati), Gainda, Gaindaa, Genda, Gultera, Taigeteej Petulaa, Taigetiz Petula, Sthulapushpa (Hindi), Chendumalli (Malayalam), Genda, Mentok, Tangla (Punjabi), Ganduga, Sandu, Sthulapushpa, (Sanskrit), Tulukka (Tamil), Bantichettu (Telugu)
Italian: Tagete Commune
Japanese: Koō-Sō
Korean: Mansugug
Majorcan: Clavell De Moro, Clavell De Mort, Clavaller De Moro, Pomposas
Nepali: Barhamase Sayaptree
Norwegian: Fløyelsblom
Polish: Aksamitka Rozpierzchła
Portuguese: Ballutets, Clavell De Moro, Cravo De Defunct, Cravo De Defunto, Cravo De Tunes
Russian: Barchatcy Otklonennye
Slovaščina: Rjavkasta Žametnica, Žametnica, Žametnica Rjavkasta
Slovencina: Aksamietnica Rozložitá
Spanish: Amapola Amarilla, Canicuba, Clavel De La India, Clavel De Las Indias, Clavel De Muerto, Clavellina Plegada, Clavellina Rizada, Copetes, Copetillo, Copetito, Damasquina, Escopetón, Escopetones, Flores De Muerto
Swedish: Sammetsblomster, Sammetstagetes

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Thai: Dao Ruang Lek
Tongaarevan: Merikō
Turkey: Kadife Çiçeği
Vietnamese: Cúc Cà Cuống, Vạn Thọ Nhỏ, Cúc Vạn Thọ Lùn

Origin/Distribution

The species is native to the Americas—Central (Mexico and Guatemala) and southwestern United States (Arizona, New Mexico and southwest Texas). It is cultivated and has naturalized elsewhere.

Agroecology

In its native range, it is found from near sea level up to altitude of 1,350 m. It is frost tender and is quite adaptable to poor soils, heat, humidity and especially drought but not adaptable to shade or water-logged sites. It thrives best in full sun, on well-drained sandy or loamy soils.

Edible Plant Parts and Uses

Flowers and leaves are edible (Kunkel 1984; Facciola 1990). Flowers are used in refreshing drinks and the leaves are used for flavouring food. The dried flowers are used as an adulterant of saffron (*Crocus sativus*) and used for colouring foods yellow. The essential oil is used as a food flavouring, though it is inferior to the oil obtained from *T. minuta* (Bown 1995).

Botany

A small, bushy, erect, branched, glabrous, herbaceous annual, 25–100 cm high with a tap root. Leaves 4–7 cm long, deeply sinuate to the midrib with linear-lanceolate segments with serrated margins (Plates 1, 2, 3, 4 and 5). Capitulum solitary and terminal, 1.5–3 cm across, on 30–15 cm long peduncle. Single flower heads have widely spreading ray florets, but double-flowered head has mounding ray florets in the shape of globular, flabellate button flower heads. Ray florets 5–9 (25+), female, ligulate, flabellate to oval-quadrate, yellow, orange to red or variegated

Plate 1 Orangey red flowers and leaves

Plate 2 Variegated reddish-brown-yellow flowers and leaves

Plate 3 Yellow flowers and leaves

Plate 4 Orangey flowers and leaves

Plate 5 Yekkow double-flowered globose flowers and leaves

blends of red-brown, yellow/red-brown (Plates 1, 2, 3, 4 and 5). Disc florets numerous, tubular, bisexual. Fruit 6–11 mm black achene, with scaly pappus.

Nutritive/Medicinal Properties

Flower Phytochemicals

Rop et al. (2012) reported that edible flowers of *Tagetes patula* had a dry matter content (%w/w) of 9.68 %, crude protein of 2.95 g/kg and the following elements (mg/kg fresh mass (FM)): P 478.25 mg, K 3808.72 mg, Ca 346.85 mg, Mg 205.19 mg, Na 114.32 mg, Fe 8.72 mg, Mn 7.86 mg, Cu 1.09 mg, Zn 13.29 mg and Mo 0.37 mg. The flowers had total antioxidant capacity of 6.70 g ascorbic acid equivalents/kg FM, total phenolic content of 4.58 g gallic acid/kg FM and total flavonoid content of 1.90 g rutin/kg FM. The flowers of *T. patula* cultivars were found to be rich in carotenoids (Kishimoto et al. 2007). Carotenoids in orange *Tagetes patula* flowers were lutein, antheraxanthin, zeaxanthin and violaxanthin. Total carotenoids in *Tagetes patula* Safari Tangerine (orange flowers) were 2019.6 μg/g FW, in Bonanza orangea (orange flowers) 1957.7 μg/g FW, in Safari Yellow (yellow flowers) 312.3 μg/g FW and in Bonanza yellow 270.3 μg/g FW (Kishimoto et al. 2007). The maximum amount of xanthophylls accumulated in the flowers with orange (or orange with claret spots) petals, where the content of carotenoids (recalculated for lutein) exceeded 5 mg/g of fresh petals against 1 mg/g for yellow and 0.2 mg/g for lemon-yellow flowers (Deineka et al. 2007). The Marigold flowers of orange colour with claret spots were characterized by a high content of anthocyanins. The main component was cyanidin-3-glucoside; some samples also contained a significant amount (10–50 %) of another cyanidin derivative identical to that of cyanidin-3-glucoside acylated with malonic acid. The main acids of isolated lutein diester were myristic and palmitic acids (accounting for 85–90 % of the total sum of acid radicals); smaller fractions represented stearic and lauric acid radicals.

Lutein (1) and eight lutein esters: (2) lutein monomyristate, (3) lutein monopalmitate, (4) lutein monostearate, (5) unknown, (6) lutein dimyristate, (7) lutein myristate-palmitate, (8) lutein dipalmitate, (9) lutein palmitate-stearate, (10) in two different parts (petals and calyces) of flower heads from different types of Marigold belonging to the species *Tagetes patula* and *T. erecta* were evaluated (Piccaglia et al. 1998). Relevant quantitative differences were found among the Marigold types which had a total content of pigments ranging from 17 to 570 mg/100 g in the petals and from 0.4 to 18.6 mg/100 g in the calyces. Marigold (*T. patula*) flowers were found to be a rich source of carotenoids mainly lutein (Bhattacharyya et al. 2008). Among the solvents methanol showed the highest extractability (52.51 %). Of three varieties (orange, yellow and red) the orange variety contained the maximum amount of lutein 154.96 mg/g of extract. The fatty acid composition of the ester fraction was determined, and saturated fatty acid content was maximum (about 75 %) and unsaturated fatty acid was about 25 %. The lutein ester was also reacted with capric acid (C_{10}) in presence of *Mucor miehei* immobilized lipase, and about 17.5 % C_{10} fatty acid was incorporated to produce modified lutein for application in various functional foods.

A new acyclic monoterpene glucoside, 2-methyl-6-methylen-2,7-octadiene-1-*O*-β-D-glucopyranoside, and known compounds, helenien, xanthophyll, patuletin and patuletrin, were isolated from *Tagetes patula* flowers (Garg et al. 1999a, b). One triterpene lupeol [lup-20-(2a)-en-3β-ol] and steroids, cholesterol, β-sitosterol (24-*R*-stigmast-5-ene-3β-ol) and stigmasterol [24-(*S*)-stigmast-5,22*E*-dien-3β-ol] were isolated from the flowers (Bano et al. 2002). A tetrahydro-β-carboline alkaloid, (+) jafrine, was isolated from the petroleum ether extract of flowers (Faizi and Naz 2002). The transformation of jafrine as well as 4-*N*-acetyl tetrahydroharmine into 2-acetyl tryptamine derivatives by autoxidation was observed.

The flavonol, patuletin, was isolated from *T. patula* flower petals (Rao and Seshadri 1941).

Flavonoids patulitrin (patuletin 7-*O*-glucoside), patuletin, quercetagetin, quercetagetin 7-*O*-glucoside, luteolin (Bhardwaj et al. 1980a), allopatuletin (3,6,7,3′,4′-pentahydroxy-5-methoxyflavone) a quercetagetin monomethyl ether (Bhardwaj et al. 1980a, b), and kaempferol) and quercetin-like structures (Ivancheva and Zdravoka 1993) (patulitrin (patuletin 7-*O*-glucoside), patuletin, quercetagetin 7-*O*-glucoside) and several unknown minor flavonoids (Guinot et al. 2008) (pateletin, patulitrin, patuletin cinnamate derivative, patuletin benzoate derivative (Faizi et al. 2008)) were isolated from the flowers. From the polar extract and fractions of yellow flowers of *Tagetes patula*, phenolic compounds (flavonoids and phenolic acids) were isolated (Faizi et al. 2011b). In the nonpolar extract, a few fatty acids, their methyl esters and thiophenes (including α-terthienyl) were detected. Patuletin, patulitrin and methyl protocatechuate were isolated from the flowers (Faizi et al. 2011a).

Thiophene derivatives were found in *T. patula* cv. Carmen flowers in solvent distillate (SE): 5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT) (3.6 %); 5′-methyl-5-(3-buten-1-ynyl)-2,2′-bithienyl (MeBBT) (nd = not detected); 5-(1-pentynyl)-2,2′-bithienyl (PBT) (50 %); 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH) (nd); 2.2′,5′,2″-terthienyl (α-T) (34.8 %); 5-(4-acetoxy-butynyl)-2,2′-bithienyl (BBTOAc) (11.6 %); 5-methylaceto-5′-(3-buten-1-ynyl)-2,2′-bithienyl (AcOCH2BBT) (nd); and 5-(3,4-diacetoxy-1-butynyl)-2,2′-bithienyl (BBT$(OAc)_2$) (nd) (Margl et al. 2002).

Of the 22 constituents identified in the hydrodistilled oil of *T. patula* capitula, grown in Lucknow, 9 were monoterpene hydrocarbons (49.4 %), 3 sesquiterpene hydrocarbons (8.5 %) and 10 oxygenated monoterpenes (32.0 %) (Garg et al. 1999*a*, *b*). The major constituents were limonene (24.5 %), terpinolene (12.1 %), (*Z*)-β-ocimene (10.4 %) and (*E*)- and (*Z*)-tagetone (9.3 %). Krishna et al. (2002) found the main constituents of the hydrodistilled oil of the capitula were (*Z*)-β-ocimene (19.9 %), (*Z*)-tagetenone (12.4 %), (*E*)-tagetenone (10.4 %), piperitenone (5.8 %) and β-caryophyllene (15.1 %). In the essential oil of *T. patula* flowers grown in Venezuela, 21 compounds were identified, and α-terthienyl (43.1 %), pentatriacontane (23.9 %) and 2-ethyl-l-dodecanol (7.9 %) were the major constituents (Martínez et al. 2009).

Flowers had significantly less volatile oil and hairy root cultures produced significantly more volatile oil than intact roots (Szarka et al. 2006). The capitula oil was rich in sesquiterpene β-caryophyllene (53.5 %); other sesquiterpenes included caryophyllene oxide (4.1 %), β-cubebene (3.5 %), spathulenol (0.9 %), traces of (*E*)-β-farnesene and α-humulene; monoterpenes (z)-tagetenone (4.2 %), (*Z*)-β-ocimene (3.8 %), terpinolene (3.3 %), (*E*)-tagetenone (1.9 %), piperitenone (1.6 %), piperitone (0.7 %), (*Z*)-tagetone (0.6 %), (*E*)-tagetone (0.6 %), piperitenone oxide(0.3 %) and limonene trace; and thiophenes 5-(3-penten-1-ynyl)-2,2′-bithienyl (PBT) (5.1 %), α-terthienyl (2.4 %) and BBT (0.8 %) BBTOAc (trace). Thirty compounds were identified in the capitula essential oil, representing 89.1 % of the total detected (Romagnoli et al. 2005). The main components were piperitone (24.74 %), piperitenone (22.93 %), terpinolene (7.8 %), dihydrotagetone (4.91 %), *cis*-tagetone (4.62 %), limonene (4.52 %) and *allo*-ocimene (3.66 %). Other minor compounds included α-terpineol (2.46 %), caryophyllene (2.09 %), *cis*-ocimene (1.8 %), 4-terpineol (1.4 %), 2-phenyl ethyl acetate (1.29 %), *trans*-tagetone (1.13 %), linalool (0.7 %), caryophyllene oxide (0.67 %), *trans*-ocimene (0.61 %), sabinene (0.43 %), 3-hexen-1-ol (0.4 %), spathulenol (0.39 %), isoborneol (0.35 %), germacrene D (0.34 %), *trans*-nerolidol (0.32 %), δ-cadinene (0.31 %), bornyl acetate (0.22 %), *p*-cymene (0.22 %), β-bisabolene (0.2 %), α-pinene (0.18 %), α-phellandrene (0.15 %), β-mircene (0.13 %) and β-copaene (0.13 %). In another study, leaf oil were richer in monoterpenes (terpinolene (21.1 %), piperitone (11.2 %), (*E*)-tagetone (9.5 %), (*Z*)-β-ocimene (6.9 %), limonene (5.9 %), (*E*)-tagetenone (5.8 %), piperitone (4.6 %), (*Z*)-tagetone (4.4 %),(z)-tagetenone (4.1 %) and piperitenone oxide (2.3 %)), sesquiterpenes (β-caryophyllene (3.5 %), β-cubebene (1.5 %), spathulenol (0.8 %) and caryophyllene oxide (0.7 %)) and thiophenes (α-terthienyl (trace), BBT (trace) and BBTOAc (trace)) (Szarka et al. 2006). In a recent study, the major compounds identified in the essential oil from *T. patula* capitula were (*Z*)-β-ocimene, (*E*)-β-ocimene, terpinolene, (*Z*)-ocimenone, (*E*)-ocimenone and δ-elemene (Prakash et al. 2012). The SPME-GC-FID analyses of live capitula showed that the volatiles were rich in monoterpenoids in comparison to the plucked capitula. In contrast, the plucked capitula recorded significant increase in sesquiterpenoids in comparison to the living capitula. *T. patula* inflorescence oil was composed mainly of β-caryophyllene (23.7 %), terpinolene (15.6 %) and *cis*-β-ocimene (15.5 %) (Armas et al. 2012).

Fruit/Seed Phytochemicals

Thiophene derivatives found in *T. patula* cv. Carmen fruits (achenes) in solvent extract comprised traces of α-T and BBTOAc (Margl et al. 2002). Phytomelanin is found in the hard, black, resistant layer in the pericarp (Pandey 1998).

Forty constituents were identified in *Tagetes patula* seed oil, comprising 94 % of the total oil (Hassanpouraghdam et al. 2011). Sesquiterpene hydrocarbons (52.7 %) and oxygenated sesquiterpenes (15.8 %) were the main subclasses of volatile oil components followed by monoterpene hydrocarbons (12.6 %). The principal constituents were (*E*)-caryophyllene (44.6 %), caryophyllene oxide (14.8 %), germacrene D (3.8 %), (*Z*)-β-ocimene (3.8 %) and limonene (3.7 %). Oxides (15.7 %) were the predominant group of components with caryophyllene oxide as their main representative. α-Terthienyl (3.8 %) comprised partially large amount in the volatile oil content despite of its polar and less volatile nature.

Leaf/Stem/Aerial Part/Seedling Phytochemicals

An enzyme with high substrate specificity and MW of 67,000, namely, 5-(4-acetoxy-1-butinyl)-2,2′-bithiophene, acetate esterase, was partly purified from the aerial parts of *Tagetes patula* (Sütfeld and Towers 1982); 3,4-diacetoxybutinylbithiophene was also detected (Pensl and Sűtfeld 1985). Thiophene derivatives were found in *T. patula* cv. Carmen shoots: (3-buten-1-ynyl)-2,2-bithie-nyl (BBT), trace from steam distillate

(SD) and 7.9 % from solvent extract (SE)); 5′-methyl-5-(3-buten-1-ynyl)-2,2′-bithienyl (MeBBT), (nd SE, trace SD; 5-(1-pentynyl)-2,2′-bithienyl (PBT) (13.7 SE; 46.4 % SD); 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH) (nd SE; nd SD); 2,2′,5,2″-terthienyl (alpha-T) (nd% SE, 31.8 % SD); 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc) (12 %SE, 11.6 % SD); 5-methylaceto-5′-(3-buten-1-ynyl)-2,2′-bithienyl ($AcOCH_2BBT$) (tr SE; nd SD); 5-(3,4-diacetoxy-1-butynyl)-2,2′-bithienyl ($BBT(OAc)_2$ (nd SE, nd SD) (Margl et al. 2002). A benzofuran, isoeuparin, was isolated from the seedling (Burke et al. 1986).

T. patula seedlings were found to contain four thiophene derivatives: bithienylbutinen, acetoxybutinylbithiophene, hydroxybutinylbithiophene and a-terthiophene in high concentrations (Bohlmann and Zdero 1979; Sütfeld and Towers 1982; Sütfeld 1982). In *T. patula* seedling, bithienylbutinen, the major thiophene compound in hypocotyls and roots, was found to accumulate earlier than the other thiophene derivatives; acetoxybutinylbithiophene was not found in cotyledons and its synthesis appeared to be light induced, while hydroxybutinylbithiophene was synthesized specifically in the roots, α-terthiophene in the cotyledons (Sütfeld 1982).

The essential oil of *T. patula* contained equal amounts of (*Z*)- and (*E*)-ocimenone and also contained limonene and β-caryophyllene (Héthélyi et al. 1986). The hydrodistilled oil of the leaves contained limonene (6.5 %), terpinolene (16.2 %), (*Z*)-tagetone (13.0 %), (*Z*)-tagetenone (5.5 %), (*E*)-tagetenone (8.2 %), piperitone (10.2 %) and piperitenone (12.5 %) as the main constituents (Krishna et al. 2002). The oil of the shoots was found to have limonene (6.8 %), (*Z*)-beta-ocimene (13.7 %), terpinolene (12.0 %), piperitone (5.8 %) and beta-caryophyllene (10.5 %) as the major constituents (Krishna et al. 2002).

The major constituents of the essential oil of the aerial parts were piperitone (33.77 %), *trans*-β-ocimene (14.83 %), terpinolene (13.87 %), β-caryophyllene (9.56 %) and limonene (7.78 %) (Rondon et al. 2006). Minor components included *cis*-β-ocimene (5.01 %), epoxy-ocimene (2.27 %), β-farnesene (1.48 %), germacrene D (1.45 %), bicyclogermacrene (1.52 %), linalool (0.73 %) and myrcene (0.53 %). The leaf oil was found to have a high content of terpinolene (21.1 %) (Szarka et al. 2006). The following compounds were found in the essential oil of *T. patula* leaves and stems: limonene (37.05 %), terpinolene (32.6 %), piperitone (14.40 %), neophytadiene (5.91 %), sabinene (2.88 %), *trans*-ocimene (2.02 %), β-caryophyllene (1.98 %), farnesol (1.84 %) and α-pinene (1.30 %) (Restello et al. 2009). *T. patula* leaf oil showed terpinolene (20.9 %) and piperitenone (14.0 %) as main components (Armas et al. 2012).

Callus cultures of *T. patula* were found to contain thiophene-biocides, mainly 5-(but-3-en-1-ynyl)-2,2′-bithiophene (BBT) and 5-(4-acetoxy-1-butynyl)-2,2′-bithiophene (BBTOAc) (Ketel 1988). Secondary calli contained about three times higher concentrations of thiophenes than tertiary calli. The occurrence of the major thiophenes (BBTOH, BBT, BBTOAc, α-T) in leaves and roots of *T. patula* (Breteler and Ketel 1993) corresponded with the data of Sütfeld (1982).

Root Phytochemicals

Two benzofurans, 4-hydroxydehydrotremetone and hydroxytremetone, were isolated from roots and hypocotyls of seedlings (Sütfeld et al. 1985). Bithiophenes 5-(4-acetoxy-1-butenyl)-2,2′-bithiophene and 5-(buten-1-nyl)-2,2′-bithiophene and a benzofuran isoeuparin (5-acetyl-4-hydroxy-2-isopropenylbenzofuran) were isolated from root cultures (Parodi et al. 1988). The benzofurans, isoeuparin and (−)-4-hydroxytremetone were isolated from *T. patula* root cultures (Margl et al. 2005). The benzenoid ring and the acetoxy group were found to be predominantly (>98 %) derived from phenylalanine via 1-deoxy-D-xylulose 5-phosphate pathway. The data indicated that isoeuparin and (−)-4-hydroxytremetone were assembled from 4-hydroxyacetophenone and dimethylallyl diphosphate via prenyl-substituted 4-hydroxyacetophenone and dihydrobenzofurans as intermediates. Root oils were rich in thiophenes (BBT (44 %), α-terthienyl (21.8 %), PBT (0.3 %), BBTOAc (6.1 %)), sesquiterpenes (α-gurjunene (4.3 %), (*E*)-β-farnesene (3.9 %),

β-caryophyllene (0.7 %), β-cubebene (0.6 %)) and monoterpene (piperitenone (0.2 %)) (Szarka et al. 2006).

α-Terthienyl was isolated from hairy roots induced by infection with *Agrobacterium rhizogenes* (Kyo et al. 1990). Depending on the hairy root line used, the level of α-terthienyl varied from 15 to 1,268 μg/g dry weight, a level that corresponded to 0.15–12.7-fold that in intact roots. Opines were also detected.

From hairy root cultures, four bithiophenes (5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT), 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH), 5-(4-acetoxy-butynyl)-2,2′-bithienyl (BBTOAc) and 5-(3,4-diacetoxy-1-butynyl)-2,2′-bithienyl (BBT(OAc)2); stigmasterol, β-farnesene) and 3 benzofurans (dehydrotremetone, 14-isobutyryloxyeuparin and 2,3,-dihydro-14-isobutyryloxyeuparin) were isolated (Menelaou et al. 1991). Thiophene production in hairy root cultures of *Tagetes patula* was found to increase with the addition of an elicitor derived from mycelial extracts of *Fusarium conglutinans* (Mukundan and Hjortso 1990). The major thiophenes produced were 5-(4-aceoxy-1-butenyl)-2,2′-bithiophene and 5-(buten-1-enyl)-2,2′bithiophene. Rajasekaran et al. (1999) found that treatment of cultured hairy roots with mycelial extract of *Aspergillus niger* (1.5 % v/v) elicited an increase in thiophene content by 1.6-folds over the control. Maximum production of thiophene was recorded at the end of the fourth week in culture with a content of 0.138 % (w/w on dry weight basis). α-Terthienyl was predominant.

Thiophene derivatives were found in *T. patula* cv. Carmen roots: BBT (65 % from steam distillate (SD) and 93.2 % from solvent extract (SE)); PBT (trace SE; nd SD); BBTOH (trace SE; nd SD); α-T (8.5 % SE, 5.2 % SD); BBTOAc (24.7 %SE, 1.6 % SD); $AcOCH_2$ BBT (tr SE; nd SD); and $BBT(OAc)_2$ (tr SE, nd SD) (Margl et al. 2002). Two thiophenes, 5′-hydroxymethyl-5-(3-butene-1-ynyl)-2,2′-bithiophene and methyl-5-[4-(3-methyl-1-oxobutoxy)-1-butynyl]-2,2′-bithiophene(2), were isolated from the roots (Bano et al. 2002).

Roots of *Tagetes* species (*T. erecta*, *T. filifolia*, *T. lucida*, *T. minuta*, *T. patula* and *T. tenuifolia*) have the highest diversity and contents of thiophenes (from 64 to 100 % of the total thiophene amount), with 5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT) as the main component followed by 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc), 2,2′:5′,2″-terthienyl (alpha-T) and 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH) (Marotti et al. 2010). The SFE (supercritical fluid CO_2) extraction of intact roots and flowers yielded 717 and 480 μg/g 2,2′:5′,2″-terthiophene (α-T), respectively, while the leaves did not contain considerable amounts of thiophenes (Szarka et al. 2010). Remarkable amounts of thiophene metabolites, 5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT) and 5-(3,4-diacetoxy-1-butynyl)-2,2′-bithienyl [BBT(OAc)2], were characteristic of the SFE of hairy root cultures. Other compounds identified in the roots included 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH), 2,2′:5′,2′-terthiophene (α-T), 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc), α-gurjunene (4.3 %), (*E*)-β-farnesene (3.9 %), β-caryophyllene, β-bisabolene, caryophyllene alcohol, methyl palmitate, palmitic acid and linoleic acid.

Four thiophenes (α-terthienyl (α-T), BBT, BBTOH, BBTOAc) and two benzofurans (euparin and 6-hydroxy-2-isopropenyl-5-acetyl, cumaranon (dihydro-euparin)) were identified in the root exudates collected from the undisturbed rhizosphere of Marigold (*Tagetes patula*) (Tang et al. 1987). Based on the total ion current chromatograms, the ratios of thiophenes in the rhizosphere were 20:25:12:1 for BBT, BBTOH, BBTOAc and α-T, respectively. These ratios were different from those obtained from the ethyl acetate extract of the roots, in which the ratios were 12:0.2:8:1. Dihydroeuparin had been isolated as a major benzofuran from *T. patula* by Bohlmann and Zdero (1979). Citric and malic acids, pyridine hydrochloride and 2-hydroxy, 5-hydroxymethyl furan, were isolated from the methanol root extract (Saleem et al. 2004).

The biosynthesis of 5-(3-buten-1-ynyl)-2,2′-bithiophene was studied in root cultures of *Tagetes patula* (Margl et al. 2001). Their data confirmed the biosynthetic route was via progressive desaturation of long-chain fatty acids precursors to C_{18} polyacetylenes and the incorporation of a suitable S-source into pentaynene (CI3) as proposed by Jente et al. (1981) who used

tritiated precursors given to soil-grown *Tagetes patula*. However, Margl et al. (2001) stated that a polyketide-like biosynthesis via a carbocyclic intermediate cannot be excluded. The monothiophene 2-(but-3-en-l-ynyl)-5-(penta-1,3-diynyl)-thiophene, present in small amounts in *Tagetes patula* hairy roots, was found to be the precursor of all bithienyls that had been described for this species but not of α-terthienyl (Arroo et al. 1995). They found that 5′-methyl-5-(3-buten-l-ynyl)-2,2′-bithienyl was converted into (5′-but-3-en-l-ynyl-[2,2′]bithiophenyl-5-yl)-methyl acetate, probably via (5′-but-3-en-l-ynyl-[2,2′] bithiophenyl-5-yl)-methanol. Substitution of the butenyl side chain of 5-(3-buten-1-ynyl)-2-2′-bithienyl resulted in the formation of 5-(3,4-dihydroxy-l-butynyl)-2,2′-bithienyl and 5-(4-hydroxy-l-butynyl)-2,2′-bithienyl, which were subsequently converted into, respectively, 5-(3,4-diacetoxy-l-butynyl)-2,2′-bithienyl and 5-(4-acetoxy-l-butynyl)-2,2′-bithienyl. The end products of this biosynthetic pathway were all bithienyl-acetate esters.

Antioxidant Activity

Of three Indian Marigold (*Tagetes patula*) cultivars, the Marigold orange (MGO) variety was found to contain the maximum amount of lutein (Bhattacharyya et al. 2010). It also had the highest DPPH radical scavenging activity and ABTS radical scavenging activity, with an EC_{50} value of 0.344 mg/ml. It was also the most effective against lipid peroxidation and hydroxyl radical scavenging activities. The MGO extract also had the maximum reducing power. Hepatic cell damage in iron-mediated Fenton reaction caused by free radicals was reduced by the Marigold extracts. The results suggested that Marigold flowers of Indian variety can be effectively utilized to produce lutein ester, which could be used as a food supplement or as an accessible source of natural antioxidants. Polar extracts, fractions and phases of the flowers demonstrated better antioxidant activity (Faizi et al. 2011a). Of the isolated constituents, methyl protocatechuate showed IC_{50} value of 2.8 μg/ml, whereas patuletin (IC_{50} = 4.3 μg/ml) was comparable to quercetin and rutin but significantly better than patulitrin (IC_{50} = 10.17 μg/ml). Toxicity test for the methanol extract and compound 2 did not elicit any behavioural changes or cause mortality in mice.

Antimicrobial Activity

Alpha-terthienyl (αT), a thiophene compound isolated from *Tagetes patula* (Asteraceae), exhibited antifungal activity towards five strains of dermatophytes (*Trichophyton mentagrophytes*, *T. rubrum*, *T. violaceum*, *Epidermophyton floccosum*, *Microsporum cookei*) (Romagnoli et al. 1994). α-T plus UVA irradiation for 90 minutes acted as a fungistatic at concentrations between 6 and 24 μM. Between 1 and 10 days after irradiation, the fungal growth was reduced or arrested with marked responses for *T. mentagrophytes*, *T. rubrum* and *M. cookei*. After UVA irradiation the photoactive compound caused damage to membranes of the nucleus, mitochondria and endoplasmic reticulum. Plasmolytic and autolytic changes resulted in plasma membrane breakage and in cell wall aberrations. 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH), the thiophene from the roots, was found to be biocidal to *Fusarium oxysporum* (Arroo et al. 1995).

The essential oil of the aerial parts of *Tagetes patula* showed strong antibacterial activity against important human pathogenic with MIC values for *Staphylococcus aureus* (30 μg/ml), *Enterococcus faecalis* (30 μg/ml), *Escherichia coli* (60 μg/ml), *Klebsiella pneumoniae* (90 μg/ml) and *Pseudomonas aeruginosa* (130 μg/ml) (Rondon et al. 2006). The hot aqueous extracts of *Tagetes patula* exerted higher antibacterial activity as compare to cold aqueous extract and methanol extract at 40 mg/ml concentration (Jain et al. 2012). It was highly inhibitory towards *Proteus vulgaris*, moderately towards *Aeromonas sobria*, *Aeromonas hydrophila*, *Staphylococcus aureus* (MTCC7405) and *Bacillus subtilis* but least so against *Staphylococcus aureus* (clinical isolate). Minimal inhibitory concentrations (MICs) were between concentrations of 20–160 mg/ml with both aqueous or methanol extracts. The methanol flower was found to possess antimicrobial activ-

ity, and its principal flavonoid patuletin was isolated as the active antibacterial principle with minimum inhibitory concentration (MIC) value of 12.5 μg/disc against *Corynebacterium* spp., *Staphylococcus* spp., *Streptococcus* spp. and *Micrococcus luteus* (Faizi et al. 2008). Its glucoside, patulitrin (4), was found to be weakly active, except against *Staphylococcus saprophyticus*, *Streptococcus faecalis* and *Streptococcus pyogenes*. The patuletin cinnamate derivative displayed antibacterial activity comparable with the parent flavonoid with a MIC value of 50 μg/disc against *Corynebacterium* spp., whereas patuletin benzoate derivative was found to be devoid of any antibacterial activity.

Two intensely mauve UV fluorescent compounds 5-(3-buten-1-ynyl)-2,2′-bithienyl and α-terthienyl isolated from *Tagetes patula* roots were found to be phototoxic to *Candida albicans* (Chan et al. 1975). The UV-mediated antibiotic activity of polyacetylenes and their thiophene derivatives from *Tagetes* species with their phototoxic effects on *Candida albicans* and certain pathogenic microorganisms and their apparent lack of phototoxicity towards the skin (except for alpha-terthienyl) suggested a potential topical therapeutic role for them in yeast, fungal and bacterial infections and light-responsive dermatoses (Towers et al. 1979).

Antiinflammatory Activity

The methanol extract of *Tagetes patula* florets inhibited acute and chronic inflammation in mice and rats when administered orally (Kasahara et al. 2002). The extract significantly suppressed hind-paw oedema induced by gamma-carrageenan in mice. Further, the extract not only inhibited the hind-paw oedema induced by various acute phlogogens, such as histamine, serotonin, bradykinin and prostaglandin E1, but also suppressed the increase of vascular permeability by acetic acid, indicating that it primarily acted at the exudative stage of inflammation. In the chronic inflammation model, the extract did not inhibit the proliferation of granulation tissue when tested by the cotton pellet method; however, it was effective on the development of adjuvant arthritis in rats.

Podiatric Therapeutic Activity

In a double-blind placebo-controlled trial carried out for 8 weeks, involving patients with bilateral hallux abducto valgus and its associated condition, bunion, administration of *T. patula* preparations, plus protective pad, was effective in reducing the width of the lesion and level of pain of hallux abducto valgus (Khan 1996).

Analgesic Activity

Patuletin, isolated from the flower, demonstrated mild analgesic activity in the acetic acid-induced writhing test and hot-plate test in mice (Faizi et al. 2011a).

Hypotensive Activity

Citric and malic acids isolated from the methanol root extract caused 71 and 43 % fall in mean arterial blood pressure (MABP) of rats at the doses of 15 and 30 mg/kg, respectively (Saleem et al. 2004). LD_{50} and LD_{100} of citric acid had been determined as 545 and 1,000 mg/kg, respectively.

Hypertensive Activity

Pyridine hydrochloride isolated from the methanol root extract produced 34 % rise in the mean arterial blood pressure of rats at the dose of 30 mg/kg (Saleem et al. 2004).

Anticataract Activity

Patulin extracted from *Tagetes patula* inhibited aldose reductase of Wistar rat lens by 100 % at 10^{-1} M, 780.0 % at 10^{-5} M and 22.7 % at 10^{-6} M (Li et al. 1991).

Acaricidal Activity

A 70 % ethanol extract from aerial parts of *T. patula* exhibited acaricidal activity against

Rhipicephalus sanguineus, the thick involved in the transmission of pathogens such as *Babesia canis*, *Ehrlichia canis*, *Coxiella burnetii*, *Rickettsia rickettsii* and *Rickettsia conorii* (Politi et al. 2012). At 50.0 mg/ml, the extract decreased oviposition rate by 21.5 % and eliminated 99.78 % of the larvae. Also it was determined that the best results were obtained with 5 minutes of immersion.

Larvicidal Activity

The thiophenes produced in callus cultures of *T. patula* showed larvicidal effect against mosquito larvae (Rajasekaran et al. 2003). *Tagetes patula* essential oil exhibited larvicidal activity against the fourth instar larvae of *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* (Dharmagadda et al. 2005). *A. aegypti* (LC_{50} 13.57, LC_{90} 37.91) was most susceptible followed by *An. stephensi* (LC_{50} 12.08, LC_{90} 57.62) and *C. quinquefasciatus* (LC_{50} 22.33, LC_{90} 71.89).

Toxicity Studies

The essential oils of *Tagetes* flowers were tested for their toxicological potential on mice; the results showed that the oils had a low toxicity with a TD_{50} 99.6 mg/kg for *T. erecta* and 112 mg/kg for *T. patula* (Martínez et al. 2009).

Allergic Dermatitis Problem

Topically applied alpha-terthienyl evoked biphasic phototoxic dermatitis and the appearance of 'sunburn' cells in human epidermis (Towers et al. 1979). None of 11 polyacetylenes had the same effect although they mimicked alpha-terthienyl in their phototoxic effects on *Candida albicans* and certain pathogenic microorganisms. Bilsland and Strong (1990) reported a case of allergic contact dermatitis from the essential oil of French Marigold (*Tagetes patula*) in an aromatherapist.

Traditional Medicinal Uses

The whole herb is aromatic, digestive, diuretic and sedative (Bown 1995). It is used internally in the treatment of indigestion, colic, severe constipation and to treat sore eyes.

In the Philippines, a flower decoction is taken internally as a carminative and used as a refreshing drink (Guerrero 1921). In Argentina, the plant extract is taken internally as a calmative and diuretic; a plant decoction is taken internally as a stimulant and stomachic (stomach strengthener) (Neher 1968). In Columbia and in Venezuela, the plant infusion is used as a bath or rub for rheumatism (Neher 1968).

Other Uses

T. patula is a popular ornamental plant especially in temperate and subtemperate areas around the world. In Argentina, the plant is used as a forage crop for sheep and goat but not cattle (Neher 1968). *T. patula* produces a significant amount of essential oil, which has characteristic antibacterial, antifungal and insecticide effects (Szarka et al. 2006). The 'Genda Attar' perfume has a beautiful and refreshing fragrance and is made from Marigold essential oil and sandalwood oil. Marigold flower garlands are used for adornment during Indian marriage ceremonies and on other special ceremonies.

Studies showed that *T. patula* essential oil (aerial parts) at concentration of 10 µl effectively control the stored grain pest, *Sitophilus zeamais* adults (Restello et al. 2009). The capitula essential oil exerted a good antifungal activity against two phytopathogenic fungi, *Botrytis cinerea* and *Penicillium digitatum*, providing complete growth inhibition at 10 and 1.25 ul/ml, respectively (Romagnoli et al. 2005). The two main compounds, piperitone and piperitenone, caused large alterations in hyphal morphology and a multisite mechanism of action. Methanol *Tagetes patula* plant extract exhibited antifungal activity against three phytopathogenic fungi: *Botrytis cinerea*, *Fusarium moniliforme* and *Pythium ultimum* (Mares et al. 2002, 2004). The extract proved to

have a dose-dependent activity on all the fungi with a marked difference between treatments in the light than in the dark. The presence of a luminous source enhanced the antifungal activity, with small differences between UVA and solar spectrum light. *Tagetes patula* extract induced alterations on *Pythium ultimum* cell membranes.

The plant contains polyacetylenic thiophenes in their roots that confer strong biocidal activity, useful for suppressing nematode populations in the soil and as sources of safe and natural pesticides (Marotti et al. 2010). *T. erecta* and *T. patula* were employed as a cover crop in Indian tea plantations to suppress nematodes (Neher 1968). Greenhouse studies by Ploeg (1999) demonstrated that preplanting of Marigold cultivars of *Tagetes patula*, *T. erecta*, *T. signata* and a *Tagetes* hybrid all reduced galling and numbers of second-stage juveniles of *Meloidogyne incognita*, *M. javanica*, *M. arenaria* and *M. hapla* in subsequent tomato plantings. Field studies found that *T. patula* diminished *Pratylenchus penetrans* populations in strawberries (Evenhuis et al. 2004). The effect of *T. patula* on *P. penetrans* population densities lasted longer than the effect of chemical soil fumigation. Strawberries were grown for 3 consecutive years after *T. patula* without damage by the root lesion nematode.

The polar extract and fractions of yellow flowers of *Tagetes patula* showing nematicidal activity against cyst nematode *Heterodera zeae* led to the isolation of phenolic compounds (flavonoids and phenolic acids). In the nonpolar extract, a few fatty acids, their methyl esters and thiophenes (including α-terthienyl) were detected. In studies of compounds obtained commercially, α-terthienyl and gallic and linoleic acids showed 100 % mortality at concentrations of 0.125 % after 24 hours. *N*-hexane extract of the roots showed nematicidal activity against *Pratylenchus penetrans* which was due predominantly to α-terthienyl (Kyo et al. 1990). Studies found that population levels of root-lesion nematode (*Pratylenchus penetrans*) were consistently lower under Marigolds (*Tagetes tenuifolia* cv. Nemakill and cv. Nemanon, *T. patula* ssp. *nana* unidentified cv. and *T. erecta* cv. Crackerjack) compared to the other cover crops tested (Kimpinski et al. 2000). Correspondingly, average potato tuber yields were significantly higher (8–14 %) when potato followed Marigolds.

Comments

Cytological and morphological evidence indicated that *Tagetes patula* L. to be an allotetraploid species ($2n=48$) which probably originated by hybridization between the diploids *T. erecta* L. and *T. tenuifolia* Cav., or species closely related to them (Towner 1961).

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Tagetes tenuifolia

Scientific Name

***Tagetes tenuifolia* Cav.**

Synonyms

Tagetes jaliscensis var. *minor* Green., *Tagetes macroglossa* Pol., *Tagetes oligocephala* DC., *Tagetes peduncularis* Cav.

Family

Asteraceae

Common/English Names

American Saffron, Lemon Marigold, Lemon Gem, Orange Gem, Signet Marigold, Striped Mexican Marigold, Slender Leaf Marigold, French Marigold

Vernacular Names

Danish: Gem Tagetes, Smalfliget Fløjlsblomst, Tangerine
Eastonian: Ahtalehine Peiulill
Finnish: Kääpiösamettikukka
French: Tagète Maculé, Tagète Taché
German: Feinblatt-Studentenblume, Gestreifte Mexikanische Studentenblume, Schmalblatt-Studentenblume
Polish: Aksamitka Wąskolistna
Slovaščina: Tankolistna Žametnica, Žametnica Tankolistna
Swedish: Litet Sammetsblomster, Liten Tagetes

Origin/Distribution

T. tenuifolia is native to Central America—Mexico, Nicaragua, Guatemala, Costa Rica Honduras, El Salvador and Panama—and is cultivated elsewhere.

Agroecology

T. tenuifolia has similar climatic requirements as other *Tagetes* species. The plant is adaptable to heavy clay and sandy soils but grows best in well-drained, fertile soil rich in organic matter and in full sun.

Edible Plant Parts and Uses

The flowers are edible and have a pleasant lemon-like flavour and can be used sparingly as a flavouring in salads, sandwiches, potato soups, wines, etc. or used as a garnish (Facciola 1990). The foliage of the signet Marigold also has a pleasant lemon fragrance.

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Botany

A small, annual, erect, branched herb, 30–50 cm high. Stem bluntly quadrangular, furrowed smooth, purplish at the basal parts. Leaves, opposite, pinnately dissected green, smooth, glossy leaves (Plate 1). Leaflets numerous, opposite to alternate, lanceolate, serrate, tip acute with a long arista and gland dotted. Flowers terminal or axillary, bright yellow, peduncle leafy generally 3 flowered, quadrangular and furrowed (Plate 1). Involucre tubular, clavate, 5 angular, 5-toothed with acute teeth, smooth. Receptacle convex, gland dotted, Ray florets 5 large, obcordate, spreading flat with style and bifid stigma, no stamens. Disc florets, numerous, tubular, 5-cleft with stamens and style, strongly 5-nerved alternating with segments, stamens 5 inserted in tube, anthers connected in tube, filament smooth, style exerted above stamens, stigma bifid. Seed linear, flat, rough, pubescent with pappus consisting of 2 paleaceous scales.

Nutritive/Medicinal Properties

The major constituents of *T. tenuifolia* essential oil were dihydrotagetone, tagetone and (*E*)-ocimenone and also contained small amounts of (*Z*)-ocimenone (Héthélyi et al. 1986).

The maximum amount of xanthophylls accumulated in the flowers with orange (or orange with claret spots) petals, where the content of carotenoids (recalculated for lutein) exceeded 5 mg per gram of fresh petals against 1 mg/g for yellow and 0.2 mg/g for lemon-yellow flowers (Deineka et al. 2007). The Marigold flowers of orange colour with claret spots were characterized by a high content of anthocyanins. The main component was cyanidin-3-glucoside; some samples also contained a significant amount (10–50 %) of another cyanidin derivative identical to that of cyanidin-3-glucoside acylated with malonic acid. The main acids of isolated lutein diester esters were myristic and palmitic acids (accounting for 85–90 % of the total sum of acid radicals); smaller fractions represented stearic and lauric acid radicals.

Plate 1 Flowers and foliage

T. tenuifolia was reported to contain the flavonoid, isorhamnetin *O*-diglycoside (De Israilev and Seeligmann 1983); quercetin 3-*O*-arabinoside, quercetin 3-*O*-galactoside and isorhamnetin 3,7-Di-*O*-galactoside (De Israilev and Seeligmann 1994); and quercetagetin, kaempferol, kaempferitrin, quercetin, quercetin-3-*O-glucoside*, quercetin-3-*O*-rhamnoside (Abdala 2001) and α-terthienyl (Vasudevan et al. 1997). *T. tenuifolia* and *T. minuta* seedlings were found to contain 5-(4-hydroxy-1-butynyl)-2-2′-bithienyl (BBTOH); 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc), while *T. campanulata* Griseb and *T. laxa* Cabrera seedlings also accumulated BBT and alpha-T (Talou et al. 1994). From the four *Tagetes* species tested, only *T. laxa* was able to produce transformed roots when infected with *Agrobacterium rhizogenes* LBA 9402. Several clones of transformed roots were obtained in which the total thiophene content present showed considerable variations (277–1,773 μg/g FW).

Roots of *Tagetes* species (*T. erecta, T. filifolia, T. lucida, T. minuta, T. patula* and *T. tenuifolia*) were found to have the highest diversity and contents of thiophenes (from 64 to 100 % of the total thiophene amount), with 5-(3-buten-1-ynyl)-2,2′-bithienyl (BBT) as the main component followed by 5-(4-acetoxy-1-butynyl)-2,2′-bithienyl (BBTOAc), 2,2′:5′,2″-terthienyl (alpha-T) and 5-(4-hydroxy-1-butynyl)-2,2′-bithienyl (BBTOH) (Marotti et al. 2010). *Tagetes lucida* and *T. tenuifolia* possessed the highest amounts

of total thiophenes (6717.3 and 6452.5 mg/kg dry weight, respectively), while *T. minuta* had the highest total thiophene yield (518.8 mg/m^2), with BBT accounting for 98 % of the total.

Traditional Medicinal Uses

In Mexico, a decoction of the entire plant is taken internally for snakebite, while a leaf poultice is used for bruises and contusions in Peru (Neher 1968).

Other Uses

Lemon Marigold is a popular ornamental bedding and pot plant. Secretions from the plant roots have an insecticidal effect on the soil, effective against nematodes and to some extent against keeled slugs; they also have an effect against some persistent weeds such as couch grass (Philbrick and Gregg 1966; Huxley et al. 1992). The plant also has an effect on asparagus beetle and bean weevils. A yellow dye is obtained from the flowers (Buchanan 1999).

The plant contains polyacetylenic thiopenes which possess strong biocidal activity, useful for suppressing nematode populations in the soil and as sources of safe and natural pesticides (Marotti et al. 2010). The root exudate of *T. tenuifolia* was found most toxic to the plant nematodes *Rotylenchulus reniformis* followed by *Tylenchorhynchus brassicae* and *Meloidogyne incognita* (Siddiqui and Alam 1988). Studies found that population levels of root-lesion nematode *Pratylenchus penetrans* were consistently lower under Marigolds (including two Marigold cultivars, *Tagetes tenuifolia* cv. Nemakill and cv. Nemanon, *T. patula* ssp. *nana*, unidentified cv. and *T. erecta* cv. Crackerjack) compared to the other cover crops tested (Kimpinski et al. 2000). Correspondingly, average potato tuber yields were significantly higher (8–14 %) when potato followed Marigolds. Another study found Marigold species and cultivars to differ in their magnitude of suppression of the root-knot nematode, *Meloidogyne incognita* (Ploeg and Maris 1999). *T. tenuifolia* cv. Tangerine Gem and the *Tagetes* hybrid Polynema allowed reproduction and root galling when grown at 30 °C and should not be used for control of *M. incognita* at temperatures close to 30 °C.

Comments

Refer also to notes under other *Tagetes* species.

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Tanacetum parthenium

Scientific Name

***Tanacetum parthenium* (L.) Sch. Bip.**

Synonyms

Aphanostephus pinulensis J.M. Coult., *Chamaemelum parthenium* (L.) E.H.L. Krause, *Chrysanthemum parthenium* (L.) Bernh., *Chrysanthemum parthenium* (L.) Pers. (illeg.), *Chrysanthemum praelatum* Vent., *Dendranthema parthenium* (*L.*) *Des Moul., Leucanthemum odoratum* (Lam.) Dulac, *Leucanthemum parthenium* (L.) Gren. & Godr., *Matricaria parthenium* L., *Parthenium matricaria* Gueldenst., *Pontia matricaria* Bubani, *Pyrethrum buschianum* Sosn., *Pyrethrum demetrii* Manden., *Pyrethrum divaricatum* (Sosn.) Sosn., *Pyrethrum glanduliferum* Sommier & Levier, *Pyrethrum grossheimii* Sosn., *Pyrethrum sericeum* var. *divaricatum* (Sosn.) Sosn., *Pyrethrum sevanense* Sosn. ex Grossh., *Tanacetum grossheimii* (Sosn.) Muradyan.

Family

Asteraceae

Common/English Names

Bachelor's Button, Bridal Roses, Camphor Geranium, Common Feverfew, Double Feverfew, European Feverfew, Feather-Fully, Febrifuge Plant, Feather Foil, Fetter-Foe, Feverfew, Feverfew Chrysanthemum, Feverfew-Chamomile, Flirtroot, Flitwort, Golden Feather, Lesser Feverfew, Matricaria Parthenium, Midsummer Daisy, Mother Herb, Nosebleed Parthenium, Pellitory, Santa Maria, White-Wort, Wild Chamomile, Wild Quinine, Eddygen Fenyw, Grande Chamomile, Mutterkraut, Vetter-Voo, Feverfew, Featherfew, Altamisa, Bachelor's Button, Featherfoil, Febrifuge Plant, Midsummer Daisy, Nosebleed, Wild Chamomile, Wild Quinine, Chamomile Grande, Chrysanthemum Atricaire, Federfoy, Flirtwort

Vernacular Names

Albanian: Karajpel Partenianr
Brazil: Crisântemo, Eston Com Febre (Portuguese)
Chile: Pireto De Jardin
Chinese: Xiao Bai Ju
Corsican: Martricaria
Croatian: Amarak, Droptiniče Koleno, Majčinski Vratić, Mater-Hćerka, Meta Gorka

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Czech: Kopretina Řimbaba, Kopretima Řimbaba, Oimbaba obecná, Řimbaba obecná
Danish: Jomfruurt, Kvindeurt, Lugtefis, Matrem, Moderurt, Pigeurt
Dutch: Boerenwormkruid, Kamille sort, Moederkruid, Wormkruidsoort
Eastonian: Lõhnav Neitsikummel, Lõhnav püreeter
Esperanto: Krizantemo ara, Tanaceto ara
Finnish: Reunuspaeivaenkakkara, Tarhakakkara
French: Camomille grande, Espargoute, Grande Camomile, Herb À Vers, Malherbe, Mandiane, Matricaire, Pyrèthre Doré, Pyrèthre Mousse, Tanaisie Parthénium
Gaelic: Bossan Pheddyr, Lus deartán, Lus Y Chiassagh
German: Bertram, Die Wucherblume, Falsche Kamille, Fieberkraut, Jungfernkraut, Metram, Mutterkamille Mutterkraut, Mutterkraut, Römische Kamille, Zierkamille
Hungarian: Anyafű, Pirétrum, Őszi aranyvirág, Őszi margitvirág
Icelandic: Glitbrá
Italian: Amarella, Amareggiola, Erba-Amara Vera, Matricale, Matricale Marga, Partenio
Juan Fernandez Islands: Santa Maria (Spanish)
Latvian: Meiteņu Biškrēsliņš
Norwegian: Matre
Polish: Wrotycz Maruna, Złocień Maruna, Złocień zwyczajny
Portuguese: Tanaceto
Russian: Piretrum Devičij
Slovaščina: Beli vratič, Materine drobtinice, Vratič beli
Slovencina: Rimbaba Obyčajná
Spanish: Altamisa, Amargaza, Botón de plata, Camomila de Aragón, Erísimo, Hierba santa, Hierba de Santa María, Matricaria, Pelitre, Piretro
Swedish: Bertram, Mattram, Parthenion
Turkey: Gümüşdüğme
Welsh: Wermod Wen, Chweryn Gwyn, Chwerwyn yr Ardd, Llysiau'r Fam, Meddygon, Menyw, Tarfgryd, Tormwyth, Tormyth

Origin/Distribution

Feverfew is indigenous to Eurasia—Balkan Peninsula in Southeastern Europe, Anatolia and the Caucasus. It is adventive by introduction in most of Europe and the Mediterranean area, also in North America and Chile in South America. Feverfew is now grown in North and South America, Europe, North Africa, China, Japan and Australia.

Agroecology

A cool climate species, feverfew occurs in mountain scrub, rocky slopes, fields, grassland, riverbeds, forest edges, along roadsides, stream banks, disturbed sites, waste places, urban sites and even walls from 10 to 2,500 m altitude. It thrives in full sun or shade (40–80 %). It occurs as a weed in gardens, yards and rubbish tips.

Edible Plant Parts and Uses

Flowers are edible and dried flowers are used as herbal tea, in wine and in certain pastries (Uphof 1968; Facciola 1990; Rop et al. 2012). The plant is used in cooking to impart a deliciously aromatic bitter taste to certain foods (Chiej 1984).

Studies found that an extraction temperature of 80 °C was optimum to provide aqueous extracts rich in parthenolide content and phenolic content and, with a desirable colour, suitable for incorporation into a functional beverage (Marete et al. 2009).

Botany

A perennial or annual, pungent, aromatic erect herb, 20–50 (–70 cm) high with numerous puberulous, grooved, terete stem branching from a rootstock with fibrous roots. Leaves alternate, radical or cauline, punctate glandular on both surfaces, lime-green, glabrous or weakly pubescent on 2.5–8 cm long petioles; upper leaves smaller and sessile to subsessile. Lamina ovate-oblong, 2–8 cm × 1.5–5 cm, bipinnate or pinnatipartite into obtuse-subacute ultimate segments. Capitula radiate, heterogamous, few to several on 2.5–3.5 cm peduncle, formed in terminal dense corymbs. Involucre hemispherical, 3-seriate phyllaries imbricate, finely pubescent, green,

Plate 1 Feverfew flowers (Louis M Landry)

outer lanceolate, inner oblong-oblanceolate, weakly pubescent to glabrescent. Receptacle convex of flattish. Ray florets, 5–12, female, with oblong, obtusely-3-lobed white ligules (Plate 1). Disc florets, numerous, yellow, tubular-infundibuliform with 5-toothed corolla tube, ovary of 2 fused carpels, stamens 5. Cypselas oblong, greyish brown, 1–1.5 mm, with 6–8 white ridges and sessile glands. Pappus membranous, coroniform with irregular lobes.

Nutritive/Medicinal Properties

Flower Phytochemicals

Rop et al. (2012) reported that edible flowers of *Chrysanthemum parthenium* (*Tanacetum parthenium*) had a dry matter content (%w/w) of 9.86 %, crude protein of 6.77 g/kg and the following elements (mg/kg fresh mass (FM)): P 501.29 mg, K 3600.34 mg, Ca 341.32 mg, Mg 159.17 mg, Na 113.31 mg, Fe 5.83 mg, Mn 7.33 mg, Cu 2.35 mg, Zn 5.94 mg and Mo 0.31 mg. The flowers had total antioxidant capacity of 4.21 g ascorbic acid equivalents/kg FM, total phenolic content of 2.72 g gallic acid/kg FM and total flavonoid content of 1.29 g rutin/kg FM. Flowers of field-grown plants had higher concentration of parthenolide (3.8 % w/w dw) than those from hydroponic plants (1.2 % w/w dw) (Pedneault et al. 2002). A hydroalcohol solution was found to extract more melatonin from the flowers than the hot water extract (Ansari et al. 2010).

The oil yield obtained by SFE (supercritical fluid extraction) of feverfew-flowering heads was similar to that resulting from hexane extraction (5.4 and 4.92 %, respectively) (Kery et al. 1999). The yield of essential oil obtained by steam distillation was only approximately one tenth that obtained by SFE or hexane extraction. Chemical analysis of the volatile constituents of feverfew revealed the presence of 17 major components, 13 of which were identified. The main constituents of each product were camphor and chrysanthenyl acetate. Other minor volatile components identified were α-pinene, camphene, β-pinene, limonene, *p*-cymene, eucalyptol, γ-terpinene, linalool, α-thujone, borneol and α-terpineol.

The essential oil contents of *T. parthenium* based on the dry weight of wild and cultivated plants from Iran were 0.1 and 0.4 % (w/w), respectively (Mirjalili et al. 2007). In total, 33 and 30 constituents were identified and quantified in wild and cultivated samples, representing 95.7 and 97.5 % of the total oil, respectively. In the oil of the wild sample, camphor (50.5 %), germacrene-D (9.2 %), camphene (7.7 %), (*E*)-sesquilavandulol (4.8 %) and (*E*)-*myrtanol* (4.7 %) were the major compounds; the minor components were tricylene (1.1 %), α-pinene (0.5 %), dihydrosabinene (0.2 %), sabinene (0.2 %), β-pinene (0.4 %), α-phellandrene (0.1 %), *p*-cymene (0.5 %), limonene (0.5 %), γ-terpinene (0.4 %), filifolone (1.4 %), chrysanthenone (1.3 %), pinocarvone (tr), borneol (0.6 %), 4-terpineol (0.5 %), lavandulyl acetate (0.1 %), bornyl acetate (1.5 %), α-capaene (0.3 %), β-elemene (0.1 %), (*E*)-caryophyllene (0.3 %), (*Z*)-β-farnesene (2.1 %), γ-gurjunene (0.1 %), (*Z,E*)-α-farnesene (1.5 %), bicyclogermacrene (1.1 %), δ-cadinene (0.2 %), spathulenol (0.4 %), viridflorol (0.6 %), α-cadinol (1.5 %), valerarone (0.1 %) and (*Z*)-nucliferol acetate (1.2 %). In the oil of cultivated plant, the major components were camphor (57.6 %), (*E*)-chrysanthenyl acetate (25.1 %), camphene (4.6 %) and bornyl angelate (2.2 %); the minor components were tricylene (0.2 %), α-pinene (0.3 %), sabinene (tr), β-pinene (tr), *p*-cymene (1.1 %), limonene (0.3 %), γ-terpinene (0.3 %),

terpinolene (tr), linalool (0.2 %), α-campholenal (0.4 %), α-cyclocitral (0.1 %), pinocarvone (tr), borneol (0.5 %), 4-terpineol (0.5 %), α-terpineol (tr), (*E*)-carveol (tr), bornyl acetate (1.4 %), neryl acetate (tr), β-terpinyl acetate (0.1 %), α-copaene (tr), (*E*)-caryophyllene (0.5 %), (*Z*)-β-farnesene (1.2 %), germacrene D (0.2 %), bornyl angelate (2.2 %), caryophyllene oxide (0.4 %), viridiflorol (0.1 %) and α-cadinol (0.2 %). It was found that (*E*)-chrysanthenyl acetate and bornyl angelate were only observed in the oil of the cultivated sample, and (*E*)-sesquilavandulol (4.8 %) and (*E*)-myrtanol (4.7 %) were completely absent in the oil of this sample. Oxygenated monoterpenes predominated in the oil of cultivated (85.9 %) and wild (60.6 %) samples. The oil of wild plants contained primarily of ten monoterpene hydrocarbons (11.6 %), nine oxygenated monoterpenes (60.6 %), eight sesquiterpene hydrocarbons (14.9 %) and six oxygenated sesquiterpenes (8.6 %), while the oil of cultivated plants consisted mainly of nine monoterpene hydrocarbons (6.8 %), 13 oxygenated monoterpenes (85.9 %), four sesquiterpene hydrocarbons (1.9 %) and four oxygenated sesquiterpenes (2.9 %).

Thirty compounds were identified in the flower-head essential oil, and the major compounds were camphor 48.4 %, chrysanthenyl acetate 26.3 % and camphene 8.76 % (Rateb et al. 2007). Other minor components included *cis*-2-octene, butyl acetate, tricylene, α-pinene, camphene, sabinene, β-pinene, *p*-cymene, limonene, 1,8-cineole, γ-terpinene, *p*-cymenene, borneol, terpin-4-ol, α-terpineol, linalool acetate, thymol, *E*-pinocarvyl acetate, *E*-caryophyllene, germacrene D, germacrene D-4-ol, *Z*-chrysanthenyl angelate, bornyl angelate, β-caryophyllene oxide, globulol, *E,E*-farnesol and *E,E*,-farnesyl acetate.

Seed Phytochemicals

Seeds were found to be rich in parthenolide and to contain tanaparthin-*α*-peroxide (Kaplan et al. 2002). Majdi et al. (2011) found that the highest expression of germacrene A synthase (*TpGAS*) was in glandular trichomes which also contained the highest concentration of parthenolide, suggesting that glandular trichomes were the secretory tissues where parthenolide biosynthesis and accumulation occurred. Expressions of (*E*)-β-caryophyllene synthase (*TpCarS*), amorpha-4,11-diene synthase, were also observed.

Aerial Parts/Plant Phytochemicals

Three pinene derivatives, two spiroketal enol ether polyines, four germacranolides and six guaianolides, two of them being endoperoxides and two secoguaianolides, were isolated from the aerial parts: germacranolide—parthenolide; eudesmolides reynosin and santamarin; guaianolides canin and artecanin; and non-lactone terpenes including camphor, β-farmesene and germacrene D, chrysanthenyl acetate, bornyl acetate, bornyl angelate, α-pinene derivatives and spiroketal enol ether polyines (Bohlmann and Zdero 1982). Compounds isolated from feverfew included sesquiterpene lactones, parthenolide, 3-β-hydroxyparthenolide, secotanapartholide A, canin and artecanin (Groenewegen et al. 1986); guaianolides, tanaparthin-α-peroxide, canin and *seco*tanapartholide-A [major group] and the corresponding 'β' series [β-peroxide, artecanin and the *seco*-B derivative] (Begley et al. 1989); significant amounts of parthenolide, camphor and chrysanthenol acetate (Smith and Burford 1992); guaianolide 3,4-epoxy-8-deoxycumambrin B and the eudesmanolide epoxysantamarine (Milbrodt et al. 1997); flavonoids, 3,6,4′-trimethyl ether and quercetagetin 3,6,3′-trimethyl ether, methyl ethers of scutellarein and 6-hydroxyluteolin, chrysoeriol 7-glucuronide, quercetin 7-glucuronide and apigenin and luteolin 7-glucuronides (Williams et al. 1999*a*); (2-glyceryl)-*O*-coniferaldehyde as the major constituent of *T. parthenium* tissue culture (Laiking and Brown 1999); and flavonoids santin 3, jaceidin 2 and centaureidin 1 (Long et al. 2003). The lipophilic flavonol, 6-hydroxykaempferol 3,7,4′-trimethyl ether, called tanetin, was found in the leaf, flower and seed of feverfew together with the known 6-hydroxykaempferol 3,7-dimethyl ether, quercetagetin 3,7-dimethyl

ether and quercetagetin 3,7,3′-trimethyl ether (Williams et al. 1995). The lipophilic flavonoids in leaf and flower were found to be methyl ethers of the flavonols 6-hydroxykaempferol and quercetagetin (Williams et al. 1999*b*). Apigenin and two flavone glucuronides were present in glandular trichomes on the lower epidermis of the ray florets. The structures of the four 6-hydroxyflavonol methyl ethers of *T. parthenium* were found to be 6- rather than 7-*O*-methylated, and tanetin was revised as 6-hydroxykaempferol 3,6,4′-trimethyl ether. The vacuolar flavonoids of feverfew were dominated by the presence of apigenin and luteolin 7-glucuronides; nine other glycosides were also present. Some rare compounds found in feverfew included guaianolides, 8α-hydroxystafiatin, endoperoxide tanaparthin-α-peroxide, canin, 10-epi-canin and secotanapartholide A and B (Todorova and Evstatieva 2001).

Three flavones, 3-hydroxyflavone, kaempferol (3,4′,5,7-tetrahydroxyflavone) and fisetin (3,3′,4′,7-tetrahydroxyflavone), and a flavanone naringenin (4′,5′,7-trihydroxyflavanone) were isolated from the aerial parts (Shafaghat and Salimi 2008).

Antioxidant phenolic acid compounds 3,5-, 4,5- and 3,4-di-*O*-caffeoylquinic acids (DCQAs) were purified from feverfew (Wu et al. 2007). Polyphenolic compounds (g/kg dry matter) in the aerial feverfew plant parts were determined as follows: chlorogenic acid 6.45 g, 3,5-DCQA (dicaffeoylquinic acid) 30.08 g, 4,5, DCQA 5.61 g, total caffeoyl derivatives 42.14 g, total dihydroxycinnamic acid derivatives 57.21 g, total flavonoids 13.97 g, total dihydroxycinnamic acid derivatives + flavonoids 71.18 g and total polyphenolic compounds 81.12 g (Fraisse et al. 2011).

Feverfew essential oil was found to increase from the beginning of stem formation (0.30 %, v/w) until full bloom (0.83 %, v/w) (Hendriks et al. 1996). During the development of the plant, the content of camphor rose from 28 to 48 %, whereas the amount of chrysanthenyl acetate decreased from 30 to 22 %. In none of the oil samples investigated could the potentially toxic monoterpenes α- or β-thujone be detected. They found that the yield of parthenolide per individual plant gradually increased from about 10 mg at study commencement to about 20 mg when the plant was in full bloom (Hendriks et al. 1997). Parthenolide was present in the leaves and flower heads, but not in the stems. Drying at ambient temperature and lyophilization had no negative influence on the yield of parthenolide per individual plant.

Twenty components were identified in the essential oil of aerial parts of *T. parthenium* in the eastern region of Kosova, constituting 885 of the oil (Haziri et al. 2009). The major components were camphor 63 % and camphene 9.6 %, indicating the occurrence of camphor/camphene chemotype in Kosova. Other components included *p*-cymene 3.3 %, bornyl acetate 3 %, chrysanthenone 1.3 % and the remainder all<1 %: tricylene, α-thujene, α-pinene, β-pinene, α-phellandrene, α-terpinene, pinocarvone, borneol, terpinene-4-ol, *p*-cymen-8-ol, α-terpineol, myrtenal, eugenol, *trans*-myrtenolacetate, isobornyl-2-methylbutanoate and caryophyllene oxide. The volatile fraction of the essential oil of feverfew grown in Belgium was characterized by high camphor (44 %) and *trans*-chrysanthenyl acetate (23 %) contents (de Pooter et al. 1989).

Twenty-three components were identified in the essential oil of *T. parthenium* aerial plant parts from Turkey representing 90.1 % of the oil (Akpulat et al. 2005). The main constituents were camphor (56.9 %), camphene (12.7 %), *p*-cymene (5.2 %) and bornyl acetate (4.6 %). Other components identified include tricylene, α-thujene, α-pinene, β-pinene, α-phellandrene, α-terpinene, γ-terpinene, chrysantheone, pinocarvone, borneol, terpinen-4-ol, ρ-cymen-8-ol, α-terpineol, myrtenal, carvacrol, eugenol, *trans*-myrtenol acetate, isobornyl 2-methyl butanoate and caryophyllene oxide. Twenty-nine components were identified in feverfew essential oil from Iran (Mohsenzadeh et al. 2011). The highest yield was extracted at the flowering stage, and the major components were camphor (18.94 %), bornyl acetate (18.35 %), camphene (13.74 %), bornyl isovalerate (3.15 %), borneol (10.93 %), juniper camphor (6.23 %) and β-eudesmol (2.65 %).

Tissue cultures of *T. parthenium* afforded significant amounts of two coumarins, scopoletin and isofraxidin together with stigmasterol and sitosterol (Banthorpe and Brown 1989). These two coumarins were either absent or were very minor compounds in the parent plant.

Leaf Phytochemicals

Water-soluble flavone glycosides detected in the leaves were identified as apigenin 7-glucuronide, luteolin 7-glucuronide, luteolin 7-glucoside and chrysoeriol 7-glucuronide (Williams et al. 1995). Murch et al. (1997) reported minute amount up to 2.45 µg/g of melatonin (N-acetyl-5-methoxytryptamine) in the leaves which was lower than that found in the flowers of St. John's wort (4.39 µg/g) and *Scutellaria baicalensis* (7.11 µg/g). The following flavonoids were detected in feverfew leaves: flavones, luteolin, scutellarein-6-methyl ether (hispidulin), scutellarein-6-4′-dimethyl ether (pectolinarigenin), 6-hydroxyluteolin 6-methyl ether (nepetin), 6-hydroxyluteolin 6,3′ -dimethyl ether (jaceosidin); flavonol, quercetagetin 3,6-dimethoxy ether (axillarin) (Ivancheva et al. 1998).

Parthenolide, tanaparthin-*α*-peroxide, tanaparthin-*β*-peroxide, 3-*β*-hydroxycostunolide and canin (Kaplan et al. 2002); parthenolide and epoxyartemorin (Sumner et al. 1992) were isolated from the leaves. Leaves of field-grown plants had higher concentration of parthenolide (1.85 % w/w dw) than those from hydroponic plants (0.38 % w/w dw) (Pedneault et al. 2002). From the leaves, isolated sesquiterpene lactones were identified as parthenolide, epoxysantamarin, 3β-hydroxyparthenolide and secotanapartholide A, and flavonoids identified as santin, apigenin, luteolin and quercetin (Rateb et al. 2007). Forty compounds were identified in the leaf essential oil, and the major compounds were camphor 37.7 %, chrysanthenyl acetate 33.8 % and terpin-1-ol 5.14 % (Rateb et al. 2007). Other minor components included butyl acetate, tricylene, α-pinene, camphene, sabinene, β-pinene, β-myrcene, *p*-cymene, limonene, β-phellandrene, 1,8-cineole, γ-terpinene, terpinolene, *p-cymenene*, pinocarvone, borneol, terpin-4-ol, α-terpineol, linalool acetate, bornyl acetate, citronellal hydrate, thymol, *E*-pinocarvyl acetate, carvacrol, α-copaene, *E*-caryophyllene, α-humulene, *E*-β-farnesene, germacrene D, Ar-curcumene, isobornyl-2-methyl butyrate, Σ-cadinene, *Z*-chrysanthenyl angelate, bornyl angelate, β-caryophyllene oxide, globulol, viridiflorol, *E,E*-farnesol and *E,E*,-farnesyl acetate. Shafaghat et al. (2009) found that feverfew leaf oil was characterized by a high amount of camphor (56.4 %), whereas in the stem oil, camphor (26.0 %), *trans*-β-ocimene (23.6 %) and germacrene-D (15.0 %) were the major constituents.

Root Phytochemicals

The roots of *Tanacetum parthenium* transformed with *Agrobacterium rhizogenes* afforded, in addition to the known coumarin isofraxidin, a new isofraxidin drimenyl ether which was elucidated as 9-epipectachol B (Kisiel and Stojakowska 1997). Twenty components (92 % of essential oil) were identified in the essential oil of *T. parthenium* roots and rhizomes (Mojab et al. 2007). Camphor (30.2 %), (*Z*)-chrysanthenyl acetate (26.5 %), α-farnesene (11.1 %) and spathulenol (8.2 %) were the major components. Other components included bornyl angelate (3.3 %), bornyl acetate (3.1 %), ethyl myristate (1.8 %), fenchone (1.5 %),1-hexanol (1.7 %), 7-benzofuranol (1.3 %), hexanal (1.1 %), β-myrcene (0.8 %), β-caryophyllene (0.4 %), α-pinene (0.3 %), *p*-cymene (0.3 %), carvacrol (0.2 %), borneol (0.1 %), isobornyl formate (0.1 %), isothujyl acetate (0.1 %) and β-bisabolene (0.1 %). The main components of the root oil were α-pinene (50.0 %), *trans*-β-farnesene (13.8 %) and bicyclogermacrene (11.0 %) (Shafaghat et al. 2009).

In feverfew hairy root cultures treated with methyl jasmonate (MJ) increased accumulation of spiroketal enol ether type diacetylenes of known deterrent activity about twofolds (Stojakowska et al. 2002). Salicylic acid (SA)

transiently reduced a content of constitutive spiroketal enol ethers, common for all root clones, but selectively enhanced accumulation of *cis*-C13-spiroketal enol ether epoxide ((*E*)-3,4-epoxy-2-(2,4-hexadiynylidene)-1,6-dioxaspiro[4.4]nonane) (2), present in clone M2. The maximum total acetylene content (≈2.5 and 1.1 % dry weight in clones M2 and I2, respectively) was observed after 72–96 hours MJ treatment. Simultaneous addition of SA and MJ to the culture medium increased accumulation of the epoxide in clone M2 (up to sixfold increase compared with the control).

Chemicals in Feverfew Extracts and Products

In the European Patent Specification EP 1 367 993 B1 titled 'Use of a feverfew extract for regulating skin ageing factors', Martin and Salio (2002) the inventors stated that to-date, the chemical constituents of whole feverfew extract include, but are not limited to apigenin-7-glucoside, apigenin-7-glucuronide, 1-β-hydroxy-arbusculin, 6-hydroxykaempferol-3,7-4′-trimethylether (tanetin), 6-hydroxykaempferol-3,7-dimethyl ether, 8-β-reynosin, 10-epicanin, ascorbic acid, β-carotene, calcium, chromium, chrysanthemolide, cosmosine, chrysanthemum, chrysarten-A, chrysarten-C, chrysoeriol-7-glucuronide, cobalt, β-costunolide, epoxyartemorin, luteolin-7-glucoside, luteolin-7-glucuronide, mangnoliolide, tanaparthin, parthenolide, reynosin, quercetagentin-3,7,3′-trimethylether, quercetagetin-3′7- dimethylether, 3,7,3′-trimethoxyquercetagetin, tanaparthin-1α,4α-epoxide and tanaparthin-1β,4β-epoxide3-β-hydroxy-parthenolide. In the US Patent US 6224875 B1, entitled '*Tanacetum parthenium* extract and method of obtaining same', the inventors Bombardelli and Morazzoni (2001) stated that *Tanacetum parthenium* contained various volatile oils having mono- and/or sesquiterpene components, flavonoids, tannins and pyrethrin, as well as terpenoids of the family of sesquiterpene lactones known as germacranolides, guaianolides and eudesmanolides. These latter compounds were found to be characterized by an α-unsaturated γ-lactone structure and to comprise in particular the compounds known as parthenolide, 3-β-hydroxy-parthenoide, costunolide, 3-β-hydroxy-costunolide, artemorin, 8-α-hydroxy-estafiatin and chrysanthemum. The presence of these sesquiterpene lactones had been considered necessary for the extracts to achieve pharmacological activity in commercial and authenticated feverfew products by (Heptinstall et al. 1992). Heptinsatll et al. (1992) found authenticated *Tanacetum parthenium* grown in the United Kingdom contained a high level of parthenolide in leaves, flowering tops and seeds but a low level in stalks and roots; the level of parthenolide in powdered leaf material declined during storage and purported feverfew products varied widely in their parthenolide content and in some products parthenolide was not detected.

Antioxidant Activity

Major polyphenolic acid compounds in feverfew with potent DPPH* scavenging activities were characterized as 3,5-, 4,5- and 3,4-di-*O*-caffeoylquinic acids (DCQAs) (Wu et al. 2007). Total antioxidant capacity (%) (DPPH scavenging activity) of feverfew aerial plant parts was 7.89 %, and contribution from the main caffeoyl derivatives was as follows: chlorogenic acid 8.49 %, 3,5- DCQA (dicaffeoylquinic acid) 48.92 %, 4,5-DCQA 9.12 % and total caffeoyl derivatives 66.53 % (Fraisse et al. 2011).

A parthenolide-depleted extract of feverfew (PD-Feverfew), which was free of sensitization potential, was found to possess free radical scavenging activity against a wide range of reactive oxygen species and with greater activity than vitamin C (Martin et al. 2008). PD-Feverfew had a fivefold greater scavenging activity for oxygen and hydroxyl radicals than ascorbic acid and threefold greater scavenging activity for ferric radicals than ascorbic acid. PD-Feverfew had the greatest scavenging activity against ferric radicals followed by oxygen, hydroxyl and peroxynitrate

radicals, respectively. PD-Feverfew was also effective in scavenging superoxide anion as measured by using a superoxide dismutase (SOD) assay kit. The IC_{50} of SOD scavenging activity for PD-Feverfew was 2.74 μg/ml and that for ascorbic acid was 34.8 μg/ml. Thus, the SOD activity of PD-Feverfew was 13-fold greater than that of ascorbic acid. In-vitro, PD-Feverfew restored cigarette smoke-mediated depletion of cellular thiols, attenuated the formation of UV-induced hydrogen peroxide and reduced pro-inflammatory cytokine release. PD-Feverfew was also found to protect keratinocytes from cigarette smoke-induced ROS formation. Cellular toxicity as measured by lactate dehydrogenase (LDH) release was also dose-dependently reversed by PD-Feverfew treatment. In-vivo, topical PD-Feverfew reduced UV-induced epidermal hyperplasia, DNA damage and apoptosis. In a clinical study PD-Feverfew treatment significantly reduced erythema versus placebo 24 hours post-UV exposure. The study showed that parthenolide-depleted extract of feverfew may protect skin from the numerous external aggressions encountered daily by the skin and reduce the damage to oxidatively challenged skin.

Anticancer/Cytotoxicity Activity

In-Vitro Studies

Parthenolide, a bioactive constituent from feverfew, induced mitochondrial dysfunction and apoptosis of human colorectal cancer cell line COLO205 (Zhang et al. 2004b). This action was found to be mediated by proapoptotic Bcl-2 family members relaying the cell death signalling elicited by parthenolide from caspase 8 to downstream effector caspases such as caspase 3 and eventually to cell death. It was also demonstrated that intracellular thiols and calcium equilibrium played a critical role in parthenolide-induced apoptotic cell death (Zhang et al. 2004a). Parthenolide rapidly depleted intracellular thiols, including both free glutathione (GSH) and protein thiols and concomitantly increased intracellular reactive oxygen species (ROS) and calcium levels in a dose- and time-dependent manner.

The alcoholic feverfew flower extract and parthenolide were the most potent, showing 100 % inhibition of Ehrlich ascites carcinoma cell viability at their highest concentration, but the alcoholic flower extract was slightly more potent than parthenolide at lower concentrations (Rateb et al. 2007). The aqueous leaf and flower extracts showed little in-vitro cytotoxic activity (60 and 65 %), respectively, at their high concentration. In an earlier study, at concentrations above 5.0 μM and an exposure time of 24 hours, parthenolide from feverfew inhibited cell growth of mouse fibrosarcoma (MN-11) and human lymphoma (TK6) cell lines in an irreversible fashion (Ross et al. 1999). However, at lower concentrations, i.e. 2.5 μM, the effect was reversible; parthenolide acted in a cytostatic fashion over multiple cell generations for both cell lines. After 24 hours exposure to 2.5 μM parthenolide, approx. 85 % of cells were able to continue cell cycling on removal of the chemical. The mechanism of the reversible growth inhibition was uncertain.

Parthenolide, from feverfew, was shown too preferentially induce acute myelogenous leukaemia stem cells to undergo apoptosis and importantly displayed no discernable effect on normal blood cells (Guzman and Jordan 2005). Anderson and Bejcek (2008) demonstrated that treatment of glioblastoma cells (brain tumour cells) with parthenolide resulted in rapid apoptosis through caspase 3/7 without a suppression of NF-kappaB activity. Studies showed parthenolide to be a promising metabolic inhibitor to retard tumorigenesis and to suppress tumour growth of cancer cells without harming normal cells (Pajak et al. 2008; Mathema et al. 2012). Parthenolide was shown to inhibit NF-kappaB- and STATs-mediated antiapoptotic gene transcription and amplified the apoptotic signal through the sensitization of cancer cells to extrinsic apoptosis, induced by TNF-alpha (Pajak et al. 2008; Mathema et al. 2012).

Kang et al. (2001) found that parthenolide potently inhibited the lipopolysaccharide (LPS)-induced interleukin IL-12 production in mouse macrophages in a dose-dependent manner. Parthenolide decreased significantly the binding activity to the kappaB site in the macrophage.

In further studies they (Kang et al. 2002) found that parthenolide strongly potentiated 1 alpha,25-dihydroxyvitamin D(3)-induced differentiation of human leukaemia HL-60 cells into monocytes via the inhibition of NF-kappa B activity and provided evidence that inhibition of NF-kappa B activation could be a prerequisite to the efficient entry of promyelocytic leukaemia cells into a differentiation pathway. In another study, parthenolide, from feverfew, induced apoptosis in pre-B acute lymphoblastic leukaemia (ALL) lines, including cells carrying the t(4;11) (q21;q23) chromosomal translocation (Zunino et al. 2007). Parthenolide induced rapid apoptotic cell death distinguished by loss of nuclear DNA, externalization of cell membrane phosphatidylserine and depolarization of mitochondrial membranes at concentrations ranging from 5 to 100 μM and production of reactive oxygen species (ROS)-specific dyes, such as nitric oxide and superoxide anion. Parthenolide-induced elevation of hypochlorite anion was observed only in the two t(4;11) lines. The data suggested parthenolide may have potential as a potent and novel therapeutic agent against pre-B ALLs. In subsequent studies, they showed that parthenolide treatment activated stress-signalling proteins in high-risk acute lymphoblastic leukaemia cells with chromosomal translocation t(4;11) (Zunino et al. 2010). Parthenolide was shown to be a potent anti-multiple myeloma cancer stem cell (MM-CSC) agent (Gunn et al. 2011). It demonstrated preferential toxicity towards MM-CSCs over non-tumorigenic MM cells. In a review of parthenolide Mathema et al. (2012) reported that parthenolide induced reactive oxygen species (ROS) exclusively in tumour cells leading to proapoptotic action; parthenolide actively interfered with microtubule formation by reducing impaired control of spindle positioning, a factor favouring tumour invasiveness in cancer cells and parthenolide-mediated STAT proteins, transcriptional factors responding to extracellular ligands that broadly mediate diverse biological functions such as cell proliferation, differentiation, transformation and apoptosis.

Parthenolide was found to inhibit proliferation of metastatic human lung cancer subline, PGCL3 cells, after 24 hours treatment the IC_{50} value was 17.60 μmol/l (Zhong et al. 2005). Parthenolide reduced significantly the activity of urokinase-type plasminogen activator secreted by PGCL3 cells and downregulated the expression level of urokinase-type plasminogen activator protein. The authors concluded that the antitumour activity of parthenolide involved the activity and expression of urokinase-type plasminogen activator. Parthenolide inhibited proliferation of human lung carcinoma (A549), human medulloblastoma (TE671), human colon adenocarcinoma (HT-29) and human umbilical vein endothelial cells (HUVEC) in-vitro with the following IC_{50} values: 4.3, 6.5, 7.0 and 2.8 μM, respectively (Parada-Turska et al. 2007). In another study, parthenolide inhibited proliferation of rabbit synoviocytes cell line HIG-82 and human rheumatoid arthritis fibroblast-like synoviocytes (RA-FLS) in-vitro (Parada-Turska et al. 2008). The proliferation of human skin fibroblasts (HSF) was inhibited less effectively.

Parthenolide exerted in-vitro stimulatory activity on tubulin assembly by inducing the formation of well-organized microtubule polymers in human breast cancer MCF-7 cells (Miglietta et al. 2004). It was found that parthenolide-induced alterations of microtubule network and nuclear morphology occurred only after combined exposures to paclitaxel. Further, the growth of MCF-7 cells was significantly inhibited by parthenolide, which enhanced paclitaxel effectiveness. The authors concluded that the antimicrotubular and antiproliferative effects of parthenolide, well-known microtubule-stabilizing anticancer agent, may influence paclitaxel activity and may be utilized in developing new combinational anticancer strategies. In separate earlier studies, Patel et al. (2000) found that parthenolide mimicked the effects of IkappaBalpha by inhibiting NF-kappaB DNA binding activity and manganese superoxide dismutase (Mn-SOD) expression and increasing paclitaxel-induced apoptosis of breast cancer cells. In other studies, feverfew ethanol extract inhibited the growth of two human breast cancer cell lines (Hs605T and MCF-7) and one human

cervical cancer cell line (SiHa) with a half-effective concentration (EC_{50}) of 1.5 mg/ml against Hs605T, 2.1 mg/ml against MCF-7 and 0.6 mg/ml against SiHa (Wu et al. 2006). Among the tested constituents of feverfew (i.e. parthenolide, camphor, luteolin and apigenin), parthenolide showed the highest inhibitory effect with an EC_{50} against Hs605T, MCF-7 and SiHa of 2.6, 2.8 and 2.7 μg/ml, respectively. Also it was found that apigenin and luteolin might have moderate to weak synergistic effects with parthenolide on the inhibition of cancer cell growth of Hs605T, MCF-7 and SiHa. In a more recent study, parthenolide and a synthetic compound, 3-isopropyl-2-methyl-4-methyleneisoxazolidin-5-one, with the same α-methylene-γ-lactone motif as in parthenolide, were found to reduce the number of viable breast cancer MCF-7 and MDA-MB-231 cells, with half maximal inhibitory concentration values between 6 and 9 μM (Wyrębska et al. 2013). Both compounds dose-dependently inhibited incorporation of [(3)H]thymidine, upregulated Bax and downregulated Bcl-2 mRNA. In MCF-7 cells, MZ-6 induced early apoptosis and cell cycle arrest in G0/G1 phase, and its effect was much stronger compared with parthenolide. In MDA-MB-231 cells, both tested compounds had similar effect and induced mostly late apoptosis.

Treatment of sesquiterpene lactones isolated from *Calea urticifolia* and *Tanacetum parthenium* at a low concentration (1 μM) significantly blocked 3-isobutyl-1-methylxanthin (IBMX)-induced melanogenesis, but did not induce the inhibitory activity of B16 melanoma cell growth (Ohguchi et al. 2009). In another study, parthenolide reduced the number of viable adherent cells in melanoma cultures with an MIC value of 4 μmol/l (Lesiak et al. 2010). Melanoma cell death accompanied by mitochondrial membrane depolarization and caspase-3 activation was observed as the result of parthenolide application. Reactive oxygen species level was not significantly increased in melanoma cells. However, preincubation of parthenolide with the thiol nucleophile *N*-acetyl-cysteine protected melanoma cells from parthenolide-induced cell death, suggesting the reaction with intracellular thiols as the mechanism responsible for parthenolide activity. Thus, parthenolide could have potential as a drug candidate for further testing in melanoma therapy.

Treatment of bladder cancer cells with parthenolide resulted in a significant decrease in cell viability (Cheng and Xie 2011). Parthenolide induced apoptosis through the modulation of Bcl-2 family proteins and poly (ADP-ribose) polymerase degradation. Treatment with parthenolide led to G1 phase cell cycle arrest in 5637 cells by modulation of cyclin D1 and phosphorylated cyclin-dependent kinase 2. Parthenolide also inhibited the invasive ability of bladder cancer cells.

Animal Studies

Mice fed with parthenolide (1 mg/day) showed a delayed onset of skin papilloma incidence induced by UVB, a significant reduction in papilloma multiplicity (papilloma/mouse) and sizes when compared with the UVB-only group (Won et al. 2004). It was found that noncytotoxic concentrations of parthenolide inhibited UVB-induced activator protein-1 DNA binding and transcriptional activity. In addition, parthenolide pretreatment also inhibited c-Jun-N-terminal kinase (JNK) and p38 kinase activation leading to the sensitization of JB6 cells to UVB-induced apoptosis. In subsequent studies, they demonstrated that parthenolide sensitized UVB-induced apoptosis via protein kinase C (PKC) pathways (Won et al. 2005). Parthenolide pretreatment of JB6 murine epidermal cells enhanced membrane translocation of PKCdelta, but inhibited the translocation of PKCzeta. Further, pretreatment with a specific PKC delta inhibitor, rotterlin, completely diminished the sensitization effect of parthenolide on UVB-induced apoptosis. Similarly when cells were transiently transfected with dominant negative PKCdelta or wild-type PKCzeta, the sensitization effect of parthenolide on UVB-induced apoptosis was also drastically reduced.

Antiviral Activity

Feverfew was one of 32 plant herbs that exhibited inhibitory activity against Epstein–Barr virus early antigen (EBV-EA) activation in Raji cells promoted by phorbol ester, 12-*O*-tetradecanoylphorbol-13-acetate (TPA) (Kapadia et al. 2002). Studies showed that parthenolide inhibited the growth of the Epstein–Barr virus (EBV)-positive Burkitt lymphoma cell line, Raji, and activated the transcription of BZLF1 and BRLF1 by inhibiting NF-κB activity (Li et al. 2012). Further, when parthenolide was used in combination with ganciclovir (GCV), the cytotoxic effect of parthenolide was amplified, suggesting that the induction of lytic EBV infection with parthenolide in combination with GCV may be a viral-targeted therapy for EBV-associated Burkitt lymphoma.

Neurological/Migraine Prophylactic Activity

The exact mechanism of migraine pathophysiology is still uncertain. Based on therapeutic and triggered migraine studies, serotonin receptors, nitric oxide, calcitonin gene-related peptide, pituitary adenylate cyclase-activating polypeptide and prostanoids have been demonstrated to be specific chemical mediators of migraine Charles (2013). Numerous mechanisms have been proposed for the action of feverfew in migraine and include inhibition of inflammation, inhibition of serotonin release, inhibition of prostaglandin synthesis, inhibition of platelet aggregation and secretion, inhibition of polymorphonuclear leucocyte degranulation, inhibition of phagocytosis of human neutrophils, inhibition of mast cell release of histamine minimizing damage to endothelium and inhibition of VSMC and modulating vasoconstriction (Biggs et al. 1992; Kemper 1999; Colodny et al. 2003). According to Rodriguez-Sainz et al. (2013) migraine, epilepsy and stroke are highly prevalent neurological disorders, often comorbid. They share diverse pathophysiological mechanisms that explain the use of similar drugs on certain occasions.

In-Vitro Studies

Sesquiterpene lactones, parthenolide, 3-β-hydroxyparthenolide, secotanapartholide A, canin and artecanin isolated from feverfew inhibited secretion of granular contents from platelets and neutrophils (Groenewegen et al. 1986). All the active compounds contained a α-methylene butyrolactone unit that could have been responsible for the antisecretory activity in extracts of feverfew. This may be relevant to the therapeutic value of feverfew in migraine and other conditions. *T. parthenium* samples established from seeds from 10 different regions were found to vary significantly within and between samples in migraine prophylactic activity in-vitro (Marles et al. 1992). Serotonin release inhibition from bovine platelets was found to correlate significantly with the content of germacranolide sesquiterpene lactone, parthenolide, although other sesquiterpene lactones from this plant and other Asteraceae species (including *T. vulgare*) were also shown to be active. Feverfew powder was found to be more potent than any of its extract or parthenolide alone in its antiserotonergic activity (Mittra et al. 2000). Feverfew extract potently and directly blocked 5-HT2B and 5-HT2A receptors and neuronally released 5-hydroxytryptamine (%-HT). Both parthenolide and Feverfew extract showed a time dependency in their action. The extract when degraded thermally up to 10 % could significantly block the 5-HT receptors and neuronal release of 5-HT; however, on further degradation it lost its inhibitory capacity markedly. Similar results were observed in rats fed orally with undergraded and degraded feverfew powder and injected i.p. with parthenolide. Feverfew powder was more effective than any of its extracts or pure parthenolide. Degraded feverfew extracts showed a marked decrease in their antiserotonergic activity.

The anti-migraine mechanism of feverfew supercritical extract was investigated in-vitro using the mouse macrophage cell line (RAW 264.7) by Aviram et al. (2012). Feverfew extract was found to inhibit both nitric oxide (NO) and TNF-α production in a dose-dependent manner with complete inhibition of NO occurring at 5 μg/ml. Feverfew inhibition of NO was attributed

to the downregulation of both eNOS and iNOS enzymes at the translational and/or posttranslational level. Fukuda et al. (2000) demonstrated that parthenolide exerted potent inhibitory effects on the promoter activity of the iNOS gene in human monocyte cell line THP-1 cells in a dose-dependent manner. The increase in iNOS promoter-dependent reporter gene activity induced by the tumour-promoting phorbol ester, 12-*O*-tetradecanoylphorbol-13-acetate (TPA), was effectively suppressed by parthenolide, with an IC_{50} of 2 μM.

In cultured lipopolysaccharide (LPS)-stimulated BV-2 microglia pretreatment with parthenolide caused a dose-dependent reduction of interleukin-6 (IL-6) secretion; at 5 μm, the highest concentration tested, it also reduced the secretion of TNF-α (54 %) (Magni et al. 2012). The reduction of microglial activation by inhibition of proinflammatory agents may help attenuate the onset and intensity of acute migraine attacks. The in-vitro results provided an additional explanation for the efficacy of orally administered *T. parthenium* as an anti-migraine agent.

Crude chloroform extracts of fresh feverfew leaves (rich in sesquiterpene lactones) and of commercially available powdered leaves (lactone-free) produced dose-dependent inhibition of the generation of thromboxane B_2 (TXB_2) and leukotriene B_4 (LTB_4) by ionophore- and chemoattractant-stimulated rat peritoneal leucocytes and human polymorphonuclear leucocytes (Sumner et al. 1992). Approximate IC_{50} values were in the range of 5–50 μg/ml. Isolated lactones (parthenolide, epoxyartemorin) were also inhibitory, with approximate IC_{50} values in the range of 1–5 μg/ml. They concluded that feverfew contained a complex mixture of sesquiterpene lactone and non-sesquiterpene lactone inhibitors of eicosanoid synthesis of high potency and that these biochemical actions may be relevant to the claimed therapeutic actions of the herb for fever, arthritis and migraine. The major flavonol and flavone methyl ethers of both *Tanacetum parthenium* and *T. vulgare* variously inhibited the major pathways of arachidonate metabolism in leucocytes (Williams et al. 1999b). There were significant differences in potency, with the tansy 6-hydroxyflavones less active than the feverfew 6-hydroxyflavonols as inhibitors of cyclooxygenase and 5-lipoxygenase. An ethanol extract of *T. parthenium* aerial parts showed high affinity for the GABA(A)-benzodiazepine site, and the bioactive apigenin isolated may be responsible for CNS (central nervous system) effects of *T. parthenium* extracts which were also used for epilepsy and convulsions in Holland (Jäger et al. 2006, 2009).

Animal Studies

Tanacetum parthenium extract enriched in parthenolide significantly reduced nitroglycerin-induced Fos expression in the nucleus trigeminalis caudalis in an animal model of migraine (Tassorelli et al. 2005). Purified parthenolide inhibited nitroglycerin-induced neuronal activation in additional brain nuclei and, significantly, the activity of nuclear factor kappaB. The findings strongly suggested parthenolide to be the component responsible for the biological activity of *Tanacetum parthenium* as regards its anti-migraine effect.

Clinical Studies

In a double-blind, placebo-controlled trial wherein eight patients received capsules containing freeze-dried feverfew leaf powder and nine placebo, those who received placebo had a significant increase in the frequency and severity of headache, nausea and vomiting with the emergence of untoward effects during the early months of treatment (Johnson et al. 1985). The group given capsules of feverfew showed no changes in the frequency or severity of symptoms of migraine. The authors concluded that feverfew taken prophylactically prevented attacks of migraine. In another randomized, double-blind, placebo-controlled crossover study involving 72 volunteers with each treatment limb lasting 4 months before crossover, treatment with feverfew was associated with a reduction in the mean number and severity of migraine attacks in each 2-month period and in the degree of vomiting; duration of individual attacks was unaltered (Murphy et al. 1988). Visual analogue scores also

indicated a significant improvement with feverfew. There were no serious side effects. In a double-blind placebo-controlled crossover trial of 57 migraine suffers, it was found that feverfew caused a significant reduction in pain intensity compared with the placebo treatment (Palevitch et al. 1997). Further, a marked reduction was recorded concerning the severity of the typical symptoms that were usually linked to migraine attacks, such as vomiting, nausea, sensitivity to noise and sensitivity to light. Transferring the feverfew-treated group to the placebo treatment resulted in an augmentation of the pain intensity as well as an increase in the severity of the linked symptoms. In contrast, shifting the placebo group to feverfew therapy resulted in a reduction of the pain intensity as well as in the severity of the linked symptoms. In another study of 24 patients (women 19–61 years old), administration of feverfew once daily (5 ml of the sap) for 30–60 days was found to significantly reduced migration index in 8 patients and less significantly in 5 patients, suggesting that feverfew may be beneficial in migraine prophylaxis as an additive drug (Prusiński et al. 1999).

In a randomized, double-blind, placebo-controlled, multicenter, parallel-group study involving 170 patients suffering from migraine, treatment of 89 patients with CO(2) extract of feverfew (MIG-99, 6.25 mg three times daily) and 81 with placebo showed that MIG-99 was effective and had a favourable benefit–risk ratio (Diener et al. 2005). The migraine frequency decreased from 4.76 by 1.9 attacks per month in the MIG-99 group and by 1.3 attacks in the placebo group. Logistic regression of responder rates showed an odds ratio of 3.4 in favour of MIG-99. Adverse events possibly related to study medication were 9/107 (8.4 %) with MIG-99 and 11/108 (10.2 %) with placebo ($P = 0.654$). Earlier in a double-blind, multicenter, randomized placebo-controlled dose–response study, they found that MIG-99 was effective only in a small predefined subgroup of patients with at least four attacks during the 28-day baseline period where the most favourable benefit–risk ratio was observed with a dosage of three capsules of 6.25 mg MIG-99 extract per day (Pfaffenrath et al. 2002). Because of the low number of patients, they asserted that the findings needed to be verified in a larger sample. In a prospective, open-label study in 12 patients diagnosed with migraine without aura, 12-week treatment with *T. parthenium* 300 mg plus *Salix alba* 300 mg (Mig-RL) twice daily was found to reduce the frequency of migraine attacks and their pain intensity and duration (Shrivastava et al. 2006). In a multicenter pilot study, 60 subjects treated 208 evaluable attacks of migraine over a 1-month period, 45 subjects treated 163 attacks with sublingual feverfew/ginger and 15 subjects treated 58 attacks with a sublingual placebo preparation (Cady et al. 2011). The study showed that sublingual feverfew/ginger appeared safe and effective as a first-line abortive treatment for a population of migraineurs who frequently experience mild headache prior to the onset of moderate to severe headache. In a recent randomized study of 69 women volunteers with chronic migraine, conducted over 10 weeks, an improvement of quality of life and better analgesic effect was found with acupuncture combined with feverfew compared with acupuncture or feverfew alone (Ferro et al. 2012).

Several clinical studies reported that feverfew had mixed results on migraine prophylaxis. In a randomized, double-blind, placebo-controlled, crossover trial to investigate migraine prophylaxis, 44 patients completed the 9-month study (De Weerdt et al. 1996). A prophylactic effect could not be demonstrated for our feverfew preparation, but the patients seemed to have a tendency to use fever symptomatic drugs during the period they used feverfew.

Review Studies

Vickers (1985) reported that in a study of feverfew users for migraine, 18 % reported adverse effects, the most troublesome being mouth ulceration (11 %). Feverfew can induce more widespread inflammation of the oral mucosa and tongue, often with lip swelling and loss of taste. In a systematic review of randomized, placebo-controlled, double-blind trials ($n = 5$ which met the inclusion/exclusion criteria), the clinical effectiveness of feverfew in the prevention of

migraine was not established conclusively (Vogler et al. 1998). The majority favoured feverfew over placebo but important caveats still existed.

In a systemic review of double-blind randomized controlled trials (RCTs) assessing the clinical efficacy and safety of feverfew versus placebo for preventing migraine, only five trials (343 patients) met the inclusion criteria (Pittler and Ernst 2004). Results from these trials were mixed and did not convincingly establish feverfew to be efficacious for preventing migraine. Only mild and transient adverse events were reported in the included trials. The authors concluded that there was insufficient evidence from randomized, double-blind trials to suggest an effect of feverfew over and above placebo for preventing migraine but that the data reviewed suggested that feverfew presented no major safety problems.

Antiinflammatory Activity

Tanacetum parthenium had been reported to inhibit the release of proinflammatory mediators from macrophages and lymphocytes Amirghofran (2012). Extracts of feverfew aerial plant parts inhibited prostaglandin production by up to 88 %; leaf extracts inhibited prostaglandin production to a lesser extent (58 %) (Collier et al. 1980). Neither the whole plant nor leaf extracts inhibit cyclooxygenation of arachidonic acid, the first step in prostaglandin biosynthesis. Feverfew was found to contain prostaglandin synthetase inhibitors: parthenolide, michefuscalide and chrysanthenyl acetate (Pugh and Sambo 1988). The IC_{50} values for the in-vitro inhibition of the prostaglandin synthetase (bovine seminal vesicle mitochondrial fraction)-mediated prostaglandin E2 production from arachidonic acid by parthenolide, michefuscalide and chrysanthenyl acetate were 11.0, 12.1 and 14.2 μM. Pharmacological tests indicated that the flavonol, tanetin, could contribute to the antiinflammatory properties of feverfew by inhibiting the generation of proinflammatory eicosanoids, although it is unlikely to be the only biologically active compound within the plant (Williams et al. 1995). The major flavonol and flavone methyl ethers of *T. parthenium* and *T. vulgare* variously inhibited the major pathways of arachidonate metabolism in leucocytes (Williams et al. 1999b). There were significant differences in potency, with the tansy 6-hydroxyflavones less active than the feverfew 6-hydroxyflavonols as inhibitors of cyclooxygenase and 5-lipoxygenase. An earlier study found that at 10–25 μg/ml feverfew had no effect on the formation of arachidonate metabolites, while at highest concentrations (50–200 μg/ml) it inhibited both cyclooxygenase and lipoxygenase metabolic products in rat leucocytes (Capasso 1986).

Pretreatment of human synovial fibroblasts with either feverfew extracts or purified parthenolide could dose-dependently inhibit the expression of intercellular adhesion molecule-1 (ICAM-1) induced by the cytokines IL-1 (up to 95 % suppression), TNF-alpha (up to 93 % suppression) and, less strongly, interferon-gamma (up to 39 % suppression) (Piela-Smith and Liu 2001). The decrease in ICAM-1 expression was accompanied by a decrease in T-cell adhesion to the treated fibroblasts. The modulation of adhesion molecule expression may be an additional mechanism by which feverfew mediates antiinflammatory effects. Studies by Kwok et al. (2001) concluded that the antiinflammatory action of parthenolide was attributed to the binding and inhibition of IkappaB kinase beta complex which was known to play a critical role in cytokine-mediated signalling. Parthenolide, the predominant sesquiterpene lactone in feverfew, inhibited the expression of COX-2 and proinflammatory cytokines (TNF alpha and IL-1) in lipopolysaccharide (LPS)-stimulated macrophages (Hwang et al. 1996). The structure–function relationship indicated that the alpha-methylene-gamma-lactone moiety conferred the inhibitory effect. Parthenolide suppressed LPS-stimulated protein tyrosine phosphorylation in the murine macrophage cell line (RAW 264.7). This suppression was correlated with its inhibitory effect on the expression of COX-2 and the cytokines. All three herbal constituents, apigenin (chamomile), ginsenoside Rb(1) (ginseng) and parthenolide (feverfew), inhibited on lipopolysaccharide (LPS)-induced proinflammatory

cytokines IL-6 and/or TNF-alpha production in murine macrophage cell culture (Smolinski and Pestka 2003). Inhibition of these two cytokines was observed in mice, but did not display the same patterns of inhibition as cell culture data. The results suggested that all three constituents possessed antiinflammatory properties but that cell culture data can only be used to approximate potential effects in animals.

Parthenolide from feverfew, inhibited the myeloid differential factor 88 (MyD88)-dependent pathway by suppressing the activity of inhibitor-κB kinase (Park et al. 2011). Parthenolide also inhibited nuclear factor-κB and interferon regulatory factor 3 activation induced by LPS or poly[I:C] and the LPS-induced phosphorylation of interferon regulatory factor 3 as well as interferon-inducible genes such as interferon inducible protein-10. These results suggested that parthenolide could modulate toll-interleukin-1 receptor domain-containing adapter-inducing interferon-β (TRIF)-dependent signalling pathways of toll-like receptors (TLRs) and may be the basis of effective therapeutics for chronic inflammatory diseases.

The alcoholic extracts of leaves and flowers and parthenolide showed significant anti-inflammatory activity (about 65–75 % of the activity of diclofenac sodium after 3 hours and about 55–60 % of the activity of diclofenac sodium after 6 hours) in the yeast-induced rat paw oedema test (Rateb et al. 2007). This was attributed to the presence of high concentration of sesquiterpene lactones, especially parthenolide, and flavonoids.

Feverfew extracts were found to inhibit mitogen-induced tritiated thymidine ([3H]-TdR) uptake by human peripheral blood mononuclear cells (PBMC), interleukin 2 (IL-2)-induced [3H]-TdR uptake by lymphoblasts and PGE2 release by interleukin 1 (IL-1)-stimulated synovial cells (O'Neill et al. 1987). Parthenolide, a major secondary feverfew, also blocked [3H]-TdR uptake by mitogen-induced PBMC. However, both crude extracts and parthenolide proved cytotoxic to mitogen-induced PBMC and IL-1 stimulated synovial cells, indicating that the pharmacological properties of feverfew may thus be due to cytotoxicity. A parthenolide-depleted extract of feverfew (PD-Feverfew) was developed to eliminate the risk of skin sensitization from feverfew (Sur et al. 2009). They ascertained that PD-Feverfew was sufficiently depleted of parthenolide since PD-Feverfew did not inhibit TNF-α induced-NF-κB activity unlike parthenolide containing whole feverfew. PD-Feverfew directly inhibited the activity of proinflammatory enzymes 5-lipoxygenase, phosphodiesterase-3 and phosphodiesterase-4 and inhibited the release of proinflammatory mediators nitric oxide, PGE_2 and TNF-α from macrophages and TNF-α, IL-2, IFN-γ and IL-4 from human peripheral blood mononuclear cells. Further, PD-Feverfew inhibited TPA-induced release of PGE_2 from human skin equivalents. In-vivo, PD-Feverfew inhibited oxazolone-induced dermatitis and was more potent than whole feverfew in reducing TPA-induced dermatitis. Finally the efficacy of PD-Feverfew was confirmed clinically by a reduction in erythema in a methyl nicotinate-induced vasodilation model. Their results indicated PD-Feverfew extract to have potent antiinflammatory activity suggesting that it would be efficacious in relieving inflammation without inducing immune sensitization. Studies showed that parthenolide suppressed inflammation by inhibiting activity of nuclear factor kappa-light-chain enhancer of activated B cells (NF-κB) (Mathema et al. 2012). Activated NF-κB is a transcription factor associated with a wide range of cellular responses, including inflammation, immune regulation, survival and proliferation. Parthenolide also acted as inhibitors of inflammasomes, large complex cytosolic proteins that are associated with autoimmunity disorders like gouty arthritis and neurodegeneration.

Vasoprotective Activity

Addition of feverfew extract to the perfusion medium protected the endothelial cell monolayer from perfusion-induced injury and led to a reversible increase in the cAMP content of rabbit aorta segments (Voyno-Yasenetskaya et al. 1988). The results indicated that feverfew may have a

vasoprotective effect in addition to its effects on platelets. Studies showed that treatment of isolated rat aortic VSMC (vascular smooth muscle cells) with parthenolide significantly inhibited the VSMC proliferation by inducing G(0)/G(1) cell cycle arrest (Weng et al. 2009). Expression of IkappaBalpha and Cox-2 were increased and were likely involved in parthenolide inhibitory effect on VSMC proliferation.

Antiplatelet/Antithrombotic Activity

Extracts of feverfew inhibited platelet aggregation and the platelet release reaction (Heptinstall et al. 1988), and the active components were held to be sesquiterpene lactones such as parthenolide. Inhibition of platelet behaviour was found to be via neutralization of sulphydryl groups either inside or outside the cell. Makheja and Bailey (1982) found that feverfew extracts inhibited ADP-, thrombin- or collagen-induced aggregation of human platelets, but, significantly, did not affect aggregation induced by arachidonic acid. Synthesis of thromboxane B2 from exogenous 14C-arachidonic acid was also not inhibited. Washed platelets prelabelled with 14C-arachidonic acid responded normally to thrombin by releasing 14C-TXB2; this was completely blocked by feverfew. A purified platelet phospholipase A2 was inhibited by feverfew with an IC_{50} of 0.1 antiplatelet units. However, in a follow-up study of ten patients who had taken feverfew extracts for up to 8 years to control migraine headaches, it was found that the platelets of all treated patients aggregated characteristically to ADP and thrombin and similarly to those of control patients (Biggs et al. 1992). However, aggregation, in response to serotonin, was greatly attenuated in the feverfew users.

The structures of two series of sesquiterpene lactones (the 'α'-series 11, 12 and 16 and the 'β'-series 15, 17 and 18) present in feverfew were revised by Hewlett et al. (1996). The activity of some of these metabolites as well as of the major sesquiterpene lactone present in feverfew, parthenolide and some simple synthetic models as inhibitors of human blood platelet function was also determined. Extracts of feverfew inhibited secretory activity in blood platelets and polymorphonuclear leucocytes (PMNs) (Heptinstall et al. 1985). Release of serotonin from platelets induced by various aggregating agents (adenosine diphosphate, adrenaline, sodium arachidonate, collagen and U46619) was suppressed by feverfew. Platelet aggregation was consistently inhibited, but thromboxane synthesis was not. Feverfew also inhibited release of vitamin B12-binding protein from PMNs induced by the secretagogues formyl-methionyl-leucyl-phenylalanine, sodium arachidonate and zymosan-activated serum. Feverfew did not inhibit the secretion induced in platelets or PMNs by the calcium ionophore A23187. Feverfew extracts were found to inhibit platelet aggregation and the platelet release reaction via neutralization of sulphydryl groups (Heptinstall et al. 1987, 1988). This was based on the observation that compounds containing sulphydryl groups such as cysteine and *N*-(2-mercaptopropionyl)glycine prevented the inhibition of platelet behaviour by feverfew. Feverfew and parthenolide dramatically reduced the number of acid-soluble sulphydryl groups in platelets. Feverfew elicited changes in the metabolism of arachidonic acid that were similar to those observed in glutathione-depleted platelets.

Feverfew extract was found to inhibit interactions of platelets with collagen substrates. (Losche et al. 1987, 1988a, b). Feverfew extract inhibited the deposition of 51-Cr-labelled platelets on both collagens types C III and C IV in a dose-dependent way. Similar concentrations of feverfew extract were needed to inhibit the formation of surface-bound aggregates and to inhibit platelet spreading in both platelet-rich plasma and suspensions of gel-filtered platelets. They found that feverfew extract inhibited uptake as well as liberation of arachidonic acid into/from platelet membrane phospholipids. When aorta segments were perfused in-situ with a physiological salt solution, the addition of feverfew to the solution protected the endothelial cell monolayer from spontaneous injury. The results indicated

that feverfew may have antithrombotic potential. In-vitro studies showed that both feverfew extract and parthenolide were more effective as inhibitors of the [14C]5-HT secretion from platelets and on platelet aggregation induced by some agents and not others and were most effective as inhibitors of the [14C]5-HT secretion (but not the aggregation) induced by phorbol-12-myristate-13-acetate (PMA) (Groenewegen and Heptinstall 1990).

Parthenolide was found to stimulate functional platelet production from human megakaryocyte cell lines and from primary mouse and human megakaryocytes in-vitro (Sahler et al. 2011). Parthenolide enhanced platelet production via inhibition of nuclear factor-κB signalling in megakaryocytes and was independent of the parthenolide-induced oxidative stress response. Additionally, parthenolide treatment of human peripheral blood platelets attenuated activation of stimulated platelets. The results revealed that parthenolide has strong potential as a candidate to enhance platelet production and to dampen undesirable platelet activation. Mathema et al. (2012) also reported that recent in-vitro studies on human megakaryotic and mouse megakaryocytic cell lines showed that parthenolide induced thrombopoiesis through the inhibitory activity of NF-κB and cell cycle arrest.

Immunomodulatory Activity

Studies showed that addition of feverfew extract inhibited phagocytosis of *Candida guilliermondii* and its overall killing in-vitro (Williamson et al. 1988). However, intracellular killing was not affected, suggesting that the apparent defect in total killing merely reflected the failure of uptake. Feverfew leaf extracts prepared in acetone–ethanol contained significantly more parthenolide than extracts in chloroform-PBS (phosphate-buffered saline) or PBS alone (Brown et al. 1997b). Extract bioactivity measured as inhibition of human polymorphonuclear leucocyte (PMNL) chemiluminescence in-vitro followed a similar trend. Extracts inhibited phorbol 12-myristate 13-acetate-induced oxidative burst by amounts which appeared not solely attributable to parthenolide alone based on the PMNL-bioassay. In another study Brown et al. (1997a) reported that the acetone leaf extracts of *T. parthenium* and *T. vulgare* inhibited phorbol myristate acetate-induced chemiluminescence of human polymorphonuclear leucocytes, with IC_{50}s from 0.79 to 2.46 mg leaf dry weight/ml whole blood Parthenolide concentration in *T. parthenium* was high 1.72 %% leaf dry weight but lower in *T. vulgare*, 0.03 %. Fractionation of crude leaf extracts revealed a number of fractions, in addition to those containing parthenolide, which influenced polymorphonuclear leucocyte activity by >5 %. The effects on phorbol myristate acetate-induced chemiluminescence suggested the activity of the responsible compound(s) was a result of inhibition of protein kinase C, or subsequent events, in polymorphonuclear leucocyte activation in-vitro.

Antiallergic Activity

Feverfew extract dose-dependently inhibited histamine release from rat peritoneal mast cells stimulated with anti-IgE or the calcium ionophore A23187 (Hayes and Foreman 1987). Greater inhibition of anti-IgE-induced histamine release was achieved with feverfew compared with the inhibition of A23187-induced release. Feverfew extract also inhibited anti-IgE-induced histamine release to the same extent in the absence and presence of extracellular glucose. It was concluded that feverfew extract contained a novel type of mast cell inhibitor.

Neuroprotective Activity

In-vitro studies in primary mouse cortical cultures showed that all feverfew sesquiterpene lactones and the α-methylene-γ-lactone moiety were able to activate a series of genes termed the antioxidant response element (ARE) and caused cellular toxicity (Fischedick et al. 2012). The guaianolides were more active and, when lacking

the endoperoxide functionality, less toxic than the germacranolides. Activation of Nrf2/ARE may be useful for the treatment of neurodegenerative disease.

Antiarthritic Activity

In the chronic adjuvant arthritic screen, compounds containing the alpha-methylene-gamma-lactone moiety, the beta-unsubstituted cyclopentenone ring and the alpha-epoxy cyclopentenone system afforded significant inhibition at 2.5 mg/kg/day (Hall et al. 1979). The sesquiterpene lactones were marginally effective against induced pleurisy. The delayed hypersensitivity was suppressed by these agents, whereas immunoglobulin synthesis was slightly stimulated. No deleterious side effects were observed with these agents from the limited tests performed. In a double-blind, placebo-controlled 6-week study of 40 female patients with symptomatic rheumatoid arthritis, no apparent benefit of oral feverfew administration and placebo was found in rheumatoid arthritis (Pattrick et al. 1989). No important differences between the clinical or laboratory variables of the groups were observed.

Antinociceptive cum Antiinflammatory Activity

Oral administration of the feverfew extract led to significant, dose-dependent antinociceptive and antiinflammatory effects against acetic acid-induced writhing in mice and carrageenan-induced paw oedema in rats, respectively (Jain and Kulkarni 1999). Parthenolide (1, 2 mg/kg i.p.), the active constituent of the extract, also produced antinociceptive and antiinflammatory effects. Naloxone, an opiate antagonist, failed to reverse feverfew extract and parthenolide-induced antinociception. Feverfew extract in higher doses (40, 60 mg/kg p.o.) neither altered the locomotor activity nor potentiated the pentobarbitone-induced sleep time in mice. It also did not change the rectal temperature in rats. The study showed that feverfew extract exerted antinociceptive and antiinflammatory effects without altering the normal behaviour of the animals.

Analgesic Activity

Parthenolide showed significant analgesic activity (about 85–90 % of the activity of paracetamol) as evaluated by acetic acid-induced writhing in mice, followed by the alcoholic extracts of flowers and leaves (about 55 and 45 % of the activity of paracetamol, respectively) (Rateb et al. 2007). The significant analgesic activity was attributed to the presence of high concentration of sesquiterpene lactones, especially parthenolide, and flavonoids.

Antipyretic Activity

Parthenolide showed significant antipyretic activity (about 60–70 % of the activity of acetyl salicylic acid (ASA)), followed by the alcoholic extracts of flowers and leaves which showed significant antipyretic activity (40–55 % of ASA activity) in the yeast-induced hyperthermia test (Rateb et al. 2007).

Antispasmodic Activity

In animal studies, feverfew extract inhibited collagen-induced bronchoconstriction by inhibiting phospholipase A2 activity (Keery and Lumley 1986). Samples prepared from chloroform extracts of fresh feverfew leaves strongly inhibited responses of rabbit aortic rings to phenylephrine, 5-hydroxytryptamine, thromboxane mimetic U46619 (9,11-dideoxy-11 alpha,9 alpha-epoxy-methano-PGF2 alpha) and angiotensin II indicating a nonspecific, most likely post-receptor site of action, but weakly inhibited contractions induced by potassium depolarization (Barsby et al. 1991, 1992). The inhibition was concentration and time dependent, noncompetitive and irreversible and also occurred in

endothelium-denuded preparations. The feverfew extracts also caused a progressive loss of tone of pre-contracted aortic rings and appeared to impair the ability of acetylcholine to induce endothelium-dependent relaxations of the tissue. Similar effects were demonstrated by parthenolide. They also found that chloroform extracts of feverfew leaf contain an as yet unidentified substance capable of producing a selective, open-channel block of voltage-dependent potassium channels in smooth muscle cells (Barsby et al. 1993a). They also found that fresh feverfew leaf extracts differing radically in their content of α-methylbutyrolactones caused time-dependent, irreversible inhibition of the contractile responses of rabbit aortic rings to all receptor-acting agonists so far tested (Barsby et al. 1993b). The presence of potentially -SH reactive parthenolide and other sesquiterpene α-methylenebutyrolactones in these extracts, and the close parallelism of the actions of pure parthenolide, suggested that the inhibitory effects were due to these compounds. Contrariwise, chloroform extracts of dried powdered leaves were not inhibitory but themselves elicited potent and sustained contractions of aortic smooth muscle that were not antagonized by ketanserin (5-HT2 receptor antagonist). These extracts were found not to contain parthenolide or butyrolactones. They concluded that the marked differences in the pharmacological potency and profiles between preparations from fresh and dried feverfew may be related to their lactone content.

Of all the extracts and major constituents, the alcoholic flower extract exhibited the most potent antispasmodic activity in the isolated rabbit duodenum, producing prolonged inhibition of intestinal motility, followed by the leaf extract (Rateb et al. 2007). Parthenolide produced moderate but not complete inhibition even at its high dose. All the aqueous extracts produced spasmogenic effect by increasing intestinal motility. Parthenolide, a sesquiterpene α-methylenebutyrolactone obtained from feverfew, inhibited smooth muscle contractility in a time-dependent, nonspecific and irreversible manner (Hay et al. 1994). They found that the characteristic smooth muscle inhibitory profile was demonstrated by the two α-methylenebutyrolactones (parthenolide and cynaropicrin), but not by the compounds lacking this functional group. Thus, the α-methylene function was critical for this aspect of the toxic pharmacological profile of the sesquiterpene butyrolactones. Béjar (1996) found that parthenolide inhibited the contractile responses of rat stomach fundus to fenfluramine and dextroamphetamine, but not serotonin. It inhibited serotonin release-mediated responses by the indirect-acting serotonin agonists on fundal tissue.

Antiulcerogenic Activity

Parthenolide from feverfew was found to exert beneficial effects in experimental murine colitis (Zhao et al. 2012). Administration of parthenolide significantly reduced the severity of dextran sulphate sodium-induced colitis and downregulated myeloperoxidase activity and phospho-NF-κB p65 expression by the blockade of phosphorylation and subsequent degradation of IκB protein, strikingly reducing the production of TNF-α and IL-1β.

Antimicrobial Activity

The essential oils from feverfew leaves, stems and roots showed inhibitory effects on *Escherichia coli* and *Salmonella typhi* but were inactive against *Staphylococcus aureus* (Shafaghat et al. 2009). Essential oil from herbal parts of feverfew from two different locations, Davutpasa-Istanbul and Savşat-Ardahan, exhibited antibacterial activity (Polatoglu et al. 2010). The oil from Davutpasa-Istanbul showed highest activity against *Bacillus subtilis* (125 μg/ml) and methicillin-resistant *Staphylococcus aureus* (125 μg/ml) and was characterized by camphor 49 %, *trans*-chrysanthenyl acetate 22.1 % and camphene 9.4 %. The oil from Savşat-Ardahan showed highest activity against *Staphylococcus aureus* (125 μg/ml) and had 60.8 % camphor and 6.8 % camphene, small amount of *cis*-chrysanthenyl acetate (0.6 %) and trace amount

of *trans*-chrysanthenyl acetate. All the oils showed toxicity to *Vibrio fischeri* in the TLC bioluminescence assay. DPPH scavenging activity was 59.3 % of the oil from Davutpasa-Istanbul at 15 mg/ml concentration and 28.2 % for the oil from Savşat-Ardahan. Feverfew essential oil exhibited antibacterial activity against *Bacillus subtilis* and *Enterobacter aerogenes*, with the minimum inhibitory concentration of 4 and 38 µl/ml, respectively (Mohsenzadeh et al. 2011).

Antimitotic/Antimutagenic Activities

Anderson et al. (1988) compared the frequency of chromosomal aberrations and sister chromatid exchanges in lymphocytes and urine mutagenicity in two groups of migraine patients chronic feverfew users ($n=30$) and matched nonusers ($n=30$). They found the mean frequency of chromosomal aberrations in the feverfew user group was lower than that in the nonuser group both in terms of cells with breaks (2.13 % vs. 2.76 %) and in terms of cells with all aberrations (4.34 % vs. 5.11 %), although the difference was not significant. Similarly the sister chromatid exchanges in the feverfew exposed group were lower than that in the control group (8.78 vs. 8.80 SCE/cell), but this difference was not significant.

Of the flavonoids isolated from *T. parthenium* extract showing activity as mitotic blocker, centaureidin 1 had an IC_{50} of 1 µM, while jaceidin 2 and santin 3 were 200 times less active (Long et al. 2003).

Antileishmanial Activity

Parthenolide, from *T. parthenium*, exhibited significant in-vitro activity against the promastigote form of *Leishmania amazonensis*, with 50 % inhibition of cell growth at a concentration of 0.37 µg/ml (Tiuman et al. 2005). For the intracellular amastigote form, parthenolide reduced by 50 % the survival index of parasites in macrophages when it was used at 0.81 µg/ml. The purified parthenolide showed no cytotoxic effects against J774G8 macrophages in culture and did not cause lysis in sheep blood when it was used at higher concentrations that inhibited promastigote forms. A guaianolide 11,13-dehydrocompressanolide purified from the hydroalcohol extract of aerial parts of feverfew showed activity against the promastigote form of *Leishmania amazonensis*, with 50 % inhibition (IC_{50}) of cell growth at a concentration of 2.6 µg/ml (da Silva et al. 2010). For the intracellular amastigote form, this guaianolide reduced by 10 % the survival index of parasites in macrophages when it was used at 20 µg/ml. The selective index (SI) ratio (CC_{50} for J774G8 cells/IC_{50} for protozoans) was 385, showing that it was more selective against the parasite than mammalian cells.

Trypanocidal Activity

Trypanocidal activity against epimastigote forms of *Trypanosoma cruzi*, by feverfew crude extracts, fractions and parthenolide, was observed (Izumi et al. 2008). The pure parthenolide showed IC_{50}/96 hours and IC_{90}/96 hours of 0.5 µg/ml and 1.25 µg/ml, respectively. The cytotoxic effect of parthenolide in LLMCK2 cells was 3.2 µg/ml (CC_{50}/96 hours) and the selectivity index was 6.4. No hemolysis was detected for parthenolide. The internalization index of *T. cruzi* in LLMCK2 cells was reduced almost 51 % at the concentration of 2 µg/ml of parthenolide and 96.6 % at 4 µg/ml. A guaianolide (11,13-dehydrocompressanolide) isolated from *Tanacetum parthenium* was shown to be effective against *Trypanosoma cruzi*, with IC_{50} values of 18.1and 66.6 µM against the multiplicative epimastigote and amastigote forms, respectively (Cogo et al. 2012). The best results were obtained against trypomastigotes, with an EC_{50} of 5.7 µM. The guaianolide presented no toxicity in $LLCMK_2$ cells (CC_{50} of 93.5 µM) and was 16.4-fold more selective for trypomastigotes. The study of the combinational effect of benznidazole and guaianolide revealed the presence of a synergistic effect against the epimastigote form and marginal additive effect against the trypomastigote form.

Toxicity Studies

Feverfew, with up to 4 mg of parthenolide, given daily as an oral tablet, was well tolerated without dose-limiting toxicity by patients with cancer but did not provide detectable plasma concentrations (Curry et al. 2004). Because of this, parthenolide pharmacokinetics was not able to be completed and was warranted especially with administration of higher doses of purified parthenolide. Feverfew is traditionally contraindicated in pregnancy, and studies by Yao et al. (2006) confirmed this warning. They found that female rats fed orally with 839 mg/kg feverfew daily on either gestation days (GD) 1–8 or 8–15 had adverse effects. Preimplantation loss appeared increased but this was not statistically significant in the feverfew GD1-8 group. Foetuses exposed to feverfew from GD8-15 were smaller than ethanol controls. Feverfew induced toxicity when GD10.5 rat embryos were cultured for 26 hours in rat serum to which feverfew extract was added. They suggested the need for a comprehensive reproductive study of feverfew.

Allergic Dermatitis Problem

Hausen (1981) reported a case of a 40-year-old female florist developed recurrent dermatitis of the face, neck, hands and forearms after a half-year handling of a new ornamental form of feverfew. Epicutaneous tests revealed positive reactions to 10 species of the Compositae family, including chrysanthemums, aster *Gaillardi*a, *Arnic*a and true chamomile. However, the strongest results were seen with petals and leaves of feverfew. A case of specific, delayed hypersensitivity induced by repeated contact with a wild form of feverfew (*Tanacetum parthenium*) was reported (Hausen and Osmundsen 1983). In the flowers investigated the content of the responsible contact allergen parthenolide appeared to be ten times greater (0.6–0.9 %) than in earlier years. Guinea pig experiments confirm the strong sensitizing potency of feverfew. Cross-reactions were elicited with 11 of 21 mostly Asteraceae plants containing chemically related sesquiterpene lactones. In a study of Compositae dermatitis, out of 686 patients tested with the sesquiterpene lactone mix and 79 with the Compositae mix, a total of 31 Compositae-sensitive patients (4.5 %) were found (Paulsen et al. 1993). Testing with the individual ingredients of the Compositae mix showed frequent positive patch test reactions to feverfew, followed in order by chamomile, tansy, yarrow and arnica.

In further studies, patch testing with constituents of sesquiterpene lactone (SL) mix, Compositae mix (CM) and other Compositae extracts and allergens in 190 Compositae-allergic patients was detected in an 8-year period (Paulsen et al. 2001). Feverfew of CM elicited positive reactions most frequently, followed by tansy, wild chamomile, yarrow and arnica, whereas dehydrocostus lactone of SL was the most frequent elicitor of positive reactions, followed by alantolactone and costunolide. In a study of chrysanthemum dermatitis among florists and amateur gardeners in South Wales, Schmidt and Kingston (1985) found that diagnosis could be conducted by patch testing with feverfew extract as all patients reacted to the feverfew extract.

Studies using a high-volume air sampler revealed that no particle-bound parthenolide was released from flowering *Tanacetum parthenium* plants (Christensen et al. 1999). Among volatiles emitted from the aerial parts of feverfew plants and collected by the dynamic headspace technique, a total of 41 compounds, mainly monoterpenes, were identified and quantified in ng; α-pinene (680.6 ng), camphene (2149.2 ng), limonene (314 ng), γ-terpinene (280.9 ng), (*E*)-β-ocimene (941.9 ng), *p*-cymene (2,247 ng), (*E*)-chrysanthenol (1,299 ng), camphor (4845.5 ng), (*E*)-chrysanthenyl acetate (2856.2 ng), (*E*)-β-caryophyllene (284.1 ng), linalool (211.7), β-farnesene (319.5 ng) and α-farnesene (251.6 ng) were the predominant monoterpenes accounting for nearly 89 % of the total volatiles emitted. The average total yield of volatiles emitted over 24 hours was 18,160 ng/g fresh weight of leaves and flowers, corresponding to the emission of approximately 8 mg volatiles per day from one full-grown feverfew plant. No parthenolide or other sesquiterpene lactones

were detected. The results did not support the theory of airborne sesquiterpene lactone-containing plant parts or of direct release of sesquiterpene lactones from living plants as the only explanations for airborne Compositae dermatitis. In another study on airborne Compositae dermatitis, of the 17 persons with + +/+ + + reactions to feverfew and parthenolide tested, 13 had positive and/or doubtful positive reactions to 1 or more monoterpenes (Paulsen et al. 2002). Only one person was allergic to several monoterpenes. Her history of gradually worsening Compositae dermatitis culminating in a probable airborne dermatitis, mimicking photosensitivity and the disappearance of symptoms upon removal of feverfew plants suggested monoterpenes as a possible contributing factor. Similar associations between doubtful positive monoterpene reactions and clinical patterns, fragrance/colophonium allergy and relevance of feverfew allergy were not established with certainty. The authors concluded sensitization to the sesquiterpene lactones of feverfew was not invariably accompanied by sensitization to its volatile monoterpenes, but the presence of monoterpene allergy, however, may contribute to airborne Compositae dermatitis.

The results of a clinical study of 12 feverfew-allergic patients confirmed that some feverfew-allergic patients were sensitive to airborne particles released from feverfew, and isolation of parthenolide from the particle-containing high-volume air sampler extract in allergenic amounts provided strong evidence of parthenolide as the responsible allergen (Paulsen et al. 2007). Out of seven patients with feverfew contact allergy who were patch tested with two creams containing the feverfew extract four of the patients tested positive to one of the creams; reactivity was associated with simultaneous positive reactions to parthenolide (Paulsen et al. 2010). This cream was analysed about 2 years later, and no parthenolide was detected, probably because of degradation of the compound.

Two cases of Compositae dermatitis exacerbated by moisturizer containing feverfew were reported in two women (Killoran et al. 2007). Patient 1 had a + reaction to sesquiterpene lactone mix, a + reaction to Compositae mix, a + reaction to parthenolide, a + reaction to *Tanacetum vulgare* and a + reaction to the calming moisturizer. Patient 2 had + reactions to sesquiterpene lactone, Compositae mix and the same calming moisturizer.

Traditional Medicinal Uses

Feverfew has a long history of use in traditional folkloric medicine among Greek and early European herbalists. Since the 1980s, feverfew has become a highly popular British, French and Canadian phytomedicine used to prevent migraine headaches, relieve menstrual cramps and treat painful joints (Awang 1989, 1997). Feverfew has been traditionally used for a wide range of ailments including psoriasis, toothache, migraine headache, insect bites, rheumatism, rheumatoid arthritis, vertigo, colic, allergies, asthma, tinnitus, dizziness, nausea, vomiting, stomach pain, menstrual problems, inflammation, fever, infertility, problems with menstruation and labour during childbirth and cleansing the kidneys and bladder (Hobbs 1989; Groenewegen et al. 1992; Pareek et al. 2011). The roots and rhizomes of feverfe*w* have been used in Iranian traditional medicine under the name of 'Aqhovan', as digestive and stomachic tonic (Mojab et al. 2007). Medieval monastic healers used it as an antipyretic (Berry 1984; de Pooter et al. 1989). A tea made from the whole plant is used in the treatment of arthritis, colds, fevers, migraine headaches, etc. and is said to be sedative and to regulate menses (Bown 1995; Foster and Duke 1998). However, pregnant women and lactating mothers are advised not to take feverfew (Awang 1993; Yao et al. 2006). The herb is applied externally as a tincture to treat bruises (Grieve 1971). An infusion of the herb is used to bathe swollen feet (Moerman 1998). Chewing 1–4 leaves per day has been used as a remedy for migraine (Foster and Duke 1998). The leaves and flower heads are deemed to be antiinflammatory, antispasmodic, aperient, bitter, carminative, emmenagogue, sedative, stimulant, astringent, stomachic, vasodilator and vermifuge (Grieve 1971; Chiej 1984; Mills 1985).

Other Uses

The dried flower buds are a source of an insecticide and are said to have similar properties to pyrethrum. The plant was also planted in house gardens to keep malaria at bay. An essential oil from the plant is used in perfumery.

Comments

Feverfew was called 'parthenium' by the ancient Greeks based on the myth that the plant was used to medically save the life of someone who had fallen from the Parthenon, during its construction in the fifth century BC; Parthenon was the Doric temple of the virgin goddess Athena on the Acropolis in Athens (Hobbs 1989).

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Tanacetum vulgare

Scientific Name

***Tanacetum vulgare* L.**

Synonyms

Chamaemelum tanacetum (Vis.) E.H.L. Krause, *Chrysanthemum asiaticum* Vorosch., *Chrysanthemum boreale* (DC.) B. Fedtsch. (illeg.), *Chrysanthemum vulgare* (L.) Bernh. (illeg.), *Chrysanthemum vulgare* var. *boreale* (Fisch. ex DC.) Makino ex Makino & Nemoto, *Dendranthema lavandulifolium* var. *tomentellum* (Hand.-Mazz.) Y. Ling & C. Shih, *Pyrethrum vulgare* (L.) Boiss., *Tanacetum boreale* Fisch. ex DC., *Tanacetum crispum* Steud., *Tanacetum umbellatum* Gilib. (inval.), *Tanacetum vulgare* subsp. *boreale* (Fisch. ex DC.) Á. Löve & D. Löve, *Tanacetum vulgare* subsp. *boreale* (Fisch. ex DC.) Kuvaev, *Tanacetum vulgare* var. *boreale* (Fisch. ex DC.) Trautv. & C.A. Mey., *Tanacetum vulgare* var. *crispum* DC.

Family

Asteraceae

Common/English Names

Bachelors buttons, Bitter Buttons, Common Tansy, Cow Bitter, Garden Tansy, Ginger Plant, Gold Leaf Tansy, Golden Buttons, Hindheel, Mugwort, Parsley Fern, Scented Fern, Stinking Willie, Tansy, Yellow Buttons

Vernacular Names

Brazil: Catinga De Mulata, Pluma, Tanásia
Chinese: Ju Hao
Czech: Kopretina Vratič, Řimbaba, Vratič, Vratič Obecný
Danish: Guldknap, Rajnfan, Regnfan, Regnfang, Rejnfan
Dutch: Boerenwormkruid, Wormkruid
Eastonian: Harilik Soolikarohi
Esperanto: Krizantemo Verma, Tanaceto, Vermoherbo
Faroe Islands: Vanlig Reinfann
Finnish: Pietaryrtit, Pietaryrtti
French: Barbotine, Tanacée, Tanaise, Tanaise Commune, Tanaisie, Tanaisie Commune
Gaelic: Franclus
German: Gemeiner Rainfarn, Gülden Knöpfle, Michelkraut, Rainfarn, Rehfarn, Revierblume, Tannkraut, Westenknöpf, Wurmkraut, Wurmsamen
Hungarian: Gilisztaűző Varádics, Közönséges Varádics, Varádics, Varádics Aranyvirág
Icelandic: Regnfang, Reinfang, Reinfáni
Italian: Erba-Amara Selvatica, Tanaceto
Norwegian: Herremann, Herremannsknapp, Reinfann, Reinfannslekta, Reinfant, Reinfar, Reinfonn, Renfang, Tangsigras, Tannsi, Tansegras, Ungkarsknapper
Peru: Palma Real

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Polish: Wrotycz, Wrotycz Pospolity, Wrotycz Zwyczajny
Portuguese: Atanásia, Atanásia-Das-Boticas, Catinga-De-Mulata, Erva-De-São-Marcos, Erva-Dos-Vermes, Joina-Das-Searas, Tanaceto, Tanásia
Russian: Dikaja Rjabina, Pižma Obyknovennaja
Slovaščina: Navadni Vratič, Vratič Navadni
Slovencina: Vratič Obyčajný
Spanish: Balsamita Menor, Hierba Lombriguera, Palma Imperial, Palmita De La India, Tanaceto
Swedish: Gubbaskägg, Rejnfånun, Renfana
Vietnamese: Cây Cúc Ngài
Welsh: Tansi, Tanclys, Dibynlor, Cynhowlen, Gwenwialen, Gwiniolen, Gwiniolwydd, Gwroeth, Gwroith, Gwyn Y Merched, Gyslys, Gystlys, Gystlys Cyffredin, Mas, Masarnwydden Leiaf, Wroith, Ystrewlys

Origin/Distribution

Tanacetum vulgare is of Eurasian origin, but was widely introduced globally and to North America where it became invasive in some areas (Wolf et al. 2012).

Agroecology

Tansy is a cool climate species. In its native and nonnative range, it occurs from near sea level to 1,600 m elevation in woodlands, meadows, rangeland, prairies, alpine grassland, montane steppe, marshes, mires, disturbed sites, gardens, pastures, railroads, roadsides, irrigation ditches, stream banks, river banks and lake shores. It is adaptable to a wide range of soil types. It can be found in dry soils, nutrient-poor soils and loamy and sandy soils to heavy, wet or moist soils but thrives in nutrient-rich, moist, well-drained soils. It occurs in sites with full sun to partial shade.

Edible Plant Parts and Uses

The young leaves and flowers are edible (Fernald et al. 1958; MacNicol 1967; Larkcom 1980; Facciola 1990; Harris 1995). Young aromatic leaves finely chopped are used in salads, puddings, cakes, biscuits, fritters, fish dishes, etc. Leaf juice has been used to flavour omelettes known as tansies. Crushed tansy leaves have been used to flavour whiskey. Tansy cheese is made by steeping the herb and pouring the extract into milk before curdling. The plant is also used as a flavouring substitute for nutmeg and cinnamon. Leaves and flowering tops are brewed into a bitter lemon-flavoured tea. Flowers have unique flavour eaten and are used for garnishing.

Botany

A robust, herbaceous perennial with erect, distally branched stems reaching 50–150 cm high (Plates 1 and 2). Leaves alternate, basal cauline, petiolate or sessile, lamina oval to elliptic in outline, 5–25 cm by 2–10 cm wide, pinnately lobed with 4–10 pairs of primary elliptic–lanceolate

Plate 1 Tansy herb

Plate 2 Tansy foliage

Plate 3 Corymbiform array of flowering heads (T. James)

Plate 4 Close-up of flowering heads of Tansy (T. Candresse)

lobes and dentate margins, surfaces sparsely hairy or glabrous, gland dotted (Plates 1 and 2). Flowering heads, axillary and terminal (Plate 5), numerous in corymbiform pattern, each head compact, oblate, flat topped, yellow, with more than 100 individual florets. Involucre 5–10 mm across, receptacle convex to conic (Plates 3 and 4). Ray florets disciform, outer ones pistillate, corolla 3–4 lobes, yellow. Disc florets with 2–3 mm yellow corolla. Achene 1–2 mm, 4–5-angled or ribbed, gland-dotted with crown-toothed pappus.

Plate 5 Axillary and terminal flowering heads (J. Holopainen)

Nutritive/Medicinal Properties

Sesquiterpene lactones tanacetin, β-hydroxyarbusculin A and reynosin were isolated from *T. vulgare* by Samek et al. (1973). Yunusov et al. (1979) isolated the following sesquiterpene lactones from the dried aerial parts: chrysanin, tamarin, tanachin and tavulin. Tanavulgarol, an oxygenated sesquiterpene, was isolated from *T. vulgare* (Chandra et al. 1987b). Two germacranolides and an *n*-decyl glucoside were isolated from the aerial parts (Chandra et al. 1987a). Four flavonoids were isolated from tansy flowers: tilianin, acacetin, cosmosiin and apigenin (Kurkina et al. 2011) besides luteolin, cinaroside, eupatilin, jaceidin and jaceoside reported earlier by the main author Kurkina. The flavonoids 6-hydroxyluteolin 6,3′-dimethyl ether (jaceosidin) and quercetagetin 3,6,3′-trimethyl ether (jaceidin) had been reported from the flowers of *T. vulgare*

(Ivancheva et al. 1998). The following flavonoids were detected in *T. vulgare* leaves: flavones (scutellarein-6-methyl ether (hispidulin), scutellarein-6-4′-dimethyl ether (pectolinarigenin), luteolin, 6-hydroxyluteolin 6-methyl ether (nepetin), 6-hydroxyluteolin 6,3′-dimethyl ether (jaceosidin)) and flavonols (quercetagetin-3- methyl ether, quercetagetin 3,6-dimethoxy ether (axillarin), quercetagetin 3,6,3′-trimethyl ether (jaceidin)) (Ivancheva et al. 1998).

Some wild tansy plants were found to produce 80–90 % β-thujone, whereas others gave the normal content (70–85 %) of α-isothujone throughout the growing season (Von Rudloff and Underhill 1965). Significant variations in the content of the minor components were found to occur only in very young plants, when appreciable amounts of ϵ-, γ- and δ-cadinene and an unidentified labile (possibly C_5) alcohol were detected.

Three tansy chemotypes were identified from tansy specimens growing in the province of Eastern Flanders (Belgium): the β-thujone, *trans*-chrysanthenyl acetate and camphor/β-thujone types (De Pooter et al. 1989). The essential oil content of Hungarian samples of *Tanacetum vulgare* varied from 0.02 to 0.66 % and exhibited a heterogeneous distribution of chemotypes (Tétényi et al. 1975). Twenty-six different chemotypes were found. Individuals and populations containing artemisia ketone and umbellulone as their main components were the most frequent. The following compounds were indentified in the essential oils of five *Tanacetum vulgare* genotypes: artemisia alcohol, γ-campholenol, davanone, lyratol, lyratyl acetate and 4-thujen-2α-yl acetate (Héthelyi et al. 1981). The essential oil from clone 409 of *Tanacetum vulgare* from Hungary was found to contain *trans*-chrysanthenyl acetate (75 %) and *trans*-chrysanthenol (5–10 %) (Neszmélyi et al. 1992).

The strained tricyclic sesquiterpene ketones vulgarone A and longipin-2-en-1-one (vulgarone B) were isolated as constituents of *Chrysanthemum vulgare* essential oil (Uchio et al. 1976, 1977; Uchio 1978). Vulgarone B was transformed into vulgarone A via a sigmatropic shift in the laboratory by irradiation with UV light. The essential oil of tansy from Eastern Kazakhstan was found to contain >50 components out of which 39 were identified (Dembitskii et al. 1984). The oil contained a substantial amount of α-thujone (19 %), artemisia ketone and *L*-camphor (12 %), while δ-terpinenol-4, (-)-borneol, bornyl acetate, neryl acetate, α-terpineol, carvone, achillenol (santolina alcohol), camphor, b-thujone, nerol geraniol, filipendulol (epichrysanthenol) and thymol were present in small amounts. The terpene hydrocarbon fraction included α-pinene (1.0 %), achillene (1.5 %), camphene (1.5 %), β-pinene, sabinene, β-myrcene, limonene, β-phellandrene, 1.8-cineole (3.0 %), γ-terpinene, *p*-cymene and terpinolene. Sesquiterpene hydrocarbons were present in an amount of 1.1 %. Among them were ylangene, longicyclene, γ-elemene, *p*-gurgunene, β-elemene, β-caryophyllene, β-selinene, δ-cadinene, γ-cadinene, ar-curcumene, 8-cadinene, calamenene and calacorene. The plant belonged to the thujone chemotype. Tansy genotypes in Finland were distributed among eight 'well-defined' main groups: sabinene, thujone, umbellulone, camphor, bornyl acetate, alpha-pinene, 1,8-cineole and germacrene D (Holopainen et al. 1987). The sesquiterpene germacrene D was identified for the first time in the present study in the essential oil of tansy. Most of these 'well-defined chemotypes' were again divided into subgroups A and B. In addition to the 'well-defined chemotypes', a number of 'mixed chemotypes' were also detected in the crossings. Those chemotypes accounted for 20 % of the whole crossing material tested.

Essential oil from aerial parts of *T. vulgare* plant from 'Tierra del Fuego' (Argentina) afforded β-thujone (91.65 %) as the major constituent (Gallino 1988), thus indicating that the plant belonged to the thujone chemotype. Some minor components included sabine, 1,8-cineol, α-thujone, germacrene D, terpinen-4-ol, γ-terpinene, *p*-cymene, pinocarvone, sabinol, eugenol and unidentified sesquiterpene alcohol. Traces of α-pinene, β-pinene, α-terpinene, α-terpineol, terpinolene, limonene, unidentified sesquiterpene hydrocarbon, myrtenol, myrcene, umbellulone and carvacrol were also found. Major constituents *T. vulgare* essential oils included camphor, isopinocamphone, *trans*-chrysanthenyl acetate, sabinene, bornyl acetate and germacrene

D (Hendriks et al. 1989). Tansy leaf oil in Holland was found to contain bicyclogermacrene trace, bornyl acetate 0.9 %, camphene 1.40 %, camphor 9.4 %, β- caryophyllene 0.7 %, 1,8-cineole 0.4 %, *p*-cymene 0.4 %, germacrene D 6.50 %, α-pinene 0.3 %, β-pinene trace, sabinene 3.9 %, sabinene hydrate 0.4 %, terpinene-4-ol 0.4 %, α-terpinene 0.3 %, γ-terpinene 0.3 %, α-thujone 0.9 % and β-thujone 67.9 % (Hendriks et al. 1990).

An investigation of 14 samples of Tansy occurring in the northeastern part of the Netherlands revealed the presence of an artemisia ketone, a chrysanthenol/chrysanthenyl acetate, a lyratol/lyratyl acetate and a β-thujone chemotype (Hendriks et al. 1990). The essential oils of the flower heads contained a higher percentage of the main constituent than the oil obtained from the leaves. Vulgarone A and B were detected in five samples; however, vulgarone A was only found in the leaf oils. *Cis*-longipinane-2, 7-dione, a component of Bulgarian Tansy, could be detected only in two samples. Examination of the essential oils and extract of tansy plant occurring in the Chicoutimi area (Quebec) revealed several chemotypes (Collin et al. 1993). Half of the plants belong to a camphor-1,8-cineole-borneol (concentration >52 %) mixed chemotype. The β-thujone chemotype (>60 %) was also present in six samples. Four specimens of a chrysanthenone type (>50 %) were also observed. Finally, one sample showed a high concentration of dihydrocarvone (>60 %). A commercial sample produced in the vicinity of Quebec City belonged mainly to the β-thujone chemotype. A small population of *T. vulgare* was found to comprise three pure chemotypes based on the sesquiterpene lactones: only germacranolides, only eudesmanolides and no sesquiterpene lactones (Todorova and Ognyanov 1999). Mixed chemotypes were not identified because probably these pure chemotypes were unable to produce hybrids. Of the 20 constituents identified in the essential oil from the aerial parts of *Tanacetum vulgare* from India, six were monoterpene hydrocarbons (3.9 %), 10 oxygenated monoterpenes (81.9 %), one sesquiterpene hydrocarbon (1.7 %), two phenolic compounds (3.0 %) and a long-chain hydrocarbon (1.5 %) (Charles et al. 1999). The oil belongs to the thujone (66.8 %) chemotype. (+)-10 Hydroxy-3-thujone was characterized from the oil. Tansy genotypes in Finland were distributed among eight 'well-defined' main groups: sabinene, thujone, umbellulone, camphor, bornyl acetate, α-pinene, 1,8-cineole and germacrene D (Holopainen et al. 1987). The sesquiterpene germacrene D was identified for the first time in the present study in the essential oil of tansy. Most of these 'well-defined chemotypes' were again divided into subgroups A and B. In addition to the 'well-defined chemotypes', a number of 'mixed chemotypes' were also detected in the crossings. Those chemotypes accounted for 20 % of the whole crossing material tested.

A total of 55 volatile compounds were detected, and 53 were identified in the air-dried flower heads of 20 Finnish tansy genotypes (Keskitalo et al. 2001). Fifteen genotypes were well defined and five were mixed chemotypes. The most frequently encountered monoterpene was camphor with or without several satellite compounds such as camphene, 1,8-cineole, pinocamphone, chrysanthenyl acetate, bornyl acetate and isobornyl acetate. In 13 genotypes, camphor concentration exceeded 18.5 %, and in seven genotypes, camphor was less than 7.2 %. Other chemotypes rich in *trans* thujone, artemisia ketone, 1,8-cineole or davadone D were also identified. Davadone-D and a mixed chemotype, containing tricyclene and myrcene, were identified from a Finnish tansy for the first time. Geographically, most chemotypes containing camphor originated from Central Finland, whereas chemotypes without camphor such as artemisia ketone, davadone D and myrcene–tricyclene originated from South or Southwest Finland. The group comprising the highest concentration of camphor chemotypes had the tallest shoots. The groups with chemotypes containing davadone-D or artemisia ketone, which originated from Southwest Finland, produced the most number of flower heads, had the tallest corymb and were last to flower. Also, the group consisting from chemotypes with a high concentration of camphor and originated from South Finland exhibited late flowering.

Forty-one constituents were identified in the essential oils from inflorescences and leaves of

tansy grown in Vilnius district (Lithuania), and the oils were distributed among four chemotypes (Mockute and Judzentiene 2004). The major constituents of the camphor chemotype (10 samples) were camphor (22.3–41.4 %) and 1,8-cineole (10.6–26.4 %); the α-thujone chemotype (six samples) was found to be dominated by α-thujone (25.7–71.5 %) and 1,8-cineole (11.3–22.3 %); the major constituents of the 1,8-cineole-chemotype (three samples) was dominated by 1,8-cineole (24.5–32.7 %) and camphor (8.3–23.8 %); and the artemisia ketone chemotype (one sample of inflorescences) predominantly featured artemisia ketone (30.5 %) and camphor (23.0 %). The oil from inflorescences of the above chemotypes contained higher amounts of the first major component and oxygenated monoterpenes (mean 83.6 %) than the leaf oils (mean 73.7 %). An opposite correlation was noticed for mono- and sesquiterpene hydrocarbons and oxygenated sesquiterpenes.

The yield of essential oils of tansy plants from 40 different locations in North, Mid- and South Norway ranged between 0.35 and 1.90 % (v/w) (average: 0.81 %); the most abundant thujone plants were especially rich in essential oil volatiles (0.95 %) (Rohloff et al. 2004). Seven chemotypes could be identified as follows: (A) α-thujone (two individuals), (B) β-thujone (22), (C) camphor (six), (D) chrysanthenyl acetate/chrysanthenol (three), (E) chrysanthenone (two), (F) artemisia ketone/artemisia alcohol (three) and (G) 1,8-cineole (two). The thujone chemotype was dominated by β-thujone (81 %) associated with α-thujone, but tansy plants rich in α-thujone were also detected (61 %). Tansy genotypes in Norway could be grouped into the following chemotypes: the mixed chemotypes Steinvikholmen (thujone–camphor), Alvdal (thujone–camphor–borneol), Goldsticks (thujone–camphor–chrysanthenyl type) and Brumunddal (thujone–camphor–1,8-cineole-bornyl acetate/borneol-α-terpineol) and the distinct chemotype Richters, with average concentrations of (*E*)-chrysanthenyl acetate >40 % in both leaf and flower essential oil (Dragland et al. 2005). The essential oil of *Tanacetum vulgare* leaves from Perú was characterized by a high amount of ß-thujone (87.83 %), and belonged to the thujone chemotype (De La Cruz et al. 2008).

Altitude, geographical, temperature gradient, as well as soil-climate conditions were found to impact on the essential oil composition of *T. vulgare* (Vaverková et al. 2006). In the lowest-lying locality with a relatively large sunshine, the content of β-thujone in the essential oil was the highest, whereas in the regions lying towards the north, the content of the essential oil was decreased and the content of camphor was increased. In the northernmost region of Slovakia, an increased number of chemovars of the camphor–cineole type was observed. The following compounds were identified in *T. vulgare* essential oil in Slovakia: α-pinene, camphene, sabinene, β-pinene, myrcene, 1,8-cineole, artemisia ketone, β-thujone, camphor, borneol, umbellulone, D-carvone, chrysantenyl acetate, bornyl acetate, thymol, germacrene and carvacrol (Mikulášová and Vaverková 2009).

Ninety-four components were detected in the essential oils from aerial parts and capitula of *Tanacetum vulgare* subsp. *siculum* (Formisano et al. 2009) Alpha-thujone, β-thujone and 1,8-cineole were the main constituents. Based on the chemical profile, this *Tanacetum* species was assigned to the thujone chemotype. Five known sesquiterpene lactones with the eudesmane skeleton, douglanin, ludovicin B, ludovicin A, 1α-hydroxy-1-deoxoarglanine and 11,13-dehydrosantonin, were isolated from the flowers of a subspecies of *T. vulgare* in Sicily (Rosselli et al. 2012). This *T. vulgare* species can be assigned to the eudesmanolide chemotype.

The water-soluble pectin complex from tansy flowers was found to consist of four different polysaccharide fractions (Yakovlev and Sysoeva 1983). Polysaccharide I contained 64 % of D-galacturonic acid and the neutral monosaccharides (PC, GLC), galactose, glucose, arabinose, xylose and rhamnose in a quantitative ratio of 5:3:3:1:4. Polysaccharide II contained 20 % of galacturonic acid and the neutral monosaccharides (PC, GLC) galactose, glucose, arabinose, xylose and rhamnose in a quantitative ratio of 10:8:3:1:2. Polysaccharide (III) contained 30 % of a uronic acid and the neutral monosaccharides galactose, glucose, arabinose, xylose and rhamnose in a quantitative ratio of 9:5:2:1:4. Polysaccharide (IV) contained 18 % of uronic acid and the neutral

monosaccharides galactose, glucose, arabinose, xylose and rhamnose in a quantitative ratio of 8:7:2:1:1.

Tanacetan TVF, isolated from floccules of tansy, was found to be a branched pectic polysaccharide with backbone of linear α-1,4-d-galacturonan (Polle et al. 2002). The ramified regions appeared to be rhamnogalacturonan-I with core of α-1,2-L-rhamno-α-1,4-d-galacturonan. The side sugar chains were attached by 1,4-linkages to the L-rhamnopyranose residues of the core and consist of single residues of β-galactopyranose and β-1,4-galactopyranan with branching points of 4,6-substituted β-d-galactopyranose residues. In addition, the branching regions contained the side chains of a branched α-1,5-arabinofuranan bearing 2,5-and 3,5-substituted α-L-arabinofuranose residues as the branching points. Some side chains of rhamnogalacturonan appeared to represent arabinogalactan, containing the branched sugar chains of α-1,5-arabinofuranan attached to the linear chains of β-1,4-galactopyranan by 1,3- and 1,6-linkages. The residues of α-L-arabinofuranose appeared to occupy the terminal positions of the arabinogalactan side chains. Four acidic polysaccharide fractions (designated T-I to T-IV) were isolated and purified from Tansy florets (Xie et al. 2007). The average *Mr* of fractions T-I through T-IV was estimated to be 326, 151, 64 and 9 kDa, respectively. Tansy polysaccharides consisted primarily of galacturonic acid, galactose, arabinose and rhamnose. Fractions T-II through T-IV contained an arabinogalactan type II structure.

β-Sitosterol was found as the major sterol and α-amyrin as the major triterpene of tansy (Chandler et al. 1982). Other sterols identified included stigmasterol, campesterol and cholesterol, and the triterpenes identified included β-amyrin, taraxasterol and pseudo-taraxasterol. *Cis*-longipinane-2,7-dione, a sesquiterpene diketone, was isolated from the flowers (Ognyanov et al. 1983). Two nonvolatile sesquiterpene alcohols designated tanacetol A, $C_{17}H_{26}O_4$, ketol sesquiterpene and tanacetol B, $C_{19}H_{30}O_5$, its monoacetyl derivative, were isolated from *T. vulgare* (Calleri et al. 1983; Appendino et al. 1983). Fifteen sesquiterpene lactones and a sesquiterpene alcohol were isolated from *T. vulgare* plant: (tatridin A, tatridin B, tanachin (=deacetyldihydrochrysanolide, 1-*epi*-tartridin B), tamarin (=deacetylchrysanolide), parthenolide, costunolide diepoxide, anhydroverlotorin 4α,5β-epoxide, artemorin, artemorin 4α,5β-epoxide, the eudesmanolides 1-*epi*-ludovicin C (=armexifolin), armefolin, 1β-hydroxyarbusculin A, reynosin, santamarin and magnolialide) and the germacrene derivative tanacetol B (Sanz and Marco 1991).

The vacuolar flavonoids of both *Tanacetum parthenium* and *T. vulgare* were *d*ominated by the presence of apigenin and luteolin 7-glucuronides; nine other glycosides were present, including the uncommon 6-hydroxyluteolin 7-glucoside in *T. vulgare* (Williams et al. 1999). The surface flavonoids of *T. vulgare* were methyl ethers of the flavones scutellarein and 6-hydroxyluteolin. Total phenolic contents reported for *T. tanacetum* (leaf) was 1.68 mg GAE/100 g DW (Wojdyło et al. 2007). Major phenolic compounds (mg/100 g DW) found were phenolic acids (894 mg caffeic acid, 335 mg neochlorogenic acid, 471 mg ferulic acid) and flavonoids (848 mg luteolin, 165 mg apigenin). Polyphenolic compounds (g/kg dry matter) in the aerial tansy plant parts were determined as follows: chlorogenic acid 4.12 g, 3,5-DCQA (dicaffeoylquinic acid) 11.82 g, 4,5, DCQA 3.54 g, total caffeoyl derivatives 19.49 g, total dihydroxycinnamic acid derivatives 41.53 g, total flavonoids 11.40 g, total dihydroxycinnamic acid derivatives + flavonoids 52.93 and total polyphenolic compounds 65.86 g (Fraisse et al. 2011).

Constituents of fresh tansy plant oil grown in two localities Ada Huja (green area) and Topčider (industrial, polluted area) in Belgrade, Serbia, respectively were as follows: α-phelandrene trace, 0.6 %; *p*-cumene trace, 0.5 %; β-phelandrene trace, 0.5 %; santolina alcohol 1.7, trace; linalool oxide trace, 1.7 %; artemisia ketone 1.1 %, 0.7 %; sabinene hydrate trace, 0.8 %; undecane 2.7 %, trace; α -thujone 0.9, trace; β-thujone 8.3 %, 1.3 %; pinocarvone 0.8 %, trace; *p*-cresol acetate trace, 0.8 %; *cis*-pinochamphone trace, 2.8 %; *trans*-carveol acetate 5.1 %, 14.5 %; piperitone 0.9 %, 3.1 %; linalool oxide acetate 0.8 %, 9.9 %; germacrene D 1.1 %, trace; *trans*-chrysanthenol trace, 1.4 %; spathulenol 5.5 %, trace; *trans*-chrysanthenyl acetate 47.9 %, 36.%; longiborneol

0.9 %, trace; and α-cadinol 3 %, trace, total 80.7 %, 75.5 % (Stevovic et al. 2011).

The biosynthesis of monoterpene ketone, (-)-camphor, a major constituent of *T. vulgare* essential oil, was reported by Croteau and Shaskus (1985). They demonstrated a geranyl pyrophosphate: (-)-bornyl pyrophosphate cyclase in soluble enzyme preparations from immature tansy leaves converted the acyclic precursor [1-3H]geranyl pyrophosphate to the bicyclic monoterpene alcohol borneol in the presence of $MgCl_2$ and oxidized a portion of the borneol to camphor in the presence of a pyridine nucleotide. The biosyntheses of irregular monoterpene artemisia ketone, the regular monoterpenes camphor and β-thujone, the sesquiterpene germacrene D, the diterpene *trans*-phytol and β-sitosterol and isofucosterol were studied in axenic cultures of *Tanacetum vulgare* (Umlauf et al. 2004). It was found that the isoprene units of the monoterpenes and the diterpene were formed via the methylerythritol phosphate (MEP) pathway, whereas the isoprene building blocks of the sesquiterpene and the sterols originated from the mevalonic acid (MVA) pathway.

Antioxidant Activity

Antioxidant activity in terms of TEAC (μM trolox/100 g DW) of *T. vulgare* leaves reported was 37.3 μM for ABTS, 469 μM for DPPH and 455 μM for FRAP (ferric reducing antioxidant power) assays (Wojdyło et al. 2007). The crude methanol extract of Tansy aerial parts displayed DPPH radical scavenging effects with an EC_{50} value of 37 μg/ml (Juan-Badaturuge et al. 2009). Three antioxidant compounds, 3,5-*O*-dicaffeoylquinic acid (3,5-DCQA), axillarin and luteolin, were isolated. 3,5-DCQA was the major constituent with antioxidant activity (IC_{50} = 9.7 μM) comparable with that of the standard quercetin (IC_{50} = 8.8 μM). Total antioxidant capacity (%) (DPPH scavenging activity) of tansy aerial plant parts was 7.42 %, and contribution from the main caffeoyl derivatives was as follows: chlorogenic acid 5.66 %, 3,5-DCQA (dicaffeoylquinic acid) 19.1 %, 4,5-DCQA 5.88 % and total caffeoyl derivatives 31.35 % (Fraisse et al. 2011).

Anticancer Activity

T. vulgare was one of several Asteraceae species that exhibited antileukaemic properties against J-45.01 human acute T leukaemia cell line and induced death via apoptosis (Wegiera et al. 2012). Five sesquiterpene lactones isolated from the flowers, douglanin, ludovicin B, ludovicin A, 1α-hydroxy-1-deoxoarglanine and 11,13-dehydrosantonin, exhibited cytotoxic activity in-vitro on A549 (human lung carcinoma epithelial-like) and V79379A (Chinese hamster lung fibroblast-like) cells using the tetrazolium salt reduction (MTT) assay (Rosselli et al. 2012). Studies by Fang et al. (2010) found that parthenolide could markedly enhance sensitivity of human lung cancer A549 cells to low-dose oxaliplatin by inhibiting NF-kappaB/p65, COX-2 and PGE(2) activation and inducing apoptosis. Parthenolide in combination with a low dose of oxaliplatin may be a beneficial chemotherapeutic strategy for patients who cannot tolerate the severe side effects of the drug at therapeutic concentrations.

Antiviral Activity

Aqueous tansy extract was found to partially inactivate in tick-borne encephalitis (TBE) virus (Fokina et al. 1991). In-vivo studies revealed that tansy extract could induce resistance of mice to TBE virus infection assessed by the increased survival rate of the animals and significant prolongation of the average longevity. Parthenolide, isolated from aerial parts of *Tanacetum vulgare*, protected Vero cells from herpes simplex virus (HSV-1) infection in-vitro (Onozato et al. 2009). The extract and parthenolide exhibited anti-HSV-1 activity with an EC_{50} of 40 μg/ml and 0.3 μg/ml, respectively, in the sulforhodamine B colorimetric assay. It was found that parthenolide interfered with virus replication after the penetration stage, inhibiting approximately 40 % of plaques formed at a concentration of 2.5 μg/ml

when compared with an untreated control. The anti-HSV-1 activity of tansy aerial parts, ethyl acetate extract and the isolated compound parthenolide, had been reported recently, and it was revealed that constituents other than parthenolide were responsible for the antiviral activity of tansy (Alvarez et al. 2011).

Antimicrobial Activity

Tansy exhibited some degree of antimicrobial activity in-vitro against both Gram-positive and Gram-negative bacteria and some fungi (Holopainen and Kaupinnen 1989; Holetz et al. 2002). Microorganisms susceptible to a hydroalcoholic extract of *T. vulgare* included *Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa*. Anticandidal activity against *Candida krusei* and *C. tropicalis* was also observed. In another study, all 5 samples of *T. vulgare* essential oils were found inhibitory to *Bacillus subtilis*, one sample (T1) was inhibitory to *Micrococcus luteus* and another sample T3 was the best, inhibiting growth of *Escherichia coli, Bacillus subtilis, Proteus mirabilis, Staphylococcus aureus* and also *Candida albicans* (Mikulášová and Vaverková 2009). MIC of *T. vulgare* essential oils for all bacteria ranged from <0.6 % to ≫2.5 %. Samples T4 and T5 exerted the lowest antibacterial effect.

Antiinflammatory Activity

Tansy chloroform leaf extract administered intraperitoneally (i.p.) inhibited in a dose-dependent way the carrageenan-induced paw oedema in rats; the calculated ED_{50} was 15.2 (7.6–30.4) mg/kg (Mordujovich-Buschiazzo et al. 1996). The extract also inhibited the subchronic inflammation induced by Freund's adjuvant in doses ranging from 80 to 160 mg/kg i.p. The major flavonol and flavone methyl ethers of both *Tanacetum parthenium* and *T. vulgare* plants variously inhibited the major pathways of arachidonate metabolism in leucocytes (Williams et al. 1999). There were significant differences in potency, with the tansy 6-hydroxyflavones less active than the feverfew 6-hydroxyflavonols as inhibitors of cyclooxygenase and 5-lipoxygenase. From the moderately lipophilic fractions of tansy plant were isolated the active principles responsible for the antiinflammatory activity of tansy against the mouse ear oedema induced by 12-*O*-tetradecanoylphorbol 13-acetate (Schinella et al. 1998). Parthenolide caused 93 % oedema inhibition at 0.5 mg/ear, with an $ID_{50} = 0.18$ µmol/ear, and the methoxyflavones jaceosidin, eupatorin, chrysoeriol and diosmetin caused 80 % oedema inhibition at 0.5 mg/ear, $ID_{50} = 0.50$ µmol/ear. The potency of parthantienolide was nearly three times greater than that of the most active of the flavones due to its more abundant amount in the plant.

Immunotherapeutic Activity

High *Mr* polysaccharide fractions T-I and T-II isolated from tansy flowers exhibited potent macrophage-/monocyte-activating activity, enhancing production of reactive oxygen species (ROS), nitric oxide (NO) and tumour necrosis factor alpha (TNF-α) by J774.A1 murine macrophages and activating nuclear factor κB (NF-κB) in THP-1 human monocytes (Xie et al. 2007). In addition, Tansy polysaccharides stimulated human neutrophil function by greatly enhancing neutrophil myeloperoxidase (MPO) release. Further, the low *Mr* fraction T-IV had potent complement-fixing activity, which may also contribute to the antiinflammatory and wound healing properties of Tansy extracts. The results elucidated at least part of the beneficial therapeutic effects of Tansy extracts and support the concept of using Tansy polysaccharides as an immunotherapeutic adjuvant.

Vasorelaxant Activity

In-vitro studies on the contractile response of Wistar rat aorta to high KCl and noradrenaline and on endothelium-dependent relaxation evoked by acetylcholine indicated that the

aqueous tansy extract exerted NO-mediated and NO-independent vasorelaxing properties (Lahlou et al. 2008b).

Antiulcerogenic Activity

Yakovlev and Sysoeva (1983) reported that an earlier pharmacological study had shown that the polysaccharide complex from tansy flowers exhibited antiulcer action in rats with various types of experimental gastric ulcers. Gastric ulcers induced by oral administration of absolute ethanol to rats were reduced dose-dependently by oral pretreatment of animals with the tansy chloroform extract (2.5–80 mg/kg) or its major constituent parthenolide (5–40 mg/kg) (Tournier et al. 1999). When administered 30 minutes before ethanol challenge, the protection ranged between 34 and 100 % for the extract and 27 and 100 % for parthenolide. When administered 24 hours before ethanol insult, 40 mg/kg of the extract and of the parthenolide reduced the mean ulcer index from 4.8 for control animals to 1.4 and 0.5, respectively. Administration of both products before ethanol treatment restored the numbers of mucosal -SH groups to values near those found for normal animals.

Diuretic Activity

Oral administration of the aqueous extracts of caraway seeds and tansy leaves to male Wistar rats significantly increased urine output at all time points (Lahlou et al. 2007). Both plant extracts increased urinary levels of Na^+ and K^+, to about the same extent, while furosemide, the reference drug, increased urinary levels of only Na^+ and decreased urinary K^+. In the 8-day subchronic study, all three substances induced significant diuresis and natriuresis; only tansy increased urinary potassium excretion. The results indicated that the water extracts of both *Carum carvi* and *Tanacetum vulgare* possessed strong diuretic action confirming their ethnopharmacological use.

Migraine Prophylactic Activity

T. parthenium samples established from seeds from ten different regions were found to vary significantly within and between samples in migraine prophylactic activity in-vitro (Marles et al. 1992). Serotonin release inhibition from bovine platelets was found to correlate significantly with the content of germacranolide sesquiterpene lactone, parthenolide, although other sesquiterpene lactones from this plant and other Asteraceae species (including *T. vulgare*) were also shown to be active.

Immunomodulating Activity

The acetone leaf extracts of *T. parthenium* and *T. vulgare* inhibited phorbol myristate acetate-induced chemiluminescence of human polymorphonuclear leucocytes, with IC_{50}s from 0.79 to 2.46 mg leaf dry weight/ml whole blood (Brown et al. 1997). Parthenolide concentration in *T. parthenium* was high, 1.72 %% leaf dry weight, but lower in *T. vulgare*, 0.03 %. Fractionation of crude leaf extracts revealed a number of fractions, in addition to those containing parthenolide, which influenced polymorphonuclear leucocyte activity by > 5 %. The effects on phorbol myristate acetate-induced chemiluminescence suggested the activity of the responsible compound(s) was a result of inhibition of protein kinase C, or subsequent events, in polymorphonuclear leucocyte activation in-vitro.

Insect Repellency Activity

A small-scale experiment confirmed the mosquito-repellent activity of *T. vulgare*, without allowing the identification of the active principle (De Pooter et al. 1989). However, the activity was much lower than that of diethyltoluamide containing commercial preparation.

The volatiles of the essential oils of tansy flower heads and the fractions exhibited strong tick (*Ixodes ricinus*) repellency (90–100 %) (Pålsson et al. 2008). Main volatiles detected from oils of

T. vulgare collected at Uppsala were α-pinene (27 %), β-pinene (11 %), pinocamphone (11 %), 1,3,3-trimethylcyclohex-1-ene-4-carboxaldehyde (11 %) and 1,8-cineole (10 %). In the sample collected in Stockholm, the main components were β-thujone (39 %) and camphor (23 %) followed by α-thujone (11 %) and 1,8-cineole (8 %). When constituents in the oils, e.g. α-terpineol, 4-terpineol, α-thujone, β-thujone, 1,8-cineol, verbenol and verbenone, were tested separately (each diluted 0.5 %, vol:vol), 64–72 % tick repellency was obtained.

Allergic Dermatitis Problem

Prolonged exposure to tansy may cause allergic contact dermatitis (Hausen and Oestmann 1988). The leading Compositae species with sensitizing properties was found to be the chrysanthemum. Most of the reactions obtained with other Compositae species such as arnica, marguerite, sunflower, tansy and yarrow were interpreted as cross-reactions due to the fact that cross-reactivity predominates within the sesquiterpene lactone constituents of the various Compositae species. In a study of 25 patients known or suspected to be allergic to different Compositae plants, 1 patient elicited positive epicutaneous reaction to tansy (Hausen 1979). Cross-reactions of patient were seen to tansy [14], yarrow [11], chamomile [10], arnica and sunflower [5]. In further studies, patch testing with constituents of sesquiterpene lactone (SL) mix, Compositae mix (CM) and other Compositae extracts and allergens in 190 Compositae-allergic patients were detected in an 8-year period (Paulsen et al. 2001). Feverfew of CM elicited positive reactions most frequently, followed by tansy, wild chamomile, yarrow and arnica, whereas dehydrocostus lactone of SL was the most frequent elicitor of positive reactions, followed by alantolactone and costunolide.

Toxicity and Toxicological Studies

According to the dispensatory of the United States of America, tansy had been used to a considerable extent as a domestic abortifacient, but was also very dangerous in its action, and had in various cases produced death (Osol and Farrar 1955). The symptoms caused included abdominal pain, vomiting, violent epileptic convulsions often followed by profound coma, dilated pupils, great disturbances of respiration, frequent and feeble pulse, and death, which had been said to be from heart failure but was probably the outcome of a paralytic asphyxia. A fluidrachm (3.75 mils) of the oil was reported to have caused death. Tansy tea had also caused death.

In the acute study in mice, the crude aqueous extract of tansy leaves caused dose-dependent adverse general behaviour effects and mortality (Lahlou et al. 2008a). The no-observed-adverse-effect levels (NOAEL) of the tansy extract were 7.0 and 1.0 g/kg, and the lowest-observed-adverse-effect levels (LOAEL) were 9.0 and 1.5 g/kg, when administered by the oral and intraperitoneal routes, respectively. Mortality increased with increasing doses, with LD_{50} of 9.9 and 2.8 g/kg for the oral and intraperitoneal modes of administration, respectively. In the chronic study in rats, daily oral administration of the crude aqueous extract of tansy leaves for up to 90 days did not result in death or significant changes in the biological (except for hypoglycaemia) and haematological parameters. Base on the high NOAEL values in the acute study in mice and lack of significant effect on biological and haematological parameters in rats after 90 days of daily doses, the authors concluded the tansy extract did not appear to have significant toxicity. Further in view of the dose of tansy consumed in traditional medicine, there appeared to be a wide margin of safety for the therapeutic use of the aqueous extract of *Tanacetum vulgare* leaves.

Traditional Medicinal Uses

For several past centuries, tansy has been commonly used as a domestic medicinal herb for treating a wide range of ailments, though it is less

commonly used in modern herbalism (Grieve 1971; Bown 1995; Chevallier 1996; Alvarez et al. 2011). The leaves and flowering heads are anthelmintic, antispasmodic, bitter, carminative, emmenagogue, stimulant, antihypertensive, diuretic and tonic. Tansy is principally used in traditional Moroccan medicine as antihypertensive remedy (Lahlou et al. 2008a; Stevovic et al. 2011). A decoction of tansy flowers and fruit is an effective agent for expelling roundworms, pinworms and tapeworms and is also used in jaundice, as a sedative in cases of rheumatism, headache and epilepsy (Dembitskii et al. 1984). Bitter tea made from the flowering heads is commonly used as an effective vermifuge for intestinal infestations especially in children and to a lesser extent to help stimulate menstrual flow. Seeds are also anthelmintic. Tansy tea or an infusion is also used as a remedy for ulcers, constipation, fever, diabetes, rheumatism, jaundice and hysteria. Common tansy in large doses has been used to induce abortion but in smaller doses was thought to prevent miscarriage and increase fertility. Tansy is also used in face wash to lighten, tonify and purify skin. Externally, tansy is also used as a poultice on swellings and some eruptive skin diseases. It is also used externally to kill lice, fleas and scabies. Tansy has also been used as an embalming substitute for corpses by early US settlers.

Other Uses

Tansy has insecticidal property. In the olden days before refrigeration, tansy foliage was used to cover meat to repel flies. Tansy is commonly used as a strewing herb in cellars, churches, etc., in order to repel insects. Both foliage and essential oil have been used to kill fleas and flies. The steam distillate of fresh leaves and flowers of tansy was found to be strongly repellent to the Colorado potato beetle, *Leptinotarsa decemlineata* (Schearer 1984). Fifty-six compounds were detected; camphor (30 %) and umbellulone (25 %) were the major components. A commercial tansy oil was also found to be highly repellent to Colorado beetles; the major component was bornyl acetate 74 %. Other components with strong repellency included 1-8-cineole, *p*-cymene, γ-terpinene and camphor. Colorado potato beetle, *Leptinotarsa decemlineata*, exhibited avoidance behaviour to tansy oil, volatiles from intact tansy plants, a 'hydrocarbon fraction' of tansy oil, obtained by fractionation on alumina, and five of the 13 known components of tansy oil (Panasiuk 1984). α-Terpinene, thujone, dihydrocarvone and carvone produced definite avoidance behaviour in Colorado potato beetles, and to a slightly lesser degree, γ-terpinene had the same effect. One constituent of tansy oil, α-pinene, attracted the beetle.

When tansy essential oil was continuously present at 0.1 and 1 % in the diet, all oblique-banded leaf-roller (OBLR) larvae from susceptible and resistant populations died (Larocque et al. 1999). The presence of 0.01 % tansy essential oil in the diet affected female pupal weight, but not larval weight gain, larval developmental time and male pupal weight. Residues of the formulation TE (tansy essential oil, ethanol 95 %) deterred oviposition of *Choristoneura rosaceana* female. The DSD (direct steam distillation) and DW (distillation in water) extracts of *T. vulgare* were more toxic (75.6 and 60.4 % mite mortality, respectively, at 4 % concentration) to the two-spotted spider mite, *Tetranychus urticae*, than the MAP (microwave-assisted process) extract (16.7 % mite mortality at 4 % concentration) (Chiasson et al. 2001). Chemical analysis of the *T. vulgare* extracts indicated that β-thujone was by far the major compound of the oil (>87.6 %) and probably contributed significantly to the acaricidal activity of the oil. Thujone is an effective insecticide, but it is highly toxic to mammals when taken in excess (Bown 1995).

A green dye is obtained from the foliage and yellow dye from the flowers and leaves. The plant also made good compost materials.

Comments

This species varies greatly in terpene composition, forming different chemotypes (Wolf et al. 2012). Refer also to the chapter on *Tanacetum parthenium*.

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Taraxacum officinale

Scientific Name

***Taraxacum officinale* G.H. Weber ex F. H. Wigg.**

Synonyms

Chondrilla taraxacum (L.) Stokes, *Crepis taraxacum* L., *Leontodon officinale* (L.) F.H. Wigg., *Leontodon taraxacum* L., *Leontodon vulgare* Lam. (illeg.), *Taraxacum almaatense* Schischk., *Taraxacum laeticolor* Dahlst., *Taraxacum officinale* var. *glabratus* Kirk, *Taraxacum officinale* var. *pygmaea* Hook.f., *Taraxacum retroflexum* H. Lindb. *Taraxacum sylvanicum* R. Doll, *Taraxacum taraxacum* (L.) H. Karst., nom. inval., tautonym

Family

Asteraceae

Common/English Names

Blowball, Broad-Lobed Dandelion, Cankerwort, Common Dandelion, Dandelion, Faceclock, Fairy Clock, Irish Daisy, Lion's-Tooth, Milk Gowan, Pissabed, Priest's Crown, Puffball, Swine's Snout, Telltime, Wet-A-Bed, Wild Endive

Vernacular Names

Albanian: Luleshurdha
Brazil: Dente De Leão, Taraxaco
Chinese: Pu Cong Ying Yao Pu Cong Ying
Czech: Pampeliška Lékařská, Smetánka Lékařská
Danish: Almindelig Mælkebøtte, Fandens Mælkebøtte, Løvetand, Mælkebøtte, Mølkebøtte
Dutch: Gewone Paardebloem, Molsla, Paardebloem
Esperanto: Oficina Taraksako, Ofta Leontodo
Estonian: Harilik Võilill
Finnish: Voikukka
French: Coq, Dandelion Officinal, Dent De Lion, Dent-De-Lion Commune, Florion D'or, Laiteron, Pissenlit, Pissenlit Commun, Pissenlit Dent-De-Lion, Pissenlit Officinal, Pissenlit Vulgaire
German: Ackerzichorie, Bimbaum, Butterblume, Echter Löwenzahl, Gebräuchliche Kuhblume, Gemeine Kuhblume, Gemeiner Löwenzahn, Gewöhnlicher Löwenzahn, Hundeblume, Kettenblume, Kuhblume, Kukucksblom, Lampe, Lichtblom, Löwenzahn, Milchstock, Pfaffendistel, Pfaffenröhrlein, Pferdeblume, Pusteblume, Ringelblume, Seicherwurzel, Wiesenlattich, Wiesen-Löwenzahn
Greek: Agrioradiko
Hawaiian: Lauhele, Laulele
Hungarian: Gyermekláncfű, Oroszlánfog, Őszi Oroszlánfog, Őszi Pitypáng, Pitypáng, Pongyola Pitypáng

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Icelandic: Fíflarætur, Túnfífill
India: Pitachumki (Bengali), Handh, Phull-Dudhi (Dogri), Baran, Barau, Dudal, Dudh-Batthal, Dudhal, Dudhali, Dudhee, Dudhi, Dudli, Dugchipheni, Kandhul, Kanphul, Karatu, Shamuke (Hindi), Kaadu Shaavanthi, Kadusevanti (Kannada), Quanti (Lahaul), Dugddhapheni (Malayalam), Dugdhapheni, Lootari, Payasvini (Sanskrit) Sarkhen Mentok (Spiti), Patri (Telugu)
Indonesia: Jombang
Italian: Dente Di Leone, Piscialette, Capo Dè Fratre, Piscacane, Piscialetto, Radichiella, Soffione, Tarasco, Tarassaco
Japanese: Hokouei, Seiyou Tanpopo, Tampopo
Korean: P'ogongyong
Nepalese: Dudal, Tuki Phul
Norwegian: Fandens Melkebøtte, Griseblom, Gulbruse, Gullbost, Hesteblom, Kaningras, Kappilaup, Koppeloppe, Løvetann, Nattsveve, Skabb, Solvender, Ugrasløvetann, Ugrasløvetenner, Vanlig Løvetann
Pakistan: Dhudhal
Polish: Mniszek Lekarski, Mniszek Pospolity
Portuguese: Amor-Dos-Homens, Dente-De-Leão, Taraxaco
Russian: Oduvanchik, Oduvanchik Lekarstvennyi, Oduvančik Lekarstvennyj
Slovaščina: Navadni Regrat, Regrat, Regrat Navadni
Slovencina: Púpava Lekárska
Spanish: Achicoria Amarga, Almirón, Amargón, Anagrón, Diente De León, Pelosilla, Taraxacón
Swedish: Fjällmaskrosor, Maskros, Ogräsmaskrosor
Turkish: Karahindiba
Vietnam: Bồ Công Anh, Bồ Công Anh Lùn, Bồ Công Anh Trung Quốc
Welsh: Dant Y Llew

Origin/Distribution

Dandelion is native to Europe and Asia Minor; it is now cosmopolitan—distributed worldwide in temperate and subtemperate areas—and is becoming a noxious weed.

Agroecology

In its native range and introduced areas in warm subtemperate and temperate zones, dandelion occurs wild in lawns, on roadsides, on disturbed banks and shores of water ways, on disturbed sunny areas, on fields, on grasslands and on other areas with moist soil from near sea level to 1,000 m elevation. It also occurs in the tropics in the cool highlands at altitudes of 1,200–1,500 m. It is a hardy plant, drought and frost tolerant, tolerating temperatures down to −29 °C. It will grow in all types of soil from sandy dunes, well-drained, humus-rich alkaline to neutral soils to thick clays including crevices in rocks and stones and brackish habitats. It grows in full sun or partial shade. *T. officinale* is considered a weedy species found in ruderal sites, lawns and grassy places.

Edible Plant Parts and Uses

The flowers, flower buds, leaves, leaf stalks, roots and sprouted seeds are edible (MacNicol 1967; Grieve 1971; Harrington 1974; Halpin 1978; Facciola 1990; Roberts 2000). The unopened flower buds while still inside the crown are eaten in pancakes, omelettes, schnapps and fritters; they can also be preserved in vinegar and used like capers. When serving a rice dish, dandelion petals are used like confetti over the rice. The young, freshly picked flowers are added to salad for colour and flavour or fried with bacon. Some recipes include dandelion flower omelette, dandelion and bacon and dandelion and beetroot salad (Roberts 2000). The flowers are used as an ingredient in the Arabic cake 'yublo'. The flowers can be made into dandelion flower jam. Mature flowers are bitter. Dandelion flowers have traditionally been used to make dandelion wine, for which there are numerous recipes. Flowers have also been used in a saison ale called 'Pissenlit' in Belgium. The flowers, leaves and roots are brewed into pleasant teas. The sprouted seeds are edible and used in salads.

Young leaves are eaten in salads, boiled like spinach, blanched steamed, sautéed, fried or braised or cooked in soups. Blanched leaves make an excellent salad either alone or in combination with other vegetables lettuce, shallot tops or chives. The blanched leaf stalks or crown can be eaten raw or as a cooked vegetable. In Vietnam, leaves are used fresh like lettuce, or boiled, made into soup, or fried like other vegetables. The young leaves make delicious sandwiches, placed between slices of bread and butter and sprinkled with salt; the addition of pepper and lemon juice varies the flavour. Dried dandelion leaves are also used as an ingredient in many digestive or diet drinks and herb beers. Dandelion beer is a rustic fermented drink common in England and Canada. Dandelion herbal beer is less intoxicating than ordinary beers, and dandelion stout ranks as a favourite. An agreeable and wholesome fermented drink can be made from dandelions, nettles and yellow dock. The roots are eaten raw or cooked and served like salsify. The roots are roasted to make dandelion coffee, a very good coffee substitute. Dandelion coffee is a natural coffee without the narcotic effects of coffee or tea. The ground roots can be mixed with coffee or chocolate and brewed.

Plate 1 Dandelion plant habit

Botany

Perennial small herb to 40 cm high with long, unbranched, tuberous tap root and milky latex. Leaves 1–20, horizontal or ascending, arranged spirally in a radical rosette; lamina—oblanceolate, 6–40 cm long by 0.7–15 cm wide, irregularly pinnatilobed to pinnatipartite, variably pubescent or glabrous, almost distinctly petiolate or tapering into a winged petiole, petiole green often tinged purplish (Plates 1 and 3). Inflorescence an axillary head, 1–25 per plant on a hollow, leafless, hairy peduncle, outer involucral bracts multiseriate, patent to recurved, ovate to lanceolate, unequal without horns (thickened clawed apices), inner involucral bracts 1-seriate, erect, oblong, receptacle flat. Florets 40 to over 100 per head, bisexual, homogamous ligulate, with yellow or orange-yellow corollas, five stamens with anthers fused to a tube, ovary inferior with one ovule, style greenish or yellowish with two spreading stigmas (Plates 1, 2 and 3). The fruits called cypselae are narrowly obovoid, 3 mm long, ribbed, olive-green or olive-brown to straw coloured to greyish in colour, with slender beaks crowned by a scabrid, silky white pappus.

Nutritive/Medicinal Properties

Plant/Aerial Parts Phytochemicals

Cadosh et al. (1978) isolated flavoxanthin and chrysanthemaxanthin from the plant. The aerial parts afforded a new eudesmanolide, a tetrahydroridentin B, a eudesmanolide- β-D-glucopyranoside and two germacranolide acids, which were esterified with B-D-glucose (Hansel et al. 1980). Scopoletin and esculetin were isolated from the

Plate 2 Dandelion lowers on long slender peduncles

Plate 3 Close view of dandelion flower and leaves

aerial parts (Komissarenco and Derkach 1982). The herb is also rich polysaccharides (primarily fructosans and inulin) and contains smaller quantities of pectin, resin and mucilage and various flavonoids (Rutherford and Deacon 1972; Cordatos 1999). Cichoric acid and the related monocaffeyltartaric acid were found to be the major phenolic constituents in flowers, roots, leaves and involucral bracts and also in the medicinal preparations tested (Williams et al. 1996).

Volatile metabolites from suspension cultures of *Taraxacum officinale* identified included acetic acid butyl ester, 2-methyl-1-propanol, *n*-butyl alcohol, 4-phenyl-1-butanol, 4-hydroxy-4-methyl-2-pentanone, acetic acid, 4-terpineol, β-terpineol and α-terpineol (Hook et al. 1991). Undifferentiated cultured cells and plants of *Taraxacum officinale* were found to contain oleanolic and ursolic acids as major triterpenoids in addition to triterpenols composed mainly of α- and β-amyrins, taraxasterol and lupeol, and negligible quantities of triterpene acids (Akashi et al. 1994). Squalene synthase activity was detected in the microsomal fractions of suspension-cultured cells of dandelion which produced cycloartane (involved in phytosterol biosynthesis) and other classes (e.g. oleanane and ursane) of triterpenoids (Komine et al. 1996). Purple-coloured dandelion callus cultures produced anthocyanin pigments when established on a cytokinin-rich medium under the light (Akashi et al. 1997). The major pigment was identified as cyanidin 3-(6″-malonylglucoside). Chalcone synthase (CHS) activity was detected in the extracts of these purple cells. Dandelion (*T. officinale*) plant was found to contain triterpenes produced by cyclization of oxidosqualene such as taraxasterol, taraxerol, lupeol, α-amyrin and β-amyrin (Masaaki et al. 2006). cDNA cloning of triterpene synthase yielded ten cDNA clones: cycloartenol synthase (TRX), lupeol synthase (TRW), BETA-amyrin synthase (TRY), taraxerol synthase (TRT), achilleol synthase (TRA), simiarenol synthase (TRE), three multifunctional triterpene synthase (TRH, TRR and TRN) and putative oxidosqualene cyclase (TRV).

Field-grown dandelion plants accumulated higher contents of polyphenolic acid compounds (mg/g dw) than hydroponic grown plants: total phenolic acids (31.2 mg vs. 5.00 mg), cichoric acid (26.5 mg vs. 3.82 %), chlorogenic acid (0.95 % vs. 0.43 %) and caftaric acid (3.75 % vs. 0.75 %), respectively (Pedneault et al. 2002). Polyphenolic compounds (g/kg dry matter) in the aerial dandelion plant parts were determined as follows: chlorogenic acid 0.84 g, cichoric acid 34.08 g, total caffeoyl derivatives 43.92 g, total dihydroxycinnamic acid derivatives 53.92 g, total flavonoids 1.62 g, total dihydroxycinnamic acid derivatives + flavonoids 55.54 g and total polyphenolic compounds 53.59 g (Fraisse et al. 2011).

The phytochemicals in various parts of the plant included ascorbic acid, caffeic acid, calcium, magnesium, potassium, chlorogenic acid, luteolin, K, isoquercetin and mannitol (Duke 2005); major sesquiterpene lactones, generally occurring as glycosides (sugars), taraxacosides, taraxacolides,

dihydrolactucin, ixerin, taraxinic acids and ainslioside (Schütz et al. 2006a); and phenylpropanoids (cinnamic acid derivatives)—cichoric acid, monocaffeoyltartaric acid, 4-caffoeylquinic acid, chlorogenic acid, caffeic acid and inulin (Schütz et al. 2006b). *Taraxacum officinale* was found to be rich in triterpenoid and sterol bitter principles (principally taraxacin and taraxacerin) which were found to be distributed uniformly in the roots, leaves and flowers (Sharafzadeh 2011). Other triterpene compounds included triterpenoids such as oleanolic and ursolic acids, and triterpenols such as lupeol, β-amyrin, α-amyrin, taraxasterol and taraxerol, as well as free phytosterols such as sitosterin, stigmasterin and phytosterin.

Leaf Nutrients and Phytochemicals

Nutrient composition of fresh raw dandelion greens (*Taraxacum officinale*) per 100 g edible portion was reported as follows (UDSDA 2012): water 85.60 g; energy 45 kcal (188 kJ); protein 2.70 g; total lipid (fats) 0.70 g; ash 1.80 g; carbohydrate 9.20 g; fibre (total dietary) 3.5 g; minerals (Ca 187 mg, Fe 3.10 mg, Mg 36 mg, P 66 mg, K 397 g, Na 76 mg, Zn 0.41 mg, Cu 0.171 mg, Mn 0.342 mg and Se 0.5 µg); vitamins (vitamin C (ascorbic acid) 35 mg, thiamine 0.190 mg, riboflavin 0.260 mg, niacin 0.806 mg, pantothenic acid 0.084 mg, vitamin B-6 0.251 mg, folate (total) 27 µg, vitamin A 10161 IU, vitamin E (α-tocopherol) 3.44 mg and vitamin K (phylloquinone) 778.4 µg); β-carotene 5,854 µg, α-carotene 363 µg, β-cryptoxanthin 121 µg and lutein + zeaxanthin 13,610 µg; total unsaturated fatty acids 0.170 g (14:0 (myristic acid) 0.009 g, 16:0 (palmitic acid) 0.145 g and 18:0 (stearic acid) 0.007 g); total monounsaturated fatty acids 0.014 g, 18:1 (oleic acid) 0.014 g; and total polyunsaturated fatty acids 0.306 g, 18:2 undifferentiated (linoleic acid) 0.261 g and 18:3 undifferentiated (linolenic acid) 0.044 g.

Dandelion is a very nutritious vegetable, rich in protein, fibre and minerals like Ca, Fe, P and K, especially K, vitamin C, vitamin A, β-carotene, α-carotene, β-cryptoxanthin, lutein and zeaxanthin. It is also a good source for vitamin E, vitamin K, folate, pantothenic acid, vitamin B-6 and vitamin Bs.

The elemental content of Br, Cu, Mn and Pb in the leaves correlated with the extent of anthropogenic pollution of the region where the plant developed (Djingova et al. 1986). A positive linear correlation was observed between the Cu and Pb, Cu and Sb, Pb and Cd, and Pb and Zn content of the leaves. The leaves had been reported to contain considerable amount of furan fatty acids (Hannemann et al. 1998).

Sitosterol (about 60 %) was the most abundant free sterol, followed by stigmasterol (25 %), then campesterol (10 %) in dandelion leaves (Westerman and Roddick 1981). Cholesterol could not be detected. With the exception of stigmasterol and campesterol, esters were present in greater quantities than were free forms, with 4,4-dimethyl sterol esters being the most abundant and principal type comprising cycloartenol (about 40 %) and 24-methylene cycloartenol (about 30 %) and 4-demethyl forms being less abundant. Of the latter, sitosterol ester was present in largest amount (about 25 % of total esters) followed by stigmasterol ester (about 1.5 %) and trace amounts of campesterol ester appearing sporadically. β-Amyrin and β-sitosterol were extracted from dandelion leaves by supercritical fluid extraction (SFE) (Simándi et al. 2002). Soxhlet extraction with *n*-hexane gave yield and recoveries of the active components similar to SFE. Among the investigated methods, extraction with ethyl alcohol resulted in the highest extraction yield and yields of β-amyrin and β-sitosterol.

A sesquiterpene fungitoxin, lettucenin, A was isolated from the leaves treated after stressing with cupric chloride (Tahara et al. 1988). Three flavonoid glycosides (luteolin 7-glucoside and two luteolin 7-diglucosides), hydroxycinnamic acids, cichoric acid, monocaffeyltartaric acid and chlorogenic acid, coumarins, cichoriin and esculin were identified in the leaf extracts (Williams et al. 1996). Esculin, cichoriin, caftaric acid, cichoric acid and mixtures of various esters of these compounds were isolated from the leaves of *T. officinale* (Budzianowski 1997). Cichoric acid and chlorogenic acid were isolated from dandelion leaves (Chkhikvishvili and

Kharebava 2001). Leaves of field-grown plants accumulated higher contents of polyphenolic acid compounds (mg/g dw) than the leaves of hydroponic grown plants: total phenolic acids (61.5 mg vs. 5.63 mg), cichoric acid (61 mg vs. 4.21 %), chlorogenic acid (0.58 % vs. 0.47 %), caftaric acid (8.95 % vs. 1.41 %), respectively (Pedneault et al. 2002). Dandelion leaves were found to be rich in triterpenes such as β-amyrin (7.920–13.750 g/100 g) and β-sitosterol (1.910–3.810 g/100g) (Kristó et al. 2003). A mammalian DNA polymerase inhibitor of D-mandelonitrile-β-D-glucoside (prunasin) was isolated from the acetone leaf extract (Mizushina et al. 2003). The dichloromethane extract of dandelion leaves afforded taraxasteryl acetate, lupeol acetate, taraxinic acid, 11,13-dihydrotaraxinic acid, phytyl fatty acid ester and squalene (Ragasa et al. 2009).

Flower/Seed Phytochemicals

The principal pigment found in dandelion flower extracts was a diester of taraxanthin designated taraxien (Booth 1964). The concentration in the flowers expressed as carotenol was about 350 ppm fresh weight. Appreciable amounts of the monoester and of free taraxanthin were found in the flowers. The monoester had solubilities and adsorption affinities between those of taraxien and taraxanthin.

Three flavonoid glycosides (luteolin 7-glucoside and two luteolin 7-diglucosides), free luteolin, chrysoeriol, hydroxycinnamic acids, cichoric acid, monocaffeyltartaric acid and chlorogenic acid were isolated from dandelion flowers (Williams et al. 1996). All-E-lutein epoxide was the major carotenoid isolated from dandelion petals and that there were also high amounts of the (9*Z*)- and (9′*Z*)-isomers, although the latter may be an artefact (Meléndez-Martínez et al. 2006). Three antimicrobial peptides designated ToAMP1, ToAMP2 and ToAMP3 were purified from *Taraxacum officinale* flowers (Astafieva et al. 2012). The peptides were cationic and cysteine rich and consisted of 38, 44 and 42 amino acid residues for ToAMP1, ToAMP2 and ToAMP3, respectively.

Storage 2S albumin proteins were found in dandelion seeds (Odintsova et al. 2010).

Root Phytochemicals

The roots had been reported to be rich in taraxacin, a crystalline, bitter substance and inulin (24 %) and also to contain gluten, potash, gum and sugar and laevulin (Grieve 1971). An aryl acylamidase (aryl-acylamine amidohydrolase) which hydrolyzes the herbicide propanil (3′,4′-dichloropropionanilide) was isolated from dandelion roots (Hoagland 1975). A serine proteinase named taraxalisin was isolated from *Taraxacum officinale* roots (Rudenskaya et al. 1998; Bogacheva et al. 1999). It was found to be a 67-kD glycoprotein containing 54 % carbohydrate; the N-terminal sequence of taraxalisin had 40 % of its residues identical to those of subtilisin. It hydrolyzed a chromogenic peptide substrate Glp-Ala-Ala-Leu-pNA optimally at pH 8.0. The substrate specificity of taraxalisin towards synthetic peptides and oxidized insulin B-chain was comparable with that of cucumisin from *Cucumis melo* and the subtilisin-like serine proteinase macluralisin from *Maclura pomifera*.

A predominant 18-kDa vegetative storage protein was found present in dandelion roots (Xu et al. 2000). A rapid decrease in temperature from 20 to 5 °C (cold shock) resulted in an increase in the relative amount of the 18-kDa protein transcript, but no change in the amount of the protein within the root. Conversely, a warm-shock treatment (the transfer of plants from 5 to 20 °C) caused a decline in the 18-kDa protein transcript and a decline in the quantity of the 18-kDa root protein. Defoliation and wounding at 5 °C both stimulated an increase in the 18-kDa protein transcript within 36 hours, but there was no change in protein amount.

Dandelion was found to contain large amounts of inulin (12–15 %) and oligofructans in its tap roots (Bacon and Eldeman 1951; Schütz et al. 2006a, b; Van Loo et al. 1995). Three β-fructofuranosidases, namely, an invertase and two hydrolases (A and B), were separated from the soluble protein extracted from dandelion

(Rutherford and Deacon 1972). The hydrolases acted on the inulin series of oligosaccharides found in the roots. Dandelion roots were found to contain fructooligosaccharides (glucose, fructose, sucrose) and fructopolysaccharides (kestoses, nystose, fructofuranosylnystose) (Schütz et al. 2006b). The contents of kestose, nystose and fructofuranosylnystose in dandelion root exceeded that of artichoke.

Olennikov et al. (2009) found that fructose, glucose, saccharose, 1-kestose and nystose were present in the free state in dandelion roots. Two dominant polymeric glucofructan compounds, TGf-1 (5.7 kDa) and TGf-2 (2.6 kDa), which were linear inulin-type macromolecules consisting of fructofuranose units bonded through *β*-(2 → 1)-bonds, were also found. TGf-1 had the structure Glc*p*-1-(2-Frc*f*-1)$_{32}$-2-Frc*f*, and TGf-2 had the following: Glc*p*-1-(2-Frc*f*-1)$_{12}$-2-Frc*f*.

Dandelion roots yielded a new eudesmanolide, a tetrahydroridentin B, a eudesmanolide- β-D-glucopyranoside and two germacranolide acids, which were esterified with β-D-glucose (Hansel et al. 1980). All three of the new glucose derivatives had a strong bitter taste. An acylated γ-butyrolactone glycoside, taraxacoside, was isolated from the roots (Rauwald and Huang 1985). Its structure was elucidated as β-*O*-[4-*O*-(*p*-hydroxyphenylacetyl)-β-D-glucopyransoyl]-β-hydroxy-γ-butyrolactone. The hydroxycinnamic acids, cichoric acid, monocaffeyltartaric acid, and chlorogenic acid were isolated from the roots (Williams et al. 1996). A triterpene, 3β-hydroxylup-18(19)-ene-21-one was isolated from the roots (Kisiel et al. 2000). Five germacrane- and guaiane-type sesquiterpene lactones, including two previously described taraxinic acid derivatives, were isolated from the roots, together with benzyl glucoside, dihydroconiferin, syringin and dihydrosyringin (Kisiel and Barszcz 2000). The other three lactones were identified as 11β, 13-dihydrolactucin, ixerin D and ainslioside. Further, the stereochemistry at C-11 in dihydrotaraxinic acid was assigned. Roots of field-grown plants accumulated higher contents of polyphenolic acid compounds (mg/g dw) than the roots of hydroponic-grown plants: total phenolic acids (9.8 mg vs. 1.23 mg), cichoric acid (7.82 mg vs. 0.96 %), chlorogenic acid (1.08 % vs. 0.1 %) and caftaric acid (0.9 % vs. 0.18 %), respectively (Pedneault et al. 2002). Sesquiterpene glucosides 14-*O*-β-D-glucosyl-11,13-dihydro-taraxinic acid and 14-*O*-β-D-glucosyl-taraxinic acid were isolated from the roots (Kashiwada et al. 2001). Dandelion roots were found to be rich in phytosterol content, e.g. β-sitosterol (1.498–2.109 g/100 g) and triterpenes β-amyrin (8.938–24.540 g/100 g) (Kristó et al. 2003). Among the 43 compounds (phenolic acids and flavonoids) detected in dandelion root and herb juice, 5 mono- and dicaffeoylquinic acids, 5 tartaric acid derivatives and 8 flavone and 8 flavonol glycosides were characterized (Schütz et al. 2005). The predominant compound was cichoric acid (dicaffeoyltartaric acid). The study revealed that even more quercetin glycosides were found in dandelion than hitherto assumed. Also the presence of di- and triglycosylated flavonoids was found.

Five lupane type of triterpenoids, namely, 3β-acetoxy-18α,19α-epoxylupan-21β-ol (1), 18α, 19α-epoxy-21β-hydroxylupan-3-one (2), lup-18-ene-3,21-dione (3), lupa-18,21-dien-3β-yl acetate (4) and (17*S*)-17,18-*seco*-lup-19(21)-ene-3, 18,22-trione (5), named officinatrione, were isolated from dandelion roots (Saeki et al. 2013).

Over the past four decades, pharmacological studies on the plant had revealed the presence of a diverse range of phytochemicals in the plant and emphasized on its diuretic, choleretic, anti-inflammatory, antioxidative, anticarcinogenic, analgesic, antihyperglycaemic, anticoagulatory, demulcent, digestive stimulant, immunomodulatory, insulin stimulant, antiangiogenic and prebiotic effects (Schütz et al. 2006a; Yarnell and Abascal 2009).

Antioxidant Activity

Dandelion extracts diminished the enzymatically induced lipid peroxidation and reduced the cytochrome c with and without NADPH in a concentration-dependent manner in the microsomal fraction of the rat liver (Hagymási et al. 2000). Total antioxidant capacity (%) (DPPH

scavenging activity) of dandelion aerial plant parts was 6.38 %, and contribution from the main caffeoyl derivatives was as follows: chlorogenic acid 1.26 %, cichoric acid 68.96 % and total caffeoyl derivatives 70.22 % (Fraisse et al. 2011).

The water and ethyl acetate fractions of dandelion flowers exhibited free radical scavenging activities in a stable 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical model and reduced the breakage of supercoiled DNA strand induced by both non-site-specific and site-specific hydroxyl radical (Hu and Kitts 2003). Both fractions also reduced the oxidation of structured phosphatidylcholine liposome induced by peroxyl radical with the ethyl acetate fraction having greater affinity to scavenge peroxyl radical than the water fraction. At low concentration, prooxidant activity of both fractions was observed in Cu^{2+}-induced structured liposome and hLDL oxidation models, thus indicating that the reducing power of the dandelion flower extract had resulted in generation of reactive cuprous ion. However, at high concentrations, the ethyl acetate did not promote oxidation in the presence of Cu^{2+}, suggesting that the free radical scavenging activity of this fraction was sufficient to minimize the potential oxidative mechanism attributed to the metal ion reducing activity associated with prooxidant activity. The dandelion flower extract was found to contain both luteolin and luteolin 7-glucoside which contributed to observed in-vitro antioxidant and Caco-2 cell cytotoxic activities. They also reported that luteolin and luteolin-7-*O*-glucoside at concentrations lower than 20 μM significantly suppressed the productions of nitric oxide and prostaglandin E2 (PGE2) in bacterial lipopolysaccharide-activated mouse macrophage RAW264.7 cells without introducing cytotoxicity (Hu and Kitts 2004). The inhibitory effects were further attributed to the suppression of both inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) protein expression, and not reduced enzymatic activity. Similar suppression for both inducible enzymes was also found with the presence of dandelion flower extract, specifically, the ethyl acetate fraction of dandelion flower extract which contained 10 % luteolin and luteolin-7-*O*-glucoside. In further studies, they showed that the dandelion flower extract possessed marked antioxidant activity in both biological and chemical models (Hu and Kitts 2005). Furthermore, the efficacy of the flower extract in inhibiting both reactive superoxide and hydroxyl radicals and nitric oxide was attributed to its phenolic content. Characteristics of chain-breaking antioxidants, such as extended lag phase and reduced propagation rate, were observed in the oxidation of linoleic acid emulsion with the addition of dandelion flower extract. DPPH-radical scavenging activity and a synergistic effect with α-tocopherol were attributed to the reducing activity derived from phenolic content of the flower extract. A significant and concentration-dependent, reduced nitric oxide production from acterial-lipopolysaccharide-stimulated mouse macrophage RAW264.7 cells was observed with the addition of the flower extract. Furthermore, peroxyl-radical-induced intracellular oxidation of RAW264.7 cells was inhibited significantly by the addition of the flower extract over a range of concentrations.

The ethanol dandelion plant extract showed a scavenging activity in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, a diminishing effect on intracellular reactive oxygen species (ROS) level (Jeon et al. 2008). *T. officinale* fruit extract was shown to have antioxidant activity and protected slices of cortex, hippocampus, and striatum of the rat's brain against sodium nitroprusside-induced cellular death (Colle et al. 2012b). Possible mechanisms of protective action included its scavenger activities against reactive oxygen species (ROS) and reactive nitrogen species (RNS), which were attributed to the presence of phenolic compounds in the extract.

Anticancer Activity

A nondialyzable hot water dandelion extract (Tof-CFr) was found to have antitumour activity (Baba et al. 1981). The extract showed an antitumour effect in the allogeneic tumour system of ddY-Ehrlich and the syngeneic C3h/He-Mm46 with intraperitoneal injection. The extract showed cytolytic activation of macrophages in

antibody-dependent macrophage-mediated cytolysis and enhancement of antitumour delayed hypersensitivity reaction in C3h/He-Mm46 syngeneic and ddY-Ehrlich allogeneic tumour systems.

Studies showed that *Taraxacum officinale* decreased human hepatoma Hep G2 cell viability by 26 % and significantly increased the tumour necrosis factor (TNF)-alpha and interleukin (IL)-1alpha production and strongly induced apoptosis of Hep G2 cells (Koo et al. 2004). Increased amounts of TNF-alpha and IL-1alpha contributed to dandelion-induced apoptosis. Recent evidence showed that *T. officinale* has anticarcinogenic activity. Crude extract of dandelion leaf decreased the growth of MCF-7/AZ breast cancer cells, whereas the aqueous extracts of dandelion flower extract and root extract had no effect on the growth of either cell line (Sigstedt et al. 2008). Furthermore, the root extract was found to block invasion of MCF-7/AZ breast cancer cells, while the leaf extract blocked the invasion of LNCaP prostate cancer cells into collagen type I. In a recent study, the aqueous dandelion root extract effectively induced apoptosis in human leukaemia cell lines in a dose- and time-dependent fashion; the apoptosis was found to be mediated by caspase activation (Ovadje et al. 2011). Interestingly, noncancerous peripheral blood mononuclear cells (PBMCs) exposed to the root extract under the same treatment conditions as leukaemia cells were not significantly affected. Lupane triterpenoids isolated from the roots, 18α,19α-epoxy-21β-hydroxylupan-3-one, and officinatrione exhibited moderate cytotoxic activities against murine leukaemia lymphocyte L1210 cell line (IC_{50} 10.5 and 10.1 μM) (Saeki et al. 2013).

Antiviral Activity

Aqueous dandelion extract exhibited potent activity against HIV-1 RT and inhibited both the HIV-1 vector and the hybrid-MoMuLV/MoMuSV retrovirus replication in-vitro (Han et al. 2011). Dandelion extracts may have potential application in the development of an antiretroviral therapy with fewer side effects.

Antiinflammatory Activity

Methanol dandelion flower extract markedly inhibited 2-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced ear oedema in mice (Yasukawa et al. 1998). Kim et al. (1999) demonstrated that stimulation of mouse peritoneal macrophages with *Taraxacum officinale* after the treatment of recombinant interferon-gamma (rIFN-gamma) resulted in increased nitric oxide (NO) synthesis. When *T. officinale* was used in combination with rIFN-gamma, there was a marked synergistic induction of NO synthesis in a dose-dependent manner. They found that the capacity of *T. officinale* to increase NO production from rIFN-gamma-primed mouse peritoneal macrophages was the result of *T. officinale*-induced tumour necrosis factor-alpha secretion. *Taraxacum officinale* was found to inhibit tumour necrosis factor-alpha production from rat astrocytes stimulated with lipopolysaccharide (LPS) by decreasing interleukin-1 production (Kim et al. 2000). The results suggested dandelion exhibited antiinflammatory activity in the central nervous system.

The methanol root extract of *Taraxacum officinale* was found to exhibit inhibitory activity on the formation of leukotriene B4 from activated human neutrophils (Kashiwada et al. 2001). The active principles identified in the extract were sesquiterpene glucosides: 14-*O*-β-D-glucosyl-11,13-dihydro-taraxinic acid and 14-*O*-β-D-glucosyl-taraxinic acid. In the carrageenan-induced air pouch model, the ethanol dandelion plant extract inhibited production of exudate and significantly diminished nitric oxide (NO) and leucocyte levels in the exudates (Jeon et al. 2008). Suppressive effects of the extract on the production of NO and expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-stimulated macrophages were also observed. Dandelion polysaccharides attenuated CCl(4)-induced hepatic damage in Sprague–Dawley rats by modulating inflammatory responses and ameliorating oxidative stress (Park et al. 2010). Pretreatment with dandelion polysaccharides markedly decreased serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

activities as well as hepatic lesions and increased free radical scavenging activity, as exhibited by a lowered TBARS concentration. Pretreatment with dandelion polysaccharides also reversed other hepatitis-associated symptoms, including glutathione (GSH) depletion, inhibited antioxidative enzyme activities, upregulation of NF-kappaB and increased expression of its regulatory inflammatory mediators, such as inducible nitric oxide synthase (iNOS), cyclooxygenase (COX)-2, tumour necrosis factor (TNF)-alpha and interleukin (IL)-1beta.

In another study, the methanol dandelion leaf extract and its fractions inhibited *LPS*-induced production of NO, proinflammatory cytokines and PGE(2) in a dose-dependent manner in the mouse macrophage cell line, RAW 264.7 (Koh et al. 2010). The chloroform fraction significantly suppressed production of NO, PGE(2) and two proinflammatory cytokines (TNF-alpha and IL-1beta) in a dose-dependent manner with 50 % inhibitory concentration values of 66.51, 90.96, 114.76 and 171.06 μg/ml, respectively. The ethyl acetate fraction also inhibited production of the inflammatory molecules. The chloroform and ethyl acetate fractions reduced LPS-induced expressions of iNOS and COX-2 and activation of MAP kinases in a dose-dependent manner. Among the fractions of the methanol extract, the chloroform and ethyl acetate fractions exhibited the most effective antiinflammatory activities. The results showed that the antiinflammatory effects of dandelion leaves were probably due to downregulation of NO, PGE(2) and proinflammatory cytokines and reduced expressions of iNOS and COX-2 via inactivation of the MAP kinase signal pathway.

Both methanol and water dandelion extracts inhibited lipopolysaccharide (LPS)-stimulated iNOS gene expression and that of its transcription factor, NF-κB, in parallel with nitrite reduction in RAW 264.7 cells (Park et al. 2011b). Both extracts significantly reduced NO production with an IC_{50} of 79.9 and 157.5 μg/ml, respectively, without cytotoxicity. Depleted glutathione (GSH) and antioxidative enzyme activities, including superoxide dismutase, catalase, GSH-peroxidase and GSH-reductase, were restored by dandelion extracts. The methanol extract showed more potent antioxidative and antiinflammatory capacities than the water extract, which was attributable to its higher total phenol, luteolin and cichoric acid content. In another study, co-treatment with luteolin and cichoric acid (both from dandelion) synergistically reduced cellular concentrations of nitric oxide (NO) and prostaglandin E2 (PGE2) and also inhibited expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells (Park et al. 2011a). Furthermore, co-treatment reduced the levels of proinflammatory cytokines, tumour necrosis factor (TNF)-α and interleukin (IL)-1β. Both luteolin and cichoric acid suppressed oxidative stress, but they did not exhibit any synergistic activity. Luteolin and cichoric acid co-treatment inhibited phosphorylation of NF-κB and Akt but had no effect on extracellular signal-regulated kinase (ERK), c-Jun NH2-terminal kinase (JNK) and p38. This antiinflammatory signalling cascade coincided with that affected by luteolin treatment alone. The results suggested that luteolin played a central role in ameliorating LPS-induced inflammatory cascades via inactivation of the NF-κB and Akt pathways and that cichoric acid strengthened the antiinflammatory activity of luteolin through NF-κB attenuation. In another study, pretreatment with taraxasterol (isolated from *T. officinale*) inhibited NO of prostaglandin E(2) (PGE(2)), tumour necrosis factor-α, interleukin IL-1β and IL-6 production in LPS-induced RAW 264.7 macrophages in a dose-dependent manner (Zhang et al. 2012). Further studies revealed that taraxasterol prevented the LPS-induced NF-κB translocation from cytoplasm into the nucleus. The results suggested taraxasterol to have antiinflammatory effect by blocking NF-κB pathway.

Hepatoprotective Activity

Carbon tetrachloride treatment decreased superoxide dismutase (SOD), catalase, glutathione

and peroxidase and increased lipid peroxidation in rats; in contrast, pretreatment of rats with 100 mg/kg (p.o.) of dandelion root hydroalcoholic extract improved the SOD, catalase, glutathione and peroxidase levels significantly and reduced lipid peroxidation (Sumanth and Rana 2006). The results suggested hydroalcoholic extract from the dandelion root possessed antioxidant activity, confirming the traditional use of the plant in treatment of liver disorders.

Studies by Colle et al. (2012a) markedly demonstrated the hepatoprotective effect of *T. officinale* leaf extract against the toxicity induced by acetaminophen. *T. officinale* decreased thiobarbituric acid-reactive substance levels induced by 200 mg/kg acetaminophen (p.o.), as well as prevent the decrease in sulphhydryl levels caused by acetaminophen treatment. Additionally, histopathological alterations, as well as the increased levels of serum aspartate and alanine aminotransferases caused by acetaminophen, were prevented by *T. officinale* (0.1 and 0.5 mg/ml). Further, dandelion leaf extract also demonstrated antioxidant activity in-vitro, as well as scavenger activity against DPPH and nitric oxide radicals. The possible mechanisms for its hepatoprotective effect may involve its scavenger activities against ROS and reactive nitrogen species, attributable to the presence of phenolic compounds in the extract.

Animal studies showed that the water ethanol dandelion root extract had therapeutic effect on CCl_4-induced liver fibrosis (Domitrović et al. 2010). The extract successfully decreased hepatic fibrinous deposits, restored histological architecture and modulated the expression of glial fibrillary acidic protein (GFAP) and alpha-smooth muscle actin (α-SMA). Concomitantly, metallothionein I/II expression increased in the extract-treated mice. Similarly, Mahesh et al. (2010) found that posttreatment of ethanol dandelion root extract and sesquiterpene lactones enriched fraction protected against CCl_4-induced hepatotoxicity in mice. Their results indicated that sesquiterpene lactones had a protective effect against acute hepatotoxicity induced by the administration of CCl_4 in mice. In another study, mice, which received hot water dandelion root extract (1 g/kg bw/day) with ethanol, revealed complete prevention of alcohol-induced hepatotoxicity as evidenced by the significant reductions of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and lactate dehydrogenase activities compared to ethanol-alone-administered mice (You et al. 2010). Dandelion extract-treated mice exhibited significant increases in hepatic antioxidant activities, including catalase, glutathione S-transferase, glutathione peroxidase, glutathione reductase and glutathione. Further, the amelioration of malondialdehyde levels indicated dandelion extract protective effects against liver damage mediated by alcohol in-vivo. The results suggested that the aqueous extract of *T. officinale* root exerted protective action against alcohol-induced toxicity in the liver by elevating antioxidative potentials and decreasing lipid peroxidation.

The HV-P411 complex, an herbal extract mixture from the seeds of *Vitis vinifera, Schisandra chinensis* and *Taraxacum officinale* elicited protective effects against D-galactosamine (D-GalN)-induced hepatitis in rats when orally administered 48, 24 and 2 hours before and 6 hours after D-GalN injection (Kang et al. 2012). Increases in serum aminotransferase activity and lipid peroxidation and a decrease in hepatic glutathione content were attenuated by the HV-P411 complex 24 hours after D-GalN treatment. The HV-P411 complex attenuated the increases in serum tumour necrosis factor-α, interleukin (IL)-6 level and cyclooxygenase-2 protein production and their mRNA expressions, while increases in seruminterleukin IL-10 level and heme oxygenase-1 protein production and their mRNA expressions were augmented by the HV-P411 complex. The increased translocation of nuclear factor-κB and c-Jun phosphorylation were attenuated by treatment with the HV-P411 complex.

Diuretic Activity

An animal study found that at high doses (2 g/kg body weight), dandelion leaves possessed diuretic

effects comparable to the prescription diuretic furosemide (Rácz-Kotilla et al. 1974). They concluded that dandelion contained three times the amount of potassium in other botanical diuretics and provided more potassium than that lost from diuresis induced by ingesting dandelion. Thus, dandelion could offer a therapeutically significant potassium contribution by replacing the potassium loss induced by most diuretics.

In a pilot study of 17 human volunteers, hydroethanol extract of dandelion leaves showed promise as a diuretic (Clare et al. 2009). There was a significant increase in the frequency of urination in the 5 hours period after the first dose. There was also a significant increase in the excretion ratio in the 5 hours period after the second dose of extract.

Adaptogenic Activity

Studies showed that *Taraxacum officinale* extract had an anti-physical fatigue effect in mice (Zhang and Chen 2011). After 6 weeks of supplementation, the extract enhanced the maximum swimming capacity of mice, effectively delayed the lowering of glucose in the blood and prevented the increase in lactate and triglyceride concentrations. In the forced swimming test, immobility time was significantly decreased on the tenth day in the group of mice treated with dandelion extract (100 mg/kg) (Lee et al. 2012). The level of lactic dehydrogenase, which is an accurate indicator of muscle damage, tended to decline after dandelion administration (10 and 100 mg/kg). When dandelion extract (100 mg/kg) was orally administered to mice, blood urea nitrogen levels decreased significantly. When dandelion extract was used in combination with recombinant interferon-gamma (rIFN-γ), a noticeable cooperative induction of tumour necrosis factor-alpha (TNF-α), interleukin (IL)-12p70 and IL-10 production was observed. Further, in peritoneal macrophages, rIFN-γ plus dandelion treatment significantly increased the production of NO through inducible nitric oxide synthase (iNOS) induction. The data suggested that dandelion improved fatigue-related indicators and immunological parameters in mice.

Probiotic Activity

The infusion of dandelion root (*Taraxacum officinale*) stimulated in-vitro the growth of 14 strains of bifidobacteria (Trojanová et al. 2004). The utilization of oligofructans, glucose, fructose and total saccharides was determined by enzymatic and phenol–sulphuric methods. Dandelion oligofructans were important source of carbon and energy for bifidobacteria tested. Bifidobacteria aid in digestion, are associated with a lower incidence of allergies and also prevent some forms of tumour growth and are being used as probiotics.

Antimicrobial Activity

Three peptides, ToAMP1, ToAMP2 and ToAMP3, purified from dandelion flowers were shown to display high antimicrobial activity both against fungal and bacterial pathogens (Astafieva et al. 2012).

Anti-obesity/Antihyperlipidemic Activity

The 95 % ethanol extract of *T. officinale* and Orlistat (an anti-obesity agent) inhibited porcine pancreatic lipase activity by 86.3 and 95.7 % at a concentration of 250 μg/ml, respectively, in-vitro (Zhang et al. 2008). Dandelion extract showed dose-dependent inhibition with the IC_{50} of 78.2 μg/ml. A single oral dose of the ethanol extract to mice significantly inhibited increases in plasma triglyceride levels at 90 and 180 minutes and reduced incremental areas under the response curves of plasma triglyceride response curve. The results indicated that *T. officinale* exhibited inhibitory activities against pancreatic lipase in-vitro and in-vivo. Diet supplementation with dandelion root and leaf root positively changed plasma antioxidant enzyme activities and lipid profiles in cholesterol-fed rabbits and thus may have potential hypolipidaemic and antioxidant effects (Choi et al. 2010). The authors concluded that dandelion root and leaf could protect

against oxidative stress-linked atherosclerosis and decrease the atherogenic index.

In a randomized double-blind, crossover study with no washout period involving men with hypercholesterolaemia, dietary inulin supplementation was found to improve blood lipid profiles and altered the colonic environment in a beneficial manner (Causey et al. 2000).

Pulmonary Protective Activity

Studies showed that *Taraxacum officinale* protected against lipopolysaccharide (LPS)-induced acute lung injury in mice (Liu et al. 2010). Dandelion treatment decreased the lung W/D ratio, protein concentration and the number of neutrophils in the bronchoalveolar lavage fluid (BALF) at 24 hours after LPS challenge. Dandelion also inhibited the production of inflammatory cytokines TNF-alpha and IL-6 in the BALF at 6 hours after LPS challenge in a dose-dependent manner. Further, histopathological examination indicated that dandelion attenuated tissue injury of the lungs in LPS-induced acute lung injury.

Antinociceptive Activity

The ethanol dandelion plant extract also possessed an inhibitory effect on acetic acid-induced vascular permeability and caused a dose-dependent inhibition on acetic acid-induced abdominal writhing in mice (Jeon et al. 2008).

Pancreas Protective Activity

Studies showed that dandelion extract had a protective effect on cholecystokinin (CCK) octapeptide-induced acute pancreatitis in rats (Seo et al. 2005). Dandelion significantly decreased the pancreatic weight/body weight ratio in cholecystokinin octapeptide-induced acute pancreatitis. It also increased the pancreatic levels of HSP60 and HSP72. Further, the secretion of interleukin 6 and TNF-alpha decreased in the animals treated with dandelion extract.

Anticolitic Activity

Taraxacum officinale in a herbal combination with *Hypericum perforatum, Melissa officinalis, Calendula officinalis* and *Foeniculum vulgare* was found effective in treating chronic colitis in 24 human patients (Chakŭrski et al. 1981). As a result from the treatment, the spontaneous and palpable pains along the large intestine disappeared in 95.83 % of the patients by the 15th day of their admission to the clinic. Defecation became daily in the patients with obstipation syndrome and in patients with diarrhoea syndrome.

Antiangiogenic Activity

The ethanol dandelion plant extract showed an antiangiogenic activity in the chicken chorioallantoic (CAM) assay (Jeon et al. 2008). Among the various fractions, the n-butanol fraction (BuOH) was identified to be most effective in the CAM assay.

Neuroprotective Activity

Studies showed that spirulina (*Arthrospira platensis*) or dandelion-enriched diet of female rats (mothers) alleviated lead acetate-induced damages in brain and cerebellum of newborn rats by reducing lead-induced oxidative stress and related cerebellum tissue damages (decrease in weight and protein content) (Gargouri et al. 2012).

Immunomodulatory Activity

Studies in mice showed that the dandelion hydroalcoholic extract had immunomodulatory property (Modaresi and Resalatpour 2012). At all three doses of 50, 100 and 200 mg/kg, the number of RBC and the rate of heart beat were significantly increased, and at 200 mg/kg dose, WBC number was significantly increased to achieve normal body balance. All three doses of dandelion increased lymphocyte numbers significantly compared with controls.

Gastroprokinetic Activity

N-butanol fraction of dandelion ethanol extract appeared to be a promising prokinetic agent in mice (Jin et al. 2011). Dandelion fraction-induced increase in the contraction of fundus and antrum contributed to an increase in the intragastric pressure. Dandelion fraction-induced decrease in the motility of pyloric sphincter contributed to a decrease in the resistance of food from the stomach to the small intestine. The acceleration of gastric emptying by the fraction was postulated to be exerted through cholinergic stimulation.

Hypoglycaemic Activity

Dandelion root extract showed hypoglycaemic activity in normoglycaemic but not in alloxan-treated hyperglycaemic (diabetic) rabbits (Akhtar et al. 1985). Studies in Croatia reported that an antidiabetic herbal preparation (Patent No. P-9801091, Zagreb) comprising leaf of *Vaccinium myrtillus*, dandelion root (*Taraxacum officinale*), chicory root (*Cichorium intybus*), juniper fruit (*Juniperus communis*), centaury plant (*Centaurium umbellatum*), beans (*Phaseolus vulgaris*), yarrow herb (*Achillea millefolium*), black mulberry leaf (*Morus nigra*), valerian root (*Valeriana officinalis*) and nettle plant and root (*Urtica dioica*), exhibited hypoglycaemic activity (Petlevski et al. 2001). The herbal preparation significantly decreased the level of glucose and fructosamine in alloxan-induced nonobese diabetic mice. In-vitro studies showed that ethanol extract of *Taraxacum officinale* at 40 μg/ml exerted insulin secretagogue activity in pancreatic insulinoma INS-1 cells, suggesting its potential as a natural resource for antidiabetic compound (Hussain et al. 2004). In contrast, a study in Europe found that 28-day treatment of normal and streptozotocin-induced diabetic mice with dandelion preparation did not affect the parameters of glucose homeostasis (basal plasma glucose and insulin, glucose tolerance, insulin-induced hypoglycaemia and glycated haemoglobin) in normal mice and did not significantly affect glucose homeostasis studied (basal glucose and insulin, insulin-induced hypoglycaemia, glycated haemoglobin and pancreatic insulin concentration) in streptozotocin-induced diabetic mice (Swanston-Flatt et al. 1998).

Goksu et al. (2010) reported the first case of hypoglycaemia caused by ingestion of dandelion. Kango (2008) found that the dandelion tap root extract induced endoinulinase synthesis in *Aspergillus niger* NK-126 and could be utilized as a potential substrate for inulinase production. This enzyme catalyzes the conversion of inulin to fructose.

Antiurolithiatic activity

T. officinale was one of seven plants tested that exhibited antiurolithiatic activity in female Wistar rats (Grases et al. 1994). It exerted beneficial effects on some urolithiasis risk factors (citraturia, calciuria, phosphaturia, pH and diuresis) evaluated, attributable to some disinfectant action and to the presence of saponins.

Bile Secretion/Digestive Stimulant Activities

Sesquiterpene lactones were found to be the bitter principles in dandelion leaves and roots which stimulate digestion and act as mild laxatives (Kuusi et al. 1985). Oral administration of extracts from the roots of *Taraxacum officinale* was found to act as a cholagogue, increasing the flow of bile (Vogel 1977).

Fertility and Antifertility Activity

Studies showed that oral intake of dandelion T-1 extract for 6 weeks upregulated oestrogen receptors (ERalpha and ERbeta), progesterone receptor (PR) and follicle-stimulating hormone receptor (FSHR) expression in mice, suggesting the potential application of dandelion extract in the clinical treatment of reproductive hormone-related disturbances (Zhi et al. 2007). In a placebo-controlled, parallel-arm, pilot study of

40 healthy premenopausal women, over five menstrual cycles, Greenlee et al. (2007) compared the effects of a naturopathic botanical and dietary interventions on sex steroid hormone metabolism. The botanical supplement comprised *Curcuma longa, Cynara scolymus, Rosmarinus officinalis, Schisandra chinensis*, *T. officinale* and *Silybum marianum*, and the dietary interventions consisted of crucifers or dark leafy greens. During the early follicular phase, compared with placebo, the botanical supplement decreased androgens dehydroepiandrosterone (−13.2 %), dehydroepiandrosterone sulphate (−14.6 %) and androstenedione (−8.6 %) and the oestrogen estrone sulphate (−12.0 %) with no significant effects on levels of any other sex steroid hormones. When comparing dietary interventions with placebo, no statistically significant differences were observed.

Administration of aqueous dandelion extract at high (1/10 LD_{50}) and low (1/20 LD_{50}) doses to male rats resulted in a significant decrease in testis weight, sperm count, motility and normal morphology, pregnancy rate and diameter and wall thickness of seminiferous tubules (Tahtamouni et al. 2011). Also, distortion of morphology of the seminiferous tubules and arrest in spermatogenesis was observed in the extract-treated group. Further, the percentage of sperm with damaged chromatin integrity was significantly higher in the two extract-treated groups. They concluded that the aqueous extract of *Taraxacum officinale* acted as an antifertility agent rather than a fertility booster as prescribed by Jordanian herbalists.

Allergy Problems

Compositae dermatitis was reported in a 9-year-old boy with a strong personal and family history of atopy (Guin and Skidmore 1987). Positive patch test reactions were 2+ for dandelion (*Taraxacum officinale*), false ragweed (*Ambrosia acanthicarpa*), giant ragweed (*Ambrosia trifida*), short ragweed (*Ambrosia artemisiifolia*), sagebrush (*Artemisia tridentata*), wild feverfew (*Parthenium hysterophorus*), yarrow (*Achillea millefolium*) and tansy (*Tanacetum vulgare*). The eruption resembled atopic dermatitis morphologically but was prominent on the palms and face and dramatically spared the area of the boy's feet covered by his shoes. In skin-prick tests, mugwort, chrysanthemum and dandelion sensitized 13.4, 10.0 and 8.5 % of the enrolled population, respectively, and 5.2 % of the population was cosensitized to all three pollens (Lee et al. 2007). In inhibition ELISA that used a pooled serum sample cosensitized to all three pollens, mugwort inhibited sIgE bindings to chrysanthemum, dandelion and mugwort up to 95, 86 and 96 %, respectively. The mugwort sIgE of this pooled serum was suppressed up to 74 and 27 % by chrysanthemum and dandelion, respectively. Chrysanthemum and dandelion were frequently cosensitized with mugwort in the general population with respiratory allergic diseases. These two species also showed extensive cross-allergenicity with mugwort.

Safety Issues

Dandelion is a commonly available food with a long history of human use and as such poses little risk or harm (Yarnell and Abascal 2009). Consumption of diets containing 33 % dandelion for months produced no toxic effects in rats (Hirono et al. 1978). The German Commission E approves the use of dandelion as a diuretic and also for use in anorexia, dyspepsia and biliary abnormalities (Blumenthal et al. 1998). Dandelion extracts are listed on the US Food and Drug Administration's 'generally recognized as safe' (GRAS) list for foods and supplements (US FDA 2012).

According to European Medicines Agency (2009) Assessment report on *Taraxacum officinale* radix cum herba, their uses for the relief of symptoms related to mild digestive disorders such as feeling of abdominal fullness, flatulence and slow digestion and for diuresis stimulation have long been recognized empirically and are plausible on the basis of bibliography and pharmacological data, although there are no data available from clinical studies. The diuretic action of preparations from Taraxaci radix cum herba may be associated with the high kalium

content and with certain flavonoids, although no studies confirm this hypothesis. Bitter principles (sesquiterpenoids) may be responsible for the stimulation of digestive fluids in stomach and bile flow stimulation. Reliable data on acute toxicity are only available for whole crude drug and some extracts. Oral administration of preparations from Taraxaci radix cum herba can be regarded as safe at traditionally used doses with the exception of patients with renal failure and/or diabetes and/or heart failure. Further, in the documentation of the traditional medicinal use within the European Union, no serious adverse effects have been reported; however, clinical safety data on extracts of Taraxaci radix cum herba is still lacking. Due to lack of data, Taraxaci radix cum herba preparations cannot be recommended for children and adolescents below the age of 12 years, in pregnancy and lactation, and must not be used in case of individuals with obstructions of bile ducts, cholangitis, liver diseases, gallstones, active peptic ulcer and any other biliary diseases. Hypersensitivity to the Asteraceae sesquiterpene lactones or other active substances from Taraxaci radix cum herba is also regarded as contraindication.

Traditional Medicinal Uses

Dandelion has been known since ancient times for its therapeutic properties in Chinese, Arabian and native American traditional medicine and has been utilized for the treatment of various ailments such as dyspepsia, heartburn, spleen and liver complaints, hepatitis and anorexia (Grieve 1971; Chiej 1984; Bown 1995; Schütz et al. 2006a, b; Yarnell and Abascal 2009). It is still used in modern phytotherapy in Europe, Asia and the Americas (Clare et al. 2009). Dandelions have long been used in herbal medicine for their choleretic, diuretic, antiinflammatory, appetite-stimulating and laxative properties (Hagymási et al. 2000; Clare et al. 2009). All parts of the plant, but especially the root, are slightly aperient, cholagogue, depurative, strongly diuretic, hepatic, antipyretic, detoxicant, galactagogue, laxative, stomachic and tonic (Grieve 1971; Chiej 1984; Lust 1974; Bown 1995; Foster and Duke 1998). The root is also experimentally cholagogue, hypoglycaemic, and a weak antibiotic against yeast infections (Foster and Duke 1998). The dried root was official in the United States Pharmacopoeia. Dandelion root is a registered drug in Canada, sold principally as a diuretic. The root is primarily considered a gastrointestinal remedy supporting digestion and liver function, while the leaf is used as a diuretic and bitter digestive stimulant. A tea made from dandelion root, black horehound herb, sweet flag root and mountain flag is taken after meals for biliousness and dizziness (Grieve 1971). A tea made from dandelion root, parsley root, balm herb and liquorice roots is taken to treat gallstones. A preparation of dandelion root, polypody root, long-leaved plantain, shepherds' purse and rhubarb is taken for piles. A mixture of dandelion root, juniper berries and broom tops is taken for liver and kidney ailments.

In the olden days, dandelion juice was the favourite preparation both in official and domestic medicine (Grieve 1971). Dandelion is used as a bitter tonic in atonic dyspepsia and as a mild laxative in habitual constipation. The German Commission E Monographs, a therapeutic guide to herbal medicine, approve *Taraxacum officinale* for dyspepsia, urinary tract infections, liver and gallbladder complaints and appetite loss. It is especially effective and valuable as a diuretic because it contains high levels of potassium salts and therefore can replace the potassium that is lost from the body when diuretics are used (Bown 1995). The plant is used internally in the treatment of gall bladder and urinary disorders, gallstones, jaundice, cirrhosis, dyspepsia with constipation, oedema associated with high blood pressure and heart weakness, chronic joint and skin complaints, gout, furuncles (boils), eczema and acne (Bown 1995). The latex contained in the plant sap can be used to remove corns, warts and verrucae; to treat inflammations of the gall bladder; and to remove stones in the liver (Chiej 1984). In Derbyshire, the juice of the stalk is applied to remove warts (Grieve 1971). A tea made from the leaves is laxative. Tea prepared from *T. officinale* has been used against fever,

insomnia, jaundice, rheumatism, eczema and other skin diseases and constipation. A leaf decoction can be drunk to 'purify the blood,' for the treatment of anaemia, jaundice, and also for nervousness. Crushed leaves are applied on lesions and insect and snake bites.

Dandelion has been traditionally used in the treatment of various liver disorders in Croatia (Domitrović et al. 2010). *Taraxacum officinale* is commonly used in Jordan folk medicine for the treatment of panophthalmitis, chronic constipation and diabetes. In addition, herbalists prescribe the aqueous extract of *Taraxacum officinale* to enhance male's fertility (Tahtamouni et al. 2011). Dandelion has been used as a remedy for anaemia, purifying the blood, and providing immune modulation in Iran (Modaresi and Resalatpour 2012). In Korean herbal medicine, dandelion has been used to improve energy levels and health (Lee et al. 2012).

Other Uses

Dandelions are important foraging plants for bees; they are an important source of nectar and pollen. The milky latex has been used as a mosquito repellent. A liquid plant feed can be made from the root and leaves. Yellow or green dye colours can be obtained from the flowers and from the roots, a magenta-brown dye is obtained.

A fungitoxin, named lettucenin A, isolated from the leaves exhibited fungitoxic effects on the growth of *Cladosporium herbarum* (Hanawa et al. 1995). The dandelion 2S albumins possessed inhibitory activity against phytopathogenic fungi and the oomycete *Phytophthora infestans* at micromolar concentrations with various isoforms differing in their antifungal activity (Odintsova et al. 2010).

Comments

Dandelion has become a nuisance weed in parks, roadsides, house gardens and yards in many temperate countries.

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Impatiens balsamina

Scientific Name

***Impatiens balsamina* L.**

Synonyms

Balsamina angustifolia Blume, *Balsamina balsamina* (L.) Huth (inval.), *Balsamina coccinea* DC., *Balsamina cornuta* DC., *Balsamina foeminea* Gaertn., *Balsamina hortensis* Desp., *Balsamina lacca* Medik., *Balsamina minutiflora* Span,. *Balsamina mollis* G.Don, *Balsamina odorata* Buch.-Ham. ex D.Don, *Balsamina racemosa* Buch.-Ham. ex D.Don, *Impatiens arcuata* Benth., *Impatiens cornuta* L., *Impatiens eriocarpa* Launert, *Impatiens lobbiana* Turcz., *Impatiens longifolia* Wight, *Impatiens malayensis* Griff., *Impatiens rosea* Lindl., *Impatiens stapfiana* Gilg

Family

Balsaminaceae

Common/English Names

Balsam, Garden Balsam, Touch Me Not Balsam, Garden Balsam, Garden Balsamine, Impatiens, Jewelweed, Rose Balsam, Spotted Snapweed.

Vernacular Names

Bangladesh: Dopati
Burmese: Dau Dalet
Chamorro: Kamantigi
Chinese: Feng Xian Hua, Ji Xing Zi
Chuukese: Pee Cca, Pee-Cha
Dutch: Juliaantje
French: Balsamine Des Jardins, Impatience
German: Balsamine, Gartenspringkraut
India: Gulmendhi (Hindi), Dushpatrijati (Sanskrit), Kasittumbai (Siddha), Kasittumbai (Tamil), Gul Mehendi (Urdu)
Indonesian: Pacar Banyu (Javanese), Paru Inai (Minangkabau), Pacar Air
Japanese: Tsurifune-Sō
Korean: Bongseonhwa
Malaysia: Bunga Embung, Bunga Tabo, Hinai Ayam, Hinai Pacak, Inai Air, Lak Kecil, Dandalet (Sarawak)
Palauan: Hosengka
Philippines: Suranga (Bikol), Solonga, Suranga (Bisaya), Kamantigi (Iloko), Kamantig (Pampangan) Saungga (Sulu), Kamantigi (Tagalog)
Russian: Nedotroga Bal'zaminovaja
Samoan: Patiale
Spanish: Balsamina, Chachupina, Chico, Madama
Swedish: Balsamin
Thai: Thian Baan, Thian Dok, Thian Suan
Tongan: Polosomo
Vietnamese: Bóng Nước, Cây Bông Móng Tay; Móc Tai, Móng Tay

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Origin/Distribution

This species is indigenous to southern Asia in India and mainland Southeast Asia. It is widely grown in gardens and has naturalized in disturbed areas as a common escape from cultivation in tropical and subtropical areas. It is has been introduced into South China, southern Europe and Turkey.

Agroecology

Although a warm-climate species, it still can be grown outdoors after the last frost in temperate areas. In its native range, the plant is found from sea level to 1,250 m elevation in wet open areas or as forest undergrowth. It is adaptable to many soils including heavy clay soils but prefers a moist, well-drained, humus-rich soil. It grows in full sun to partial shade.

Edible Plant Parts and Uses

The flowers (Paul 2011), seeds (Kunkel 1984; Phuphathanaphong 1992; Paul 2011), leaves and young shoots (Read 1946; Heyne 1950; Kunkel 1984) have been reported to be edible. Stella Paul (2011) uses the flowers in a vegetarian 'Kofta', wherein the petals are made into little balls, dipped in a batter (chickpea powder or rice powder or corn flour), shallow fried and then cooked in a curry with sliced potatoes. She also adds petals to salad. The dried seeds are ground and a pinch added to tea. The seeds are also eaten raw or cooked and also afford an edible oil (Kunkel 1984; Phuphathanaphong 1992). In China the leaves and shoots are cooked and eaten (Read 1946; Kunkel 1984) and also in Bali (Heyne 1950).

Botany

An erect, annual herb, 20–60 (–90) cm high. The stem is glabrous or weakly pubescent when young, succulent and sparsely branched with swollen nodes. Leaves alternate but lower ones occasionally opposite, sessile to shortly petiolate 1–2 cm, lamina lanceolate, narrowly elliptic or oblanceolate, 4–12 × 1.5–3 cm, with a pair of sessile black glands towards base, both surfaces glabrous or sparsely pubescent and with stipitate glands, lateral veins 4–7 pairs, base cuneate, margin deeply serrated, apex acuminate (Plate 1). Flowers solitary or in fascicles of 2–3 in leaf axils, on densely pubescent, 2–3 cm across on 1–2 cm pedicels with linear bracts. Flowers white, pink or purple, red or variegated, simple or double petalous (Plate 1). Sepals 3, lateral sepals, ovate to ovate–laceolate, sparsely ciliate; lower sepal conical pubescent, abruptly narrowed into an incurved spur 10–20 mm long. Petals 5, upper petal orbicular, apex retuse, long mucronulate; lateral four petals pairwise connate and shortly clawed. Stamens 5; filaments linear; anthers ovoid, apex obtuse. Ovary superior, fusiform, densely pubescent. Capsule 4–5 valved, broadly fusiform, 1–2 cm, densely tomentose, narrowed at both ends, explosively dehiscent. Seeds many, black-brown, subglobose, 1.5–3 mm across, tuberculate.

Plate 1 Foliage and flowers of garden balsam

Nutritive/Medicinal Properties

Flower Phytochemicals

Of the genes at four loci (H, L, P, W) that determine floral pigmentation in balsam phenotypes, only L was correlated with the presence

of a flavonol which was probably myricetin (Clevenger 1958). Kaempferol was found in the petals and sepals of all types analyzed, while quercetin was limited to the sepals of these. Leucoanthocyanins were detected in both sepals and petals of the earliest bud stages, and cyanidin and delphinidin were detected from buds of all phenotypes with cyanidin generally predominating (Alston and Hagen 1958).

Klein and Hagen (1961) reported anthocyanin production in various coloured balsam flower phenotypes as follows: In pink flower phenotype, intact petal anthocyanidins (pelargonidin) and flavonols (kaempferol); cultured petal anthocyanidins (pelargonidin, cyanidin, peonidin) and flavonols (kaempferol, quercetin); and sepals anthocyanidins (pelargonidin, cyanidin, peonidin) and flavonols (kaempferol, quercetin). In red flower phenotype: intact petal anthocyanidins (pelargonidin) and flavonols (kaempferol); cultured petal anthocyanidins (pelargonidin, cyanidin) and flavonols (kaempferol, quercetin); and sepals anthocyanidins (pelargonidin, cyanidin) and flavonols (kaempferol, quercetin). In purple flower phenotype: intact petal anthocyanidins, lacking flavonols (malvidin, kaempferol, myricetin); cultured petal anthocyanidins (cyanidin) and flavonols (malvidin, kaempferol, myricetin); and sepals anthocyanidins lacking and flavonols (malvidin, kaempferol, quercetin, myricetin).

Petals of mature flowers were pigmented by *p*-coumaroyl and feruloyl esters of pelargonidin-3,5-diglucoside supplemented by highly substituted derivatives of pelargonidin and by large amounts of kaempferol as the aglycones and two glucosides, while balsam stems were found to have 3-monoglucosides of kaempferol, quercetin, pelargonidin, cyanidin and delphinidin (Hagen 1966a). Hagen (1966a) reported a progressive elaboration of anthocyanin in red balsam flower by dividing it into four developmental stages: stage I had no anthocyanin, stage 2 pelargonidin-3-monoglucoside appeared as the only anthocyanin, stage 3 with multiple pelargonidin intermediate compounds and stage 4 at anthesis many of the compounds disappeared leaving one major pigment, *p*-coumaroyl pelargonidin-3,5-diglucoside. Mansell and Hagen (1966) found that when pelargonidin-3-monoglucoside was introduced into genetically white petals, it was converted to acylated pelargonidin-3,5-diglucoside. Miles and Hagen (1968) found that balsam flower contained enzymes that catalyzed the glycosylation of phenolic compounds. Enzymes were extracted which glycosylated hydroquinone to arbutin and at least three different flavonols to the 3-monoglucoside. It was suggested that the flavonol glucosylating enzyme acted naturally to glucosylate a precursor of both flavonols and anthocyanins to the 3-monoglucoside. The only elaboration of an anthocyanin observed with petal extracts was an acylation of pelargonidin-3-monoglucoside.

A flavonoid-3-β-D-glucosidase was purified from balsam petals of *Impatiens balsamina* (Boylen et al. 1969). When the petal preparation was incubated with pelargonidin-3-monoglucoside, hydrolysis of the glucoside was followed by a spontaneous decomposition of the aglucone nucleus. Both glucosidase and galactosidase activities were detected.

The following compounds were isolated from the flowers: kaempferol, quercetin and 1,4-naphthoquinone derivatives (Ishiguro and Oku 1997); a kaempferol 3-rhamnosyldiglucoside, isolated from white petals of and its structure determined as kaempferol-3-*O*-[2″-*O*-α-l-rhamnopyranosyl-3″ *O*-β-D-glucopyranosyl]-*P*-D-glucopyranoside (Fukumoto et al. 1994); kaempferol 3-rutinoside and 2-hydroxy-1,4-naphthoquinone (lawsone) (Oku and Ishiguro 2001); sodium 3-hydroxide-2[[sodium 3-hydroxide-1,4-dioxo(2-naphthyl)] ethyl]naphthalene-1,4-dione (impatienolate) and sodium 2-hydroxide-3-(2-hydroxyethyl)naphthalene-1,4-dione (balsaminolate) (Oku and Ishiguro 2002); kaempferol and its derivatives kaempferol-3-glucoside, kaempferol-3-glucosylrhamnoside and kaempferol-3-(*p*-coumaroyl)glucoside (Hua et al. 2001); and kaempferol and quercetin (Lim et al. 2007).

Fruit/Seed Phytochemicals

Five novel baccharane glycosides, hosenkosides A–E, were isolated from the seeds (Shoji et al. 1994a). Hosenkol A was the genin of hosenkosides

A and D, and hosenkol B was the genin of hosenkosides B and E. Hosenkol C, the genin of hosenkoside C, was determined as (3*S*,4*R*,17*R*, 20*S*,24*Z*)-3,17,21,26,28-pentahydroxybaccharan-24-ene. Another four rare baccharane glycosides, hosenkosides L–*O*, were isolated and their structures elucidated as hosenkoside L as hosenkol A 3-*O*-sambubiosyl-28-*O*-glucoside, hosenkoside M as hosenkol as 3-*O*-sambubiosyl-26-*O*-glucosyl-28-*O*-glucoside, hosenkoside N as hosenkol C 3-*O*-glucosyl-28-*O*-glucoside and hosenkoside *O* as hosenkol D 3-*O*-sophorosyl-28-*O*-glucoside (Shoji et al. 1994c). Another six baccharane glycosides were isolated: hosenkoside F (hosenkol 3-*O*-sambubiosido-26-*O*-glucoside), hosenkoside H (hosenkol B 3-*O*-sambubioside), hosenkoside I (hosenkol 3,26-*O*-diglucoside), hosenkoside G (hosenkol C 3-*O*-sambubiosido-28-*O*-glucoside), hosenkosides J (hosenkol A 3-*O*-sophoroside) and hosenkoside K (hosenkol 3-*O*-sophorosido-26-*O*-glucosyl-28-*O*-glucoside) (Shoji et al. 1994b).

Dinaphthofuran-7,12-dione derivatives, named balsaminones A and B, and 2-methoxy-1,4-naphthoquinone were isolated from the pericarp (Ishiguro et al. 1998). A high molecular weight protein has been isolated as a major polypeptide comprising 85 % of the total extractable proteins in balsam fruit pericarp (Pal and Biswas 1994). This protein appeared to be a homo-tetramer consisting of subunits, Mr 75 K. Four closely related highly basic, antimicrobial peptides of 20 amino acids long, containing four cysteine residues forming two intramolecular disulfide bonds, designated Ib-AMP1, Ib-AMP2, Ib-AMP3 and Ib-AMP4 (Tailor et al. 1997) and Ib-AMP1 and Ib-AMP4 peptides, were isolated from the seeds (Thevissen eYIb-AMP1, a highly basic, 20-residue peptide was found to have five arginine residues and to contain four cysteines forming two intramolecular disulfide bonds (Patel et al. 1998). Two new flavone glycosides isolated from the seeds were determined as quercetin-3-*O*-[α-L-rhamnose-(1 → 2)-β-D-glucopyranosyl]-5-*O*-β-D-glucopyranoside and quercetin-3-*O*-[(6‴-*O*-caffeoyl)-α-l-rhamnose-(1 → 2)-β-D-glucopyranosyl]-5-*O*-β-D-glucopyranoside (Lei et al. 2010). 2-Methoxy-1,4-naphthoquinone (MeONQ) abounds in the *I. balsamina* pod at the level of 4.39 % (w/w db) (Wang et al. 2011). Eight major baccharane glycosides, namely, hosenkosides A, B, C, F, G, K, L and M, were isolated from the seeds (Li et al. 2011).

The major fatty acids of *I. balsamina* seed oil reported included 4.7 % palmitic acid, 5.8 % stearic acid, 2.8 % arachidic acid, 18.3 % oleic acid, 9.2 % linoleic acid, 30.1 % linolenic acid and 29.1 % α-parinaric acid (9c, 11t,13t,15c-octadecatetraenoic acid) (Gunstone 1996).

Leaf Phytochemicals

2-Methoxy-1,4-naphthoquinone (Ding et al. 2008), lawsone, lawsone methyl ether and methylene-3,3′-bilawsone (Sakunphueak and Panichayupakaranant 2010b, 2012) were isolated from the leaves.

Stem Phytochemicals

Two new tetrahydronaphthalenes, 1α, 2α-diol-4α-ethoxy-1, 2, 3, 4-tetrahydronaphthalene (1) and 1α, 2α, 4β-triol-1, 2, 3, 4-tetrahydronaphthalene (2), were isolated from the stem (Chen et al. 2010).

Root Phytochemicals

A natural bisnaphthoquinone, methylene-3,3′-bilawsone, two naphthoquinones (lawsone and 2-methoxy-1,4-naphthoquinone), two coumarin derivatives (scopoletin and isofraxidin) and a sterol (spinasterol) were isolated from balsam roots (Panjchayupakaranant et al. 1995). A biscoumarin, 4,4′-biisofraxidin, was isolated from balsam root cultures (Panichayupakaranant et al. 1998). Different elicitors, namely, yeast extract, *Candida albicans* homogenate, *Trichophyton rubrum* homogenate, chitosan, and methyl jasmonate (MJ), depending on concentrations used exerted differential effects on the production of the three main naphthoquinones, lawsone (2-hydroxy-1,4-naphthoquinone), lawsone methyl ether and methylene-3,3′-bilawsone in balsam root cultures

(Sakunphueak and Panichayupakaranant 2010a). Treatment with MJ (400 μM) was capable of increasing production of lawsone and lawsone methyl ether up to 8.6- and 11.3-fold higher, respectively, compared to the level in untreated cultures. Treatment of 21-day-old root cultures with 300 μM MJ for 36 hours resulted in the production of 10.0, 0.78 and 0.23 mg/g DW of lawsone, its methyl ether and methylene-3,3′-bilawsone, respectively. Such levels were sufficient for commercial production. These compounds were found to possess various pharmacological activities that had been shown to assist with the treatment of skin diseases.

Optimization of the feeding conditions showed that adding 500 mg/l methionine to a 21-day-old balsam root cultures increased production of lawsone methyl ether and 3,3′-methylenebislawsone up to 2.6- and 3.1-fold higher, respectively, compared to the controls (Sakunphueak et al. 2013). In addition to lawsone, lawsone methyl ether and 3,3′-methylelnebislawsone, various pharmacologically interesting secondary metabolites were isolated such as a flavonoid, luteolin; a naphthoquinone, 2,3-dihydroxy-1,4-naphthoquinone; and a triterpenoid, echinocystic acid.

Plant/Cell Culture Phytochemicals

2-Hydroxy-1,4-naphthoquinone was isolated from the aerial plant parts (Glennie and Bohm 1965). Shikimic acid was shown to be an excellent precursor of 2-hydroxy-1,4-naphthoquinone in *I. balsamina* aerial parts (Chen and Bohm 1966). p-Hydroxybenzoic acid was also found to be a precursor of 2-hydroxy 1,4-naphthoquinone balsam (Bohm 1967). A bisnaphthoquinone derivative named impatienol, 3-hydroxy-2-{[3-hydroxy-1,4-dioxo (2-naphthyl)] ethyl} naphthalene-1, 4-dione from aerial parts (Ishiguro et al. 2000), and 2-methoxy-naphthalene-1,4-dione were isolated from balsam plants (Jin et al. 2011). The cell culture-derived parent plants yielding high levels of 2-methoxy-1,4-naphthoquinone as initiated explants were found capable of producing two naphthoquinones, lawsone and an unknown, which was more polar than lawsone (Panichayupakaranant 2001).

Some of the published pharmacological properties of the plant are elaborated below.

Antioxidant Activity

Studies revealed that the different balsam flower extracts exhibited antioxidant activity, with the water extract showing the strongest activity (Hu et al. 2007). The antioxidant capacity of balsam flower extract (per 100 g) was equivalent to the antioxidant capacity of vitamin C 2.3 g, quercetin 0.76 g and rutin 0.02 g, respectively. All balsam stem extracts possessed moderate antioxidant potential in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging and reducing power assays (Su et al. 2012). The total phenolic and flavonoid contents ranged from 2.88 to 13.63 mg gallic acid equivalents/g dried extract and 0.98 to 7.87 mg quercetin equivalents/g dried extract, respectively.

Anticancer Activity

A pilot study demonstrated that ethanol or chloroform leaf extracts had in-vitro antitumour activity against the HepG2 human hepatocellular carcinoma cell line (Ding et al. 2008). The MTT assay showed that only the chloroform CHE2 fraction had a strong tumour inhibition ratio (IC_{50} = 6.47 mg/l), which was superior to that of curcumin (IC_{50} = 13.95 mg/l). The active component of the fraction was identified as 2-methoxy-1,4-naphthoquinone which exerted potent in-vitro antitumour activity against HepG2 cells.

2-Methoxy-1,4-naphthoquinone (MeONQ) from *Impatiens balsamina* exhibited high ability to induce gastric adenocarcinoma necrosis, showing good potential as a candidate agent for *Helicobacter pylori* infection-related disease therapy (Wang and Lin 2012). MeONQ resulted in serious necrosis via superoxide anion catastrophe when the treatment doses were higher than 50 μM, whereas apoptosis occurred at low treatment doses (25–50 μM) through the caspase-dependent

apoptosis pathway. Necrosis was the dominant mode of adenocarcinoma cell death.

Antimicrobial Activity

The naphthoquinone, 2-methoxy-1,4-naphthoquinone exhibited antimicrobial activity (Kang and Moon 1992). A bioactive antimicrobial compound (LC_{50} = 26 ppm) isolated from the 95 % ethanol extract of the dried aerial parts of *Impatiens balsamina* was identified as 2-methoxy-1,4-naphthoquinone (MNQ) (Yang et al. 2001). Five Gram-positive and two Gram-negative bacteria as well as all eight fungi (including multidrug-resistant strains) tested were highly sensitive to MNQ. A tea prepared according to traditional methods was found to contain sufficient MNQ to account for its antimicrobial properties. All balsam stem extracts showed good antimicrobial activity especially antifungal activity against all of the tested microorganisms (Su et al. 2012).

A set of related antimicrobial peptides (Ib-AMPs) was isolated from *I. balsamina* seeds (Thevissen et al. 2005; Tailor et al. 1997; Patel et al. 1998). Native Ib-AMPs showed no haemolytic nor toxic activity up to a concentration of 100 μM, demonstrating the potential of the native Ib-AMPs to combat fungal infections. Kaempferol and quercetin from balsam flowers were found to have antibacterial activity against an acne-inducing agent, *Propionibacterium acnes* (Lim et al. 2007). Minimum inhibitory concentrations (MICs) for both compounds were ≤32 and ≤64 μg/ml for clindamycin-sensitive and clindamycin-resistant *P. acnes*, respectively. The four combination formulations (kaempferol and either erythromycin or clindamycin; quercetin and either erythromycin or clindamycin) exhibited a synergic inhibition of *P. acnes* growth. The combination of kaempferol with quercetin showed an indifferent effect. The combination of clindamycin with kaempferol or quercetin showed a greater synergic effect than that of erythromycin with kaempferol or quercetin.

All parts (root/stem/leaf, seed and pod) of *I. balsamina* extracts exhibited bactericidal activity against multiple antibiotic-resistant *Helicobacter pylori* (Wang et al. 2009). Specifically, the pod extract had significantly lower MICs and MBCs (1.25–2.5 and 1.25–5.0 μg/ml, respectively). Of the five pod-extraction solvents, both ethyl acetate and acetone were the most efficient for the anti-*H. pylori* compounds of the pod extraction. This activity exceeded that of metronidazole and approximated to that of amoxicillin. 2-Methoxy-1,4-naphthoquinone (MeONQ) and stigmasta-7,22-diene-3β-ol (spinasterol) isolated from the pods and roots/stems/leaves of *I. balsamina*, respectively, exhibited anti-*H. pylori* (Wang et al. 2011). The minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) for MeONQ were in the ranges of 0.156–0.625 and 0.313–0.625 μg/ml, respectively, and in the ranges of 20–80 μg/m both of MICs and MBCs for spinasterol against antibiotic (clarithromycin, metronidazole and levofloxacin)-resistant *Helicobacter pylori*. Notably, the potent activity of MeONQ was equivalent to that of amoxicillin (AMX) and its action was dose dependent. The ethanol and rectified spirit balsam seed extracts showed promising antibacterial activity against the growth of bacteria species *Escherichia coli* and *Bacillus anthracis*, whereas the ethanol and petroleum ether extracts showed better results against the fungal growth of *Aspergillus niger* and *Fusarium* sp. (Jain 2011).

Among the naphthoquinones isolated from balsam leaves, lawsone methyl ether showed the highest antimicrobial activity (Sakunphueak and Panichayupakaranant 2012). It showed antifungal activity against dermatophyte fungi and *Candida albicans* with the MICs and MFCs in the ranges of 3.9–23.4 and 7.8–23.4 μg/ml, respectively, and also had some antibacterial activity against aerobic, facultative anaerobic and anaerobic bacteria with MICs in the range of 23.4–93.8, 31.2–62.5 and 125 μg/ml, respectively. Lawsone showed only moderate antimicrobial activity against dermatophytes (MICs and MFCs in the ranges of 62.5–250 and 125–250 μg/ml, respectively), but had low potency against aerobic bacteria, and was not active against *C. albicans* and facultative anaerobic bacteria. In contrast, methylene-3,3′-bilawsone showed significant antimicrobial activity only against *Staphylococcus*

epidermidis and *Bacillus subtilis* (MIC and MBC of 46.9 and 93.8 μg/ml, respectively).

Antianaphylactic Activity

Ethanol extract (35 %) of *I. balsamina* white petals was found to exhibit significant antianaphylactic activity in the murine immediate hypersensitivity reaction system induced by hen egg-white lysozyme (Ishiguro et al. 1992). A 35 % ethanol petal extract from *Impatiens balsamina* was found inhibitory against platelet-activating factor (PAF)-induced hypotension (Oku and Ishiguro 1999). One mechanism of the antianaphylactic effects of *Impatiens balsamina* was characterized as PAF-antagonist effects. The 35 % ethanol petal extract exhibited antianaphylactic effect by preventing hen egg-white lysozyme (HEL)-induced decrease in blood flow in mice (Ishiguro et al. 2002). Its active components, kaempferol 3-rutinoside and lawsone also significantly inhibited the decrease of blood flow. They also found that platelet-activating factor (PAF) and serotonin participated in decreasing the blood flow, but histamine did not.

Analgesic/Antiinflammatory Activities

Significant selective cyclooxygenase-2 (COX-2) inhibitory activities were observed for two new 1,4-naphthoquinone sodium salts; sodium 3-hydroxide-2[[sodium 3-hydroxide-1,4-dioxo (2-naphthyl)]ethyl]naphthalene-1,4-dione (impatienolate); and sodium 2-hydroxide-3-(2-hydroxyethyl)naphthalene-1,4-dione (balsaminolate), isolated from the corolla of *Impatiens balsamina* (Oku and Ishiguro 2002). The results supported the use of *I. balsamina* to treat articular rheumatism, pain and swelling.

WNT Signalling Inhibitory Activity

2-Methoxy-1,4-naphthoquinone from *I. balsamina* inhibited the TCF/β-catenin (TOP) transcriptional activity (IC_{50} 2.9 μM), while it decreased the transcriptional activity of FOP (mutated TCF-binding site)-transfected cells at >5 μM.

Antipruritic/Antidermatitic Activity

A 35 % ethanol petal extract significantly inhibited the scratching behaviour induced by Dextran T40 and compound 48/in mice (Ishiguro and Oku 1997). Kaempferol, quercetin and 1,4-naphthoquinone derivatives in the extract were demonstrated to show antipruritic effects. Dinaphthofuran-7,12-dione derivatives named balsaminones A and B and 2-methoxy-1,4-naphthoquinone isolated from the pericarp exhibited significant antipruritic activity (Ishiguro et al. 1998).

The 35 % ethanol petal extract at 100 mg/kg significantly inhibited serious scratching behaviour in the NC mouse with established dermatitis when administered i.v. 1 hour before or p.o. 24 hours before the measurement (Oku and Ishiguro 2001). A 10 μg/kg dose of kaempferol 3-rutinoside and 2-hydroxy-1,4-naphthoquinone (lawsone) isolated from the extract also inhibited scratching behaviour in the dermatitis NC mouse. When 4-week-old NC mice with no symptoms were administered orally 100 mg/kg/day of IB until 13 weeks of age, protection was also noted against scratching behaviour during the development of dermatitis. The results suggested the extract to be effective for the prevention and treatment of atopic dermatitis. 2-Hydroxy-3-(2-hydroxyethyl)-1,4-naphthoquinone; ferulic acid; 2,2′-methylenebis(3-hydroxy-1,4-naphthoquinone); and 2,2′-ethylidenebis(3-hydroxy-1,4-naphthoquinone) (impatienol) all exhibited significant antipruritic activity in 48/80-induced scratching behaviour in mice (Oku et al. 2002). However, 2-methoxy-3-(2-hydroxyethyl)-1,4-naphthoquinone (balsaquinone) did not show any activity. The results indicated these compounds to be promising for treating allergic diseases with chronic and severe pruritus.

Antinociceptive Activity

Methanol balsam flower extract demonstrated strong and dose-dependent antinociceptive activity in all the chemical- and heat-induced mice models (Imam et al. 2012). The use of naloxone confirmed the association of opioid receptors in the

central antinociceptive effect. The extract also exhibited significant central nervous system depressant effect.

Antityrosinase Activity

Kaempferol isolated from the methanol balsam flower extract exhibited inhibitory activity against mushroom tyrosinase with an ID_{50} of 0.042 mM (Lim et al. 2006). Kaempferol also strongly inhibited melanin production by *Streptomyces bikiniensis*, in a dose-dependent manner, without inhibiting cell growth.

Testosterone 5-Alpha-Reductase Inhibition Activity

A bisnaphthquione derivative named impatienol isolated from the aerial parts exhibited significant testosterone 5-alpha-reductase inhibitory activity (Ishiguro et al. 2000). It may have potential therapeutic use in male benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS).

Anthelmintic Activity

Balsam seed oil exhibited moderate anthelmintic activity against *Pheretima posthuma* in-vitro (Jalalpure et al. 2007).

Traditional Medicinal Uses

Impatiens balsamina has been used as an indigenous medicine in Asia for the treatment of rheumatism, fractures and fingernail inflammation (Wang et al. 2009). The plant is cathartic, diuretic and emetic and prescribed for treatment of pains in the joints (Chopra et al. 1986). In Korea, *Impatiens balsamina* has been used in traditional oriental medicine to treat scrofulosis, carbuncles, tuberculosis and dysentery (Kang and Moon 1992). The Korean folk medicine 'Bong Seon Wha Dae' (prepared from balsam stems) has been used to cure constipation and acute gastritis (Park et al. 2003). In China, all parts of the plant are for all sorts of foreign bodies, e.g., metal in the throat that had been inadvertently swallowed, as well as for thorns and splinters in the flesh, and the powdered seeds are used for difficult labour (Stuart 1979). The seeds are expectorant and also used for cancer treatment.

The flowers are mucilaginous and cooling and are employed for snakebites, lumbago and intercostal neuralgia (Duke and Ayensu 1985). The flowers, and their alcoholic extract, possess marked antibiotic activity against some pathogenic fungi and bacteria (Chopra et al. 1986). Flowers of the plant are used in folk medicine to treat lumbago, neuralgia, burns and scalds in Bangladesh (Imam et al. 2012). Juice obtained from white petals is applied topically for dermatitis and urticaria (Khare 2004).

In the Philippines, the leaves are pounded and used in poultices to dissolve felons (Guerrero 1921). In Malaysia, the leaves are used for poulticing broken and torn nails (Burkill 1966). In Brunei, root decoction is administered for irregular menstruation (Khare 2004).

Other Uses

The plant is widely cultivated as a garden ornamental. The flowers are used to prepare a red dye and used as a substitute for henna (*Lawsonia inermis*) for finger and toe nails and in cosmetics. The seed oil can be used for burning lamps and in the surface-coating industry. The leaves are used for dyeing.

Comments

Garden balsam is easily propagated from seeds.

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Impatiens walleriana

Scientific Name

***Impatiens walleriana* Hook.f.**

Synonyms

Impatiens episcopi H.J. Veitch, *Impatiens giorgii* De Wild., *Impatiens holstii* Engl. & Warb., *Impatiens lujai* De Wild., *Impatiens sultanii* Hook.f.

Family

Balsaminaceae

Common/English Names

Balsam, Bizzy-Lizzie, Busy Lizzy, Garden Impatiens, Impatiens, Japanese Balsam, Jewel Weed, Patience Plant, Patient Lucy, Shady Lady, Snapweed, Sultan's Balsam, Sultan's Flower, Sultana, Touch Me Not, Zanzibar Balsam

Vernacular Names

Brazil: Beijo De Frade
Chinese: Su Dan Feng Xian Hua
Czech: Netýkavka Turecká
Dutch: Juliaantje
East Africa: Sunguala (Chagga), Matuanange (Zanzibar)
French: Balsamine Sauvage
German: Fleissiges Lieschen
India: Khujuang Lei (Manipuri)
Samoan: Patiale
Spanish: Balsamina, Chico
Swedish: Flitiga Lisa
Thai: Dtôn Tian Fà-Ràng
Tongan: Polosomo
Vietnamese: Móng Tay Suitan

Origin/Distribution

The species is native to East Africa (i.e. south-eastern Kenya, Tanzania, southern Malawi, western Mozambique and eastern Zimbabwe). The species is widely cultivated as an ornamental in many parts of the world and has also become naturalized in many of these areas.

Agroecology

In its native range and countries where it has naturalized, it is found in coastal forest areas, riverine thickets, bushland, waterway margins, damp and shady places, and in riparian habitats. It has become a weed of roadsides, disturbed sites and waste areas in populated areas. It grows best in uniformly moist, organic rich, well-drained soils in partial to full shade. It is drought and frost intolerant.

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Edible Plant Parts and Uses

The flowers are edible and have a sweet taste (Anonymous 2012; Deane 2007–2012; Rop et al. 2012). They can be added to salads or mixed into fancy drinks.

Botany

A perennial or annual herb, simple or branched with succulent, translucent, green or reddish tinged, glabrous stem, slightly thickened and semi-woody at the base, 30–90 cm high. Leaves alternate, simple, glabrous broadly elliptic, or ovate to oblong-elliptic-13 cm long and 2.5–5.5 cm wide, with 5–8 pairs of lateral veins and 1–2 (sometimes more) extrafloral stipitate basal glands, apex acute or acuminate, base cuneate, margin crenate denticulate (Plates 1, 2, 3 and 4).

Plate 1 Pink flowered balsam

Plate 2 Purple flowered balsam

Flowers predominantly in pairs or threes in the axils of upper stem and branches, pedicels 2–4 cm with linear-lanceolate to subulate bracts. Lateral sepals 2, ovate-lanceolate or linear-lanceolate, green, small, 3–7 mm long. Lower sepal whitish, shallow, abruptly constricted into 2.5–4.5 cm long, curved, narrow spur. Petals 5, free, 3 cm across, various shades of pink, rose, orangey red, red, white, or variegated (Plates 1, 2, 3 and 4). Upper petal broadly obcordate or obovate and crested, lateral petals connate towards base. Ovary fusiform and glabrous. Fruit fusiform, 15–25×4–6 mm wide in the middle, glabrous, pale green capsule, dehiscing explosively to eject numerous small, brownish seeds.

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Impatiens walleriana* had a dry matter content (%w/w) of 14.75 %, crude protein of 4.60 g/kg

Plate 3 Red flowered reddish leaves balsam

Plate 4 Orange flowered green leaves balsam

and the following elements (mg/kg fresh mass (FM)): P 382.73 mg, K 2835.25 mg, Ca 405.62 mg, Mg 203.34 mg, Na 94.29 mg, Fe 7.26 mg, Mn 6.05 mg, Cu 1.31 mg, Zn 8.72 mg and Mo 0.39 mg. The flowers had total antioxidant capacity of 6.89 g ascorbic acid equivalents/kg FM, total phenolic content of 4.85 g gallic acid/kg FM and total flavonoid content of 1.93 g rutin/kg FM.

Traditional Medicinal Uses

Leaves and roots dried, pounded mixed with water, juice drank as abortifacient (Kokwaro 2009).

Other Uses

It is widely cultivated as an ornamental in masses in shady beds, borders and woodland gardens, as ground cover or edging along walks or paths in parks and gardens. It is also cultivated in containers, window boxes and hanging baskets as a house plant.

Comments

Busy Lizzie is readily propagated from seeds and stem cuttings.

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Begonia cucullata var. *cucullata*

Scientific Name

Begonia cucullata* Willd. var. *cucullata

Synonyms

Begonia cucullata var. *hookeri* (A.DC.) L.B.Sm. & Schub., *Begonia cucullifolia* Hassk., *Begonia dispar* Rchb., *Begonia hookeri* Sweet, *Begonia nervosa* Kunth (Inval.), *Begonia paludicola* C. DC., *Begonia sellowii* Klotzsch, *Begonia semperflorens* Hook. (illeg.), *Begonia semperflorens* Link & Otto, *Begonia semperflorens* Link & Otto var. hookeri (Sweet) A.DC., *Begonia semperflorens* f. *flavescens* C.DC., *Begonia semperflorens* var. *sellowii* (Klotzsch) C. DC., *Begonia setaria* Graham

Family

Begoniaceae

Common/English Names

Bedding Begonia, Begonia, Club Begonia, Clubed Begonia, Fibrous Begonia, Paraguayan Begonia, Perpetual Begonia, Semperflorens Begonia, Wax Begonia

Vernacular Names

Argentina: Flor Flor-de-nácar
Brazil: Azeda-do-brejo, Begônia-do-brejo, Erva-de-sapo
Czech: Kysala květnatá
French: bégonia, bégonia annuel, bégonia des jardins, bégonia d'interieur, bégonia semperflorens, coeur de Jélsus
German: Beetbegonie, Begonie, Eisbegonie, Eisblume, Gottesauge, Semperflorens-Begonie
Italian: begonia, begoniette
Paraguay: Agrial
Portuguese: azeda-do-brejo, azedinha, Azedinha do brejo, begônia, begônia-cerosa, begônia-de-jardim, Begônia-do-banhado, begônia-do-brejo, begônia-sempre-florida, erva-de-sapo
Spanish: begonia alta, begonia de cera, begonia perpetua, begonia vírgin, flor de nácar, semperflorens auténtica

Origin/Distribution

The species is native to South America—Argentina, Brazil, Paraguay, Peru and Uruguay (Golding 1982; Smith et al. 1986; Golding and Wasshausen 2002) It has naturalized elsewhere in the tropics and subtropics. In Hawaii and in La Réunion, where the species has naturalized, it has become invasive in natural and seminatural environments.

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Agroecology

The natural habitat of many begonias including this species consists of moist, cool forests and tropical rainforests from 0–1,000 m altitude in its native range. Elsewhere the species has naturalized in planted forests, ruderal/disturbed and urban areas. It is tolerant of hot and humid summers but is sensitive to low temperature below 12 °C, dying back in frost and resprouting from underground rootstocks in spring in subtemperate areas. It abhors water-logged conditions and is tolerant of short dry periods due to their thick and waxy leaves which help minimize water loss. The species does best in dappled shade but will grow in full sun or considerable shade but is less floriferous under the latter. Reddish-coloured or bronze-leaved varieties are more tolerant of full sun than green-leaved varieties. The species thrives best in moist, well-drained, acidic (pH 5.5–6.5) sandy loams or loamy soils rich in organic matter.

Edible Plant Parts and Uses

Begonia semperflorens (*B. cucullata*) and *Begonia elatior* have potential to be cultivated as edible flowers with an acceptable taste (Friedman et al. 2007). The fleshy leaves and flowers are edible raw or cooked and can have a slight bitter after taste (Laferriere 1990, 1992; Deane 2007–2012). Sauteed alligator meat with Begonia sauce represents a musty challenge to the palate. Chopped begonia petals are mixed into a food processor or mixer with soft cream cheese, strawberry, or other jelly or jam and some juice or liquid to prepare Begonia spread (Deane 2007–2012). In Paraguay the leaves of the *B. cucullata* are eaten fried or in soup or salads, while the sap is used to treat sore throats (Gonzfilez-Torres 1980).

Botany

A glabrous, caulescent, stoloniferous, monoecious herb, 30–80 cm high with green or reddish succulent stems. Leaves are alternate, simple, weakly asymmetric, broadly ovate with truncate, usually incurved base, 8–12 cm long by 6–9 cm wide, 6–7 palmately nerved, margin undulating or weakly crenate-serrate, reddish at times, glossy dark green adaxially, paler green abaxially; some varieties have bronzed, reddish, or variegated leaves (Plates 1, 2 and 3). Stipules oblong, 1.5–3 by 1.5–2.5 cm, persistent. Flowers are either staminate (male) or pistillate (female) occurring in few-flowered axillary cymes on 3–5 cm long peduncles, bracts, ovate and serrulate. Male flowers with four white, red, or pink tepals in decussate arrangement, outer tepals suborbicular 10–15 mm across, inner ones smaller and narrowly obovate 10–12 mm long by 6–8 mm wide, stamens yellow, free, numerous, filaments short, anthers linear. Female flowers 4–5; obovate tepals; white, red, or pink, styles 3; bifid; the stigmatic tissue linear; spiral; continuous; ovary inferior with three fused carpels; placentae bilamellate (Plates 1, 2, 3 and 4). Fruit a dehiscent capsule, unequally 3-winged, the largest deltoid. Seeds tiny and acute.

Plate 1 Cluster of pink Begonia flowers

Plate 2 Close view of pink Begonia flower and leaves

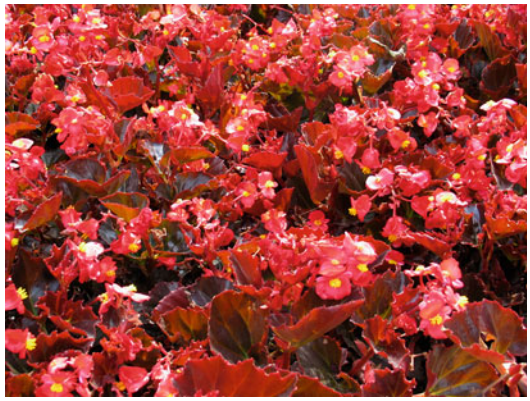

Plate 3 Red Begonia flowers and red leaves

Plate 4 Close-up of red begonia flower

Nutritive/Medicinal Properties

Seed Phytochemicals

The major storage substances in the tiny seed of *Begonia semperflorens* were found to be lipids sequestered in lipid vesicles and proteins in the form of protein crystalloids and electron-dense globoid crystals in protein bodies (West and Lott 1991). The globoid crystals contained high Mg, K and P levels characteristically found in phytin from large-sized seeds. Small traces of Ca were found in globoid crystals within protein bodies found in the provascular tissue of the embryo.

Flower Phytochemicals and Antioxidant Activity

Six anthocyanins, cyanidin *3-O*-(2″-xylosyl,6″-*trans* caffeoyl)-glucoside, *cis* and *trans* isomers of cyanidin 3-*O*-(2″-xylosyl,6″-*p*-coumaroyl)-glucoside and cyanidin 3-*O*-(2″-glucosyl,6″-*p*-*coumaroyl*)-glucoside were isolated from flowers of different horticultural *Begonia* (Chirol and Jay 1995).

Growing of *B. semperflorens* in a greenhouse was found to improve the flower yield as compared to netting house, but long-day treatment did not enhance further the yield in both growth habitats (Friedman et al. 2007). These results indicated *B. semperflorens* to be indifferent to long day, but *B. elatior* was highly sensitive. The antioxidant levels of closed and open flowers of *B. semperflorens* were not reduced during storage. However, the level of anthocyanins was reduced especially in the closed flowers. Antioxidant activity of opened *B. semperflorens* 'Imperial Red' flowers was determined as 11.1 μM Trolox equivalent/g DW, the anthocyanin content of the flower was 0.37 O.D./520 g DW and its acid content was 1.58 % citric acid equivalent. Antioxidant activity of closed flowers was 21.1 μM Trolox Equivalent/g DW, its anthocyanin content 0.35 O.D/520 g DW and its acid content 1.90 % citric acid equivalent.

Leaf Phytochemicals and Antioxidant Activity

Begonia cucullata was reported to contain 4.8 meq oxalate per gram dry weight, representing 96 % of the total acidity present in plant sap (Tavant and Mange 1965).

The maximum quantum yield of PSII (Fv/Fm) [photosystem II (Maximal fluorescence-minimal fluorescence/maximal fluorescence)] in red leaves (cv. Cocktail) was significantly higher than that in green leaves (cv. Super Olympia) during and after high-light stress (Zhang et al. 2010). High light also induced significant increases in anthocyanins in both genotypes. Before light stress exposure, red-leaved plants showed an average anthocyanin content 9.5-fold higher than that of 'Super Olympia' green-leaved plants. In contrast, high light induced a dramatic increase in anthocyanin content in 'Cocktail' plants, and anthocyanin content was 14-fold

higher in 'Cocktail' than in 'Super Olympia'. In red-leaved 'Cocktail' anthocyanin content increased from 55.1 U/g FW before light stress exposure to 290.4 U/g FW after 3-day light stress exposure. In green-leaved 'Super Olympia', anthocyanin content increased from 5.3 U/g FW before to 18.9 U/g FW after 3-day light stress exposure. After high-light stress, anthocyanins in 'Super Olympia' reverted to the initial level, whereas 'Cocktail' leaves retained most of their accumulated anthocyanins. The two genotypes had similar chlorophyll and carotenoid content before and after exposure to high light, whereas chlorophyll and carotenoids were lower in 'Cocktail' during exposure to high-light stress. The Chl a/b ratio of 'Cocktail' was not significantly different from that of 'Super Olympia' throughout the experiment, suggesting that there was no difference in light-harvesting capacity between the two genotypes.

There were no significant differences in flavonoid or phenolics content between the two genotypes either before or after high-light stress (Zhang et al. 2010). However, 'Cocktail' contained more flavonoids and phenolics than 'Super Olympia' under high-light stress. In red-leaved 'Cocktail', from zero-day light stress exposure to after 3-day light stress exposure, flavonoids increased from 3.06 mg/g FW to 8.66 mg/g and phenolics increased from 0.88 to 2.59 mg/g FW, respectively, while in green-leaved 'Super Olympia', flavonoids increased from 3.46 mg/g FW to 6.94 mg/g and phenolics increased from 1.0 to 1.93 mg/g FW, respectively.

High-light stress enhanced the pool size of the xanthophyll cycle (violaxanthin (v) + antheraxanthin (A) + zeaxanthin (Z)) in green-leaved plants, whereas no significant change in pool size was observed in red-leaved plants (Zhang et al. 2010). However, high light increased the de-epoxidation state of the xanthophylls cycle [(A + Z)/(V + A + Z)] in both cultivars.

Under high-light stress, DPPH antioxidant activity increased dramatically in 'Cocktail', which was maintained at a high level even after recovery (Zhang et al. 2010). However, DPPH antioxidant activity in 'Super Olympia' exhibited no obvious changes, and its level remained low throughout the experiment. The activities of superoxide dismutase and peroxidase were induced to similar level in both genotypes, while the activities of catalase, dehydroascorbate reductase and ascorbate peroxidase (APX) were significantly higher in 'Super Olympia' during light stress. After recovery, antioxidant enzyme activities gradually declined in both genotypes, despite the increased APX activity in 'Super Olympia'. The results indicated that 'Cocktail' had greater nonenzymatic antioxidant capacity, but lower overall enzymatic antioxidant activities in response to high-light stress. Overall, the results suggested that anthocyanins primarily functioned as photoprotective light filters rather than as antioxidant molecules during high-light stress in *B. semperflorens* and that red-leaved varieties afforded greater photoprotection than green-leaved varieties.

Traditional Medicinal Uses

B. cucullata has been reported to have analgesic, antiinflammatory, antimalarial, febrifuge, vulnerary and diuretic properties and used as herbal medicine for diarrhoea, dysentery, fever, inflammations, hiccups, malaria, sore throat, stomatosis, thirst, warts, wounds, sores, toothache and pharyngosis (Duke et al. 2009). The macerated plant is employed for fever, hiccup and thirst by the Guarani. Paraguayans apply mashed roots to toothache, apply juice on warts and moles, apply leaves on inflammation and wounds and charred plant parts on sores in mouth and throat. Most species have oxalic acid.

Other Uses

Wax begonia with single or double flowers in shades of white, pink, or red plus bicolour versions and green, reddish, or variegated foliage is an extremely popular garden annual grown for mass planting in beds, container, or baskets.

Comments

The plant is readily propagated from seeds, leaf and stem cuttings and root division. The rhizomes (thickened rootstock), tubers, and roots are poisonous.

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Begonia x tuberhybrida

Scientific Name

Begonia x tuberhybrida Voss

Synonyms

Begonia × *tuberhybrida* var. *grandiflora* Voss, Begonia Tuberhybrida Group, *Begonia tuberosea* hort

Family

Begoniaceae

Common/English Names

Hybrid Tuberous Begonia, Tuberous Begonia

Vernacular Names

French: Bégonia Tubéreux
German: Knollenbegonie
Spanish: Begonia Tuberosa
Swedish: Knölbegonia

Origin/Distribution

Begonia tuberhybrida is a complex group of cultivars developed from hybridization of several Andean species such as *B. boliviensis* with pink flowers or *B. pearcei* with yellow flowers (Dewitte et al. 2011; USDA, ARS 2012). Other parental Andean species used in hybridization include *Begonia veitchii* and *B. davisi.* Tuberous begonias are cultivated and not found wild.

Agroecology

Tuberous begonias thrive best in a mild cool summer climate and are totally intolerant of high temperatures or very high humidity levels or frost. The ideal conditions for tuberous begonias are areas where evening temperatures do not fall below 15 °C and where day temperatures are less than 27 °C (on average). They grow best in partial to dappled shade, in well-drained fertile loamy-acidic soil rich in humus. The plants need frequent watering and fertilization and need protection from strong winds. Container plants may be brought indoors in fall and grown as winter houseplants.

Edible Plant Parts and Uses

The fleshy leaves and flowers are edible (Laferriere 1990, 1992; Deane 2007–2012) raw or cooked and used in salads (Deane 2007–2012). Chopped begonia petals are mixed into a food processor or mixer with soft cream cheese, strawberry or other jelly or jam and some juice or liquid to prepare Begonia spread. The brightly coloured flowers have a delicious light, lemon taste and a crisp texture (Anonymous 2012).

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Snipped petals are used as a garnish in salads and sandwiches or whole petals dipped in flavoured yogurt and serve as an appetizer.

Botany

A large heterogeneous Begonia group with tuberous roots, complex and diversified because of crossing and backcrossing. Plants are small annual/perennial, tuberous herb growing to 30–45 cm high in a compact bushy habit with thick tuberous roots. Leaves alternate, 5–10 cm long, cordate to ovate with undulating or dentate margin, glossy green simple with lobed margin and pinnate venation with succulent green or reddish petioles (Plate 1). Flowers in few-flowered axillary cymes. Flower with male and female flowers on the same plant. Flowers small 1.5–2 cm to large, 5–7 cm, showy, waxy, roselike, single (4–5 tepals) or double flowers with multiples whorls of tepals of variable brightly colours of red, pink, purple, orange, yellow with ruffled-toothed or smooth margins (Plates 1 and 2).

Plate 1 Leaves and flowers

Nutritive/Medicinal Value

Six anthocyanins, cyanidin 3-*O*-(2″-xylosyl,6″-trans caffeoyl)-glucoside, *cis* and *trans* isomers of cyanidin 3-*O*-(2″-xylosyl,6″p-coumaroyl)-glucoside and cyanidin 3-*O*-(2″-glucosyl,6″-p-coumaroyl)-glucoside were isolated from flowers of different horticultural *Begonia* (Chirol and Jay 1995).

Studies showed that the content of chlorophyll a, chlorophyll b and carotene increased with 10, 40 and 50 Gy ^{60}Co-γ ray irradiation of *B. tuberhybrida* flowers (Ding et al. 2004). However, the content of chlorophyll a and carotene increased more with 50 Gy and chlorophyll b content increased more with 40 Gy. Co-γ ray irradiation of *Begonia tuberhybrida* improved SOD, CAT activities at higher dosages (40, 50 Gy). Higher dose increased malondialdehyde (MDA) content. Irradiation also increased the flavonoid, and the 20 and 10 Gy irradiation gave better effects.

Cucurbitane triterpenes: cucurbitacin B (Doskotch et al. 1968, 1969; Doskotch and Hufford 1970), cucurbitacin D, dihydrocurbitacin B and very small quantities of a degraded cucurbitacin compound and hexanor–cucurbitacin D were isolated from *B. tuberhybrida* tubers (Doskotch and Hufford 1970). Cucurbitacin B

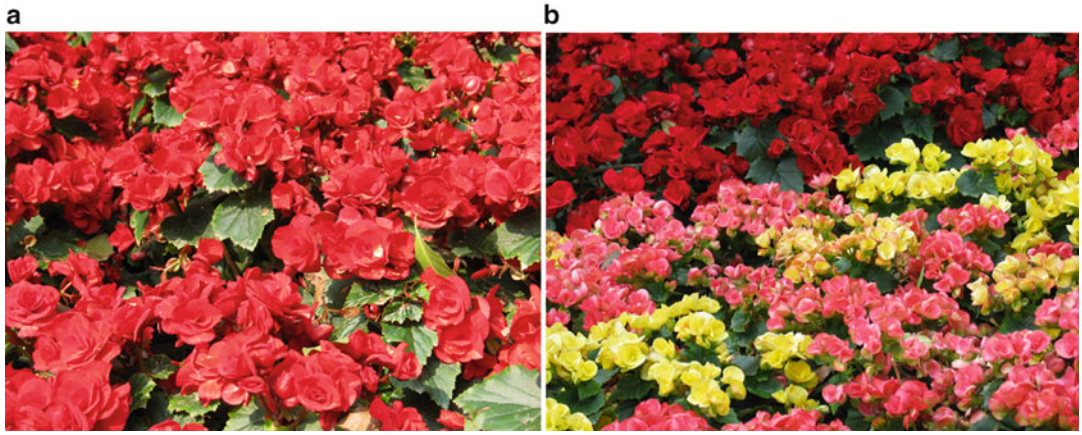

Plate 2 (**a**) and (**b**) Mass planting of different coloured tuberose Begonia

was found to have antitumour activity against human nasopharynx carcinoma (KB cells) in-vitro (Doskotch et al. 1968, 1969).

B. tuberhybrida was reported to have a crassulacean acid metabolism (CAM) and to contain with oxalic acid as the predominant acid, followed by malic, citric, and succinic acids, and phorbic acid was present in small amounts (Nordal and Resser 1966).

Other Uses

Begonia x tuberhybrida is a very popular and attractive ornamental plant for pots, baskets, containers or window boxes, flower beds, borders and houseplant.

Comments

Hybrids are arranged into 13 different groups based upon the floral structure and habit (Perry 2012):

(S) Single—large single flowers with flat tepals

(S-Fr)—large single flowers, tepal margins frilled or ruffled

(S-Cr)—large single flowers, frilled or tufted centre of tepals

(D-N)—large, double flowers, like Narcissus, central tepals forming a trumpet

(D-C)—large, double flowers, like camellia, unruffled edge

(D-CR)—large, double flowers, like camellia, ruffled edge

(D-R)—large double flowers with rose bud-like centre

(D-Car)—large double carnation-like flowers, tepals fringed on margins

(D-P)—large usually double flowers like camellias, picotee, tepals with different colours on margin blending with other colours

(D-M)—like picotee only distinct non-blending line of colour on margins

(D-Mar)—like camellia but rose coloured, blotched or spotted with white

(S-D-HB)—single or double pendant flowers with trailing/cascading stems, hanging basket

(S-D-Mul)—bushy compact multiflora, with single and double flowers

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Spathodea campanulata

Scientific Name

***Spathodea campanulata* P. Beauv.**

Synonyms

Bignonia tulipifera Schum., *Bignonia tulipifera* Thonn., *Spathodea campanulata* subsp. *congolana* Bidgood, *Spathodea danckelmaniana* Büttner, *Spathodea nilotica* Seem., *Spathodea nilotica* f. *bryanii* O. Deg. & I. Deg., *Spathodea tulipifera* (Schum.) G. Don

Family

Bignoniaceae

Common/English Names

African Flame Tree, African Tulip Tree, African Tuliptree, African-Tuliptree, Fireball, Firebell, Fire Tree, Flame of the Forest, Flame-of-the-Forest, Flame Tree, Fountain Tree, Indian Cedar, Nandi Flame, Nile Flame, Pichkari, Nandi Flame, St. Dominic's Mahogany, Santo Domingo Mahogany, Scarlet Bell Tree, Squirt Tree, Tuliptree, Ugandan Flame

Vernacular Names

Afrikaans: Afrikaanse Vlamboom, Vlamboom
Benin: Adada, Vikissè (Fon, Goun), Tulipier Du Gabon (French), Orourou (Yoruba)
Brazil: Bisnagueira, Espatódea, Tulipeira-Da-África
Burmese: A-Hpa.Ri.Ka. Kyu:Lis
Cameroon: Evovone (Ewondo), Bamileke (Mafou)
Carolinian: Apär
Columbia: Tulipán Africano
Cook Islands: Kō'Ī'Ī, Kō'Ī'Ī, Mata Kō'Ī'Ī, Mimi, Patiti Vai, Pātītī Vai, Pititi Vai (Maori)
Cote D'ivoire: Boro (Abe), Kokomayur (Abure), Asrélé (Agni), Sinséré (Akan-Asante), Kotchu, Sé (Aye), Asrélé (Anyi), Biébié, Biébié Biébié, Biébié Sirili, Diébéserélé (Baoulé), Vovo (Gagu), Pautu, Zabré, Zéblé Zébré (Guere), Zéblé Zébré, Zibli (Kru-Bété), Gbagbihia (Kyama), Missiboiri, Tiéré (Manding- Dioula), Kokwè (Maninka), Assien (Senufo-Tagwana, Tagouana), Zéblé Zébré (Shien)
Cuba: Espatodea
Danish: Afrikansk Tulipantræ
Democratic Republic Of Congo: Tulipier Du Gabon (French), Mbika (Kiboa), Zowa-Zowa (Kikongo), Aro (Kilur), Rruu (Kilendu), Mbina (Kinande), Igifuratura (Kinyarwanda), Isalasala (Kirega), Bobo (Kiyanzi), Oteko

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(Lokele), Langalanga (Mashi), Oteko (Turumbu), Kuon-Kusu

Dominican Republic: Amapola, Mampolo

Dutch West Indies: Tulpenboom

Eastonian: Kellukspatoodea

Esperanto: Spatodeo

Fijian: Taga Mimi

French: Arbre-Flamme, Baton Du Sorcier, Immortel Éntranger, Pissat De Singe, Pisse L'eau, Pisse-Pisse, Tulipeira-Do-Gabão, Tulipier Du Gabon

Gabon: Tsogolo (Apindji), Asuba, Akondo-Kondo (Bakèlè), Mutsongo (Banzabi), Muntsogu (Bavarama, Bavungu, Eshira), Mutsongo, Mutsotsogu (Bapunu), Muyayaga (Bavili), Éhuba (Benga), Isubo (Béséki), Évung-Vunghe, Évunghele-Vunghele (Fang), Ntsogo (Galoa, Mpongwè, Nkomi, Orungu), Tsogo (Ivéa, Ngowé), Nyinga (Loango), Mulèlè, Mulèlè-Kusu (Masango), Ndjobi-Likoto (Mindumu), Égombé (Mitsogo)

Gambia: Sukunde (Fula-Pulaar), Sula-Selo (Manding-Mandinka)

German: Afrikanischer Tulpenbaum, Spathodea, Telpenbaum

Ghana: Edumanki, Vot ʃO (Adangme), Akuakuo Ninsuo, Akuɔkɔ, Kɔkɔ-Anidua (Akan-Asante), Kookoo Nisua, Kuokuonesuo (Asante-Twi), Biebie (Baule), Adadase, Adatsigo (Gbe-Vhe), Osisiri (Kwawu), Abeni (Senufo-Tagwana), Akuakuaninsu, Akuakuo-Ninsuo, O-Sisiriw (Twi), Osisiri (Wasa)

Guinea: Diapélédé, Sukunde (Fula-Pulaar), Tunda (Manding-Maninka)

Guinea-Bissau: Pikeriko, Piquério (Balanta), Cafauano, Culassaque, Sekunde, Suncúndè (Fula-Pulaar), Sula-Selô (Mandémg-Mandinka), Teme (Pepel)

Haiti: Immortel Éntranger (French)

India: Rudra Palash (Bengali), Pichkari, Rugtoora (Hindi), Lujjekaye, Neerukaye, Ucche Kaayi (Kannada), Pichkari (Marathi), Patadi (Tamil), Patade, Patadiya (Telugu)

Indonesia: Kecrutan, Ki Engsrot, Sepatu Diat

Kenya: Sebetaiyat

Laotian: Khae Daeng

Luganda: Kifabakazi

Malaysia: Pancut-Pancut

Mexico: Flamboyán, Galeana

Nigeria: Kenshie (Bokyi), Ókuèkuè, Ókwèkwè (Edo), Èsèńnīm (Efik), Ekok (Ejagham), Akpoti, Ímí Éwū, Ogbolo Ḿmìrì, Oruru, Ugwogo (Igbo), Okiníkene (Mbembe), E-Nko Nebang (Mungaka), Mójútòrò, Orórù (Yoruba)

Palauan: Orsachel Kui

Pohnpeian: Dulip En Aprika, Tuhke Dulip

Polish: Tulipanowiec Afrykański

Polynesia: Pisse L'Eau

Popular Republic Of Congo: Voulou (Akwa), Ontsountsoko (Koukouya), Tulipier Du Gabonn (French)

Portuguese: Bisnagueira, Espatódea, Tulipeira-Da-África

Puerto Rico: Meaito

Samoan: Fa'Apasi, Tulipe

Senegal: Blalo (Balanta), Sisal (Banyun), A-Tyilil (Konyagi), Mam (Serer), Fèr, Fèhr, Tidômô (Wolofé)

Sierra Leone: Dumɛntili, Dundunturi (Manding-Maninka), Baine, Gobane, Gele-Gɔ, Ngele Gɔwɔ, Tombo-Lɛmbi, Tombo, Lɛmbi (Mende), A-Leop-A-Ro-Bath (Temne)

Spanish: Espatodea, Amapola, Mampolo, Tulipán Africano, Árbol De La Fontana, Llama-Del-Bosque, Llama Nandi, Árbol De La Fontana, Llama-Del-Bosque, Llama Nandi, Árbol De La Fontana, Llama-Del-Bosque, Llama Nandi, Tulipan Africano, Tulipán De África, Tulipero Del Gabón

Sri Lanka: Kudulu, Kudaella Gaha (Sinhalese)

Swahili: Kifabazakazi, Kibobakasi

Swedish: Afrikanskt Tulpanträd

Thai: Khae-Saed

Togo: Dudu (Fon), Dadassé, Datsigolo, Adatsigolo (Ewé), Tulipier Du Gabon (French), Adadase (Gbe-Vhe), Gbetachi-Gbetschi (Yoruba-Ife)

Tongan: Tiulipe

Tongarevan: Tiale Akapisipisi, Tiare Akapisipisi

Uganda: Munyalisha

Vietnamese: Chuông Đỏ, Hồng Kỳ, Sò Đo Cam

Venezuela: Caoba De Santo, Gallito, Tulipán Africano

West Cameroons: Bwèle Ba Mbonjì (Duala), Mbako (Kpe), Etoto, Etutu (Kundu)

Yapese: Ramingobchey

Origin/Distribution

African Tulip Tree is native of West and Central Africa and western East Africa: Angola, Ethiopia, Democratic Republic of Congo, Ghana, Kenya, Sudan, Tanzania, Uganda and Zambia. It is planted as an ornamental elsewhere in Africa, e.g. in Cape Verde, Zimbabwe and Madagascar. African Tulip Tree is widely grown in tropical and subtropical regions outside Africa. It has become naturalized and is an important component of secondary vegetation, e.g. in Mexico and Puerto Rico, and is considered a weed in Guam and Hawaii.

Agroecology

In its native range in Africa, the species occurs naturally in secondary forests in the high forest zone; in riverine forests; in deciduous, transition and savannah forests from sea level to 2,000 m altitude; and in areas receiving 1,300–2,000 mm annual precipitation and with mean annual temperatures of 27–30 °C. The biggest trees grow in moist, sheltered ravines. The species thrives in full sun and is frost and shade intolerant. It prefers rich, moist, well-drained loamy, sandy soils but will grow in poor infertile soils including clayey soils and limerock. It is adaptable in soils of a wide pH range of 4.5–8.

Edible Plant Parts and Uses

In Thailand the flowers are eaten (Wetwitayaklung et al. 2008). Young leaves used in soups by Igbo in Nigeria (Okeke et al. 2009). The seeds are also eaten in many parts of Africa.

Botany

A medium-sized deciduous perennial tree, reaching a height of 10–25 (–35 m), with a round, compact crown of dense, dark-green foliage, with stout, buttressed trunk, thick lenticellate branches;

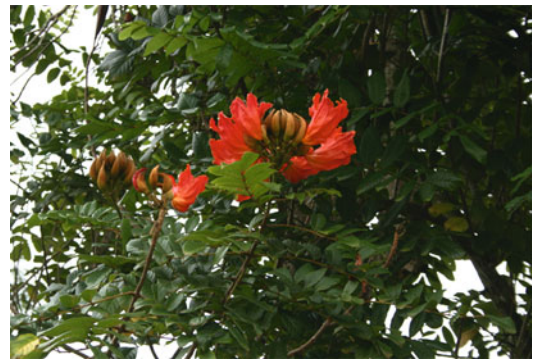

Plate 1 African Tulip flowers

Plate 2 Imparipinnate leaves

young bark pale, grey-brown and smooth turning grey-black, scaly and fissured vertically and horizontally with age. Leaves opposite, exstipulate and imparipinnate (Plates 1 and 2). Each leaf comprising 5–7 pairs of opposite leaflets and a terminal one, petioles 7–15 cm long. Leaflet elliptical to ovate or ovate-oblong, (3–)7–16 cm by (1.5–)3–7 cm, entire margin, base asymmetrically truncate to cuneate, apex acuminate or acute, glabrous to pubescent below, with (6–)8–11 pairs of lateral veins, dark green adaxially and light green abaxially, on 5 mm long petiolule. Inflorescence a terminal corymb-like raceme. Flowers hermaphrodite, zygomorphic, large and showy; pedicel up to 6 cm long; calyx spathaceous, 4–8 cm long, recurved, long-acuminate, ribbed, tomentellous, green, splitting at anthesis; corolla widely campanulate from a contracted base, 8–15 cm long, 5-lobed, lobes obtuse with strongly crispate margins, scarlet or orange-red with yellow margin and throat; stamens 4 with

yellow filaments, inserted on corolla tube, didynamous, more or less exserted, anthers linear, dark brown; ovary superior, 2-celled, style filiform, yellow, slender, stigma 2-lamellate, reddish (Plate 1). Fruit a narrowly ellipsoidal woody capsule 15–27 cm by 3.5–7 cm, blackish-brown, dehiscing by two valves, many-seeded. Seeds thin and flat, 1.5 cm by 2 cm, very broadly winged.

Nutritive/Medicinal Properties

Flower/Fruit Phytochemicals

The following phytochemicals were obtained from the petroleum ether extracts of the flowers: hexadecanoic acid, methyl ester (13.42 %), tricosane (9.64 %), n-heneicosane (13.57 %), bis(2-ethylhexyl) phthalate (22.50 %), 1,2-benzenedicarboxylic acid, oleic acid (19.58 %), diisooctyl ester (14.71 %) and levodopa (18.49 %) (Zaheer et al. 2011). From the methanol extract of the flowers, the following compounds were identified: 4,8-methanoazulen-9-ol, decahydro-2,24,8-tetramethyl-, stereoisomer (77.31 %) and thujopsene (22.69 %). The flowers also contained verminoside and specioside and the fruits caffeic acid and ajugol (Elusiyan et al. 2011). The flowers were also found to contain phenols and flavonoids (Wetwitayaklung et al. 2008; Hareesh et al. 2010) and anthocyanins (Banerjee and De 2001). Four compounds were identified from the flowers: butane 1, 1-diethoxy-3-methyl- (35.11 %) and n-hexadecanoic acid (30.22 %), 1,2-benzenedicarboxylic acid, diisooctyl ester (21.78 %) and oleic acid (12.89 %) (Kumaresan et al. 2011).

Leaf Nutrients and Phytochemicals

The nutrient composition of the young leaves (ulumiri) used as vegetables had been analysed by the Federal University of Technology, Akure, and the University of Nigeria as follows per 100 g edible portion: moisture 44 g, energy 212 kcal, protein 8.6 g, fat 0.3 g, carbohydrate 43.7 g, fibre 0.1 g, ash 2.6 g, vitamin A 28 μg RE, thiamin 1.3 mg, riboflavin 0.30 mg, niacin 1.12 mg, folic acid 44 μg, vitamin C 17.64 mg, Ca 13gmg, P 600 mg, Fe 9.7 mg and Zn 4.2 mg (CINE 2007).

Caffeic acid was isolated from the leaves (Subramanian et al. 1973). Spathodol, a new polyhydroxysterol with the structure (24S)-5α-stigmasta-7,25-diene-2α,3β-diol plus triterpenoids β-sitosterol, 3β-acetoxyoleanolic acid; siaresinolic acid; 3β-acetoxy-12-hydroxyoleanan-28, 13-olide; oleanolic acid and β-sitosterol-3-*O*-β-D-glycopyranoside were isolated from the dried leaves of *S. campanulata* (Ngouela et al. 1991). Phenolic compounds, namely, *p*-hydroxybenzoic acid and iridoid glucoside, were isolated from the leaves (El-Hela 2001a, b). Three new iridoids determined as 6-*O*-*trans*-caffeoyl-decinnamoyl globularimin, 6-*O*-*trans*-caffeoyl-asystasioside E and 6-*O*-*trans*-caffeoyl-5,7-bisdeoxycynanchoside and provisionally named as spatheosides A, B and C, respectively, were isolated from *S. campanulata* leaves (Gouda 2009). Also isolated were four known iridoids identified as verminoside, 6′-*O*-*trans*-caffeoyl-loganic acid, catalpol and ajugol. Leaves were reported to contain tannins, saponins, anthraquinone glycosides and flavonoids (Ilodigwe et al. 2010a, b). Elusiyan et al. (2011) reported the leaves to contain verminoside, kaempferol diglucoside, caffeic acid and phytol. Akharaiyi et al. (2012) reported the leaves to contain alkaloids, flavonoids, saponins, phenols, steroids and terpenoids.

The chloroform/ethyl acetate fraction of the alcoholic extract of *Spathodea campanulata* aerial parts afforded the isolation of phenolic acids, caffeic acid and ferulic acid; the fraction ethyl acetate/methanol on further fractionation afforded three flavonoids: kaempferol 3-*O*-glucoside, quercetin 3-methyl ether and 8-methoxy kaempferol 3-*O*-glucoside (Nazif 2007). The predominant components of the cuticular wax of *S. campanulata* leaves were n-alcohols (35 %), with octacosanol and triacontanol as the most abundant ones (Gormann et al. 2004). Other notable constituents were sterols, albeit present in trace amounts.

Stem/Root Phytochemicals

A pentacyclic triterpenoid acid, spathodic acid, with the structure 3β,19α,24-trihydroxyolean-12-ene-28-oic acid, and the sitosterol-3-*O*-β-D-glucopyranoside were isolated from the stem bark of *S. campanulata* (Ngouela et al. 1990). Three antimalarial principles were isolated from the stem bark: 3β-hydroxyurs-12-en-28-oic acid (ursolic acid) and two of its derivatives, 3β-hydroxyurs-12,19-dien-28-oic acid (tomentosolic acid) and 3β,20β-dihydroxyurs-12-en-28-oic acid (Amusan et al. 1996). Spathoside, a new cerebroside, was isolated from *Spathodea campanulata* stem bark, besides known compounds (n-alkanes, linear aliphatic alcohols, sitosterol and their esters, β-sitosterol-3-*O*-β-D-glucopyranoside, oleanolic acid, pomolic acid, *p*-hydroxybenzoic acid and phenylethanol esters) (Mbosso et al. 2008). The stem bark was also found to contain verminoside and ajugol (Elusiyan et al. 2011), flavonoids, terpenoids and phenols (Ngouela et al. 1988).

The stem bark of *S. campanulata* used as a drug in traditional medicine was found to contain the following nutraceutical (mg/kg): carbohydrates 1.36 mg, protein 0.32 mg, fats 0.03 mg and energy 5.69 kcal/g; and phytoconstituents (mg/kg), alkaloids 1.92 mg, flavonoids 2.50 mg, tannin 0.35 mg, lignin 0.29 mg, glycosides 0.05 mg, serpentines 0.05 mg, terpenoids 0.03 mg and saponins 0.01 mg and 0.12 mg (Brindha et al. 2012). The bark also contained the following elements: organic carbon 1.82 %, nitrogen 1.12 %, phosphorus 0.36 %, potassium 3.89 %, sodium 0.18 %, calcium 3.25 %, magnesium 2.56 %, sulphur 0.32 %, zinc 1.02 ppm, copper 0.11 ppm, iron 56.23 ppm, manganese 5.36 ppm, boron 0.08 ppm and molybdenum 0.03 ppm.

An iridoid glucoside, ajugol, and two phenolic derivatives (*p*-hydroxy-benzoic acid and methyl *p*-hydroxybenzoate) were isolated from the root bark (Pianaro et al. 2007).

Antioxidant Activity

The flower had a low TEAC (Trolox Equivalent Antioxidant Capacity) value of 0.07 and an IC_{50} value of 157.72 μg (Wetwitayaklung et al. 2008). The total polyphenol content in the flowers was 2.38 g/100 g dried flower and 6.38 g/100 g in the methanol crude flower extract. Recent studies by Hareesh et al. (2010) showed that *S. campanulata* flowers exhibited good free radical scavenging activity. At 500 μg/ml concentration, the ethanol flower extract exhibited about 82 % of lipid peroxidation inhibition and the IC_{50} value for the flower extract was 201 μg/ml. In the hydroxyl radical activity using the deoxyribose method, 500 μg/ml of the extract showed about 84 % inhibition and the IC_{50} value was 200 μg/ml. In the DPPH radical inhibition activity, the flower extract showed around 68 % at 500 μg/ml concentration and the IC_{50} value was 225 μg/ml.

Ethanol extract of *Spathodea campanulata* leaves showed significant dose-dependent antioxidant activity in-vitro (Kowti et al. 2010a). The extract showed an effective free radical scavenging activity towards the nitric oxide and superoxide radicals with IC_{50} values of 160 and 198 μg/ml, respectively. Total antioxidant capacity at 50 and 500 μg/ml of *Spathodea campanulata* extract was equivalent to 29.2 and 199.4 μg/ml of α-tocopherol. At 500 μg/ml, in nitric oxide radical and superoxide radical scavenging assay, it elicited maximum inhibition of 81 and 79 %, respectively.

The methanol extracts of *Commelina diffusa* herb and *Spathodea campanulata* bark reduced the peroxidation of bovine brain extract with an IC_{50} value of 1.39 and 0.24 mg/ml, respectively (Mensah et al. 2006). In addition the extracts also exhibited significant antioxidant activity by protecting MRC-5 cells from hydrogen peroxide-induced oxidant injury at concentrations between 1 and 10 μg/ml. The extracts showed no inhibition of NF-kappaB at 100 μg/ml.

Alcoholic extract of *Spathodea campanulata* aerial parts and two of the isolated fractions showed strong antioxidant activity (92, 94 and 89 % RSA, radical scavenging activity) (Nazif 2007). The antioxidant principles isolated from the various parts of *Spathodea campanulata* plant included verminoside (leaf, stem bark and flowers; $EC_{50} = 2.04$ μg/ml), specioside

(flowers; $EC_{50} = 17.44$ µg/ml), kaempferol diglucoside (leaf; $EC_{50} = 8.87$ µg/ml) and caffeic acid (leaf and fruits) (Elusiyan et al. 2011). The non-antioxidant components isolated in the study included ajugol (stem bark and fruits) and phytol (leaf).

Wound/Burn Healing

Topical applications of methanol *S. campanulata* bark extract ointment (2, 10 and 49 %) dose dependently decreased the score damage of the burn site in rats (Sy et al. 2005). Treatment with 10 and 49 % of the bark ointment reduced the score damage from 5 to 1 and 5 to 0.2, respectively, at day 15 after experimental burn. The bark ointment (10 and 49 %) induced a complete burn healing on the 19–20th post-burn day. The results supported the rational use of the *S. campanulata* barks in traditional medicine to promote burn healing.

For *Spathodea campanulata, Hoslundia opposita* and *Pycnanthus angolensis*, which were reported by the healers to be used also for wound healing, in the case of stomach ulcers, strong anti-adhesive activity against *Helicobacter pylori,* was demonstrated, while the extracts did not exhibit any direct cytotoxicity against the bacterium (Agyare et al. 2009).

Antimicrobial Activity

The methanol extracts of *Commelina diffusa* herb and *Spathodea campanulata* bark showed some level of antimicrobial activity with *C. diffusa* exhibiting selective antifungal activity against *Trichophyton* species (Mensah et al. 2006) and also antioxidant activity. Methanol extracts of *Tridax procumbens* and *Spathodea campanulata* showed significant activity against bovine mastitis bacterial pathogens coagulase-positive *Staphylococcus aureus* (8.0) and *Streptococcus agalactiae* (7.6), respectively (Das et al. 2009). The crude *S. campanulata* methanol extract was found to contain saponins, steroids, terpenoids, flavonoids, alkaloids and tannins.

The petroleum ether extract of *S. campanulata* leaf showed good inhibitory activity against *Klebsiella pneumoniae* and compared with standard antibiotic streptomycin (Dhanabalan et al. 2008). The methanol extract also showed inhibitory activity. Ethanol flower extract inhibited the in-vitro growth of *Proteus vulgarisms, Escherichia* coli and *Klebsiella pneumonia* but was less effective against *Staphylococcus aureus* and *Salmonella typhimurium* (Kowti et al. 2010b). The flower extract showed greater potency than the leaf extract. In another study, the crude ethanol extract of *S. campanulata* leaf potently inhibited growth of nine clinical bacteria isolates, namely, *Pseudomonas aeruginosa* (wound), *Serratia marcescens, Escherichia coli* (urine), *Staphylococcus aureus* (wound), *Klebsiella pneumoniae* (urine), *Bacillus cereus* (wound), *Proteus mirabilis* (faeces), *Salmonella typhi* (faeces) and *Enterococcus faecium* (faeces) (Akharaiyi et al. 2012). This was followed by the methanol extract and the petroleum ether extract was least inhibitory. The crude ethanol leaf extract contained alkaloids 1.5 %, flavonoids 0.56 mg/ml QE (quercetin equivalent), saponins (3.92 mg/ml), phenols 0.04 mg/ml TAE (tannic acid equivalent), steroids and terpenoids.

Two phenolic derivatives *p*-hydroxybenzoic acid and methyl *p*-hydroxybenzoate isolated from the roots exhibited antifungal activity against the fungus *Cladosporium herbarum* (Pianaro et al. 2007). Spathoside, a new cerebroside, and known compounds (n-alkanes, linear aliphatic alcohols, sitosterol and their esters, β-sitosterol-3-*O*-β-D-glucopyranoside, oleanolic acid, pomolic acid, *p*-hydroxybenzoic acid and phenylethanol esters) isolated from *Spathodea campanulata* stem bark, inhibited significantly the growth of some Gram-positive and Gram-negative bacteria (Mbosso et al. 2008).

Four topical products prepared by incorporating the methanol extract of *S. campanulata* stem bark (20 % w/w) into aqueous cream, soft paraffin, emulsifying ointment and simple ointment bases were evaluated for their in-vitro antimicrobial efficacy (Ofori-Kwakye et al. 2009). The methanol and ethanol extracts showed good activity while the aqueous and petroleum ether extracts

exhibited little activity. The methanol extract showed the best antibacterial activity. The MIC of the methanol extract was *Candida albicans* (45–50 mg/ml), Bacillus *subtilis* and *Escherichia coli* (50–55 mg/ml), *Pseudomonas aeruginosa* (60–65 mg/ml) and *Staphylococcus aureus* (145–150 mg/ml). Antimicrobial activity of *S. campanulata* in the topical bases was in the order: aqueous cream > emulsifying ointment > simple ointment > white soft paraffin. Antimicrobial activity of *S. campanulata* in aqueous cream decreased upon storage at room temperature for 6 months. The antifungal activity of the methanol extract of *S. campanulata* was reduced upon storage, while antibacterial activity was largely unaffected. Excision wounds infected with *Staphylococcus aureus* in Sprague–Dawley rats when treated with 20 % w/w *Spathodea campanulata* stem bark cream, and Cicatrin(®) cream showed a rapid and comparable decrease in wound size (Ofori-Kwakye et al. 2011). In uninfected wounds, both 20 % w/w *Spathodea* cream and Cicatrin(®) cream application resulted in ~95 % wound closure seen on day 20 and a complete closure seen on day 24. In infected wounds, both 20 % w/w *Spathodea* cream and Cicatrin(®) cream administration led to ~91 % wound closure on day 24 and a complete wound contraction on day 28. The results supported the folkloric use of *S. campanulata* stem bark in wound healing treatment.

Anticonvulsant Activity

Spathodea campanulata leaf extract exhibited anticonvulsant activity (Ilodigwe et al. 2010a). Administration of ethanol leaf extract (250–1,000 mg/kg, p.o.) 30 minutes prior to intraperitoneal administration of pentylenetetrazole (70 mg/kg) or picrotoxin (5 mg/kg) protected the treated mice against the respective pentylenetetrazole- and picrotoxin-induced convulsion in a dose-dependent manner, offering 100 % protection at the maximum dose of 1,000 mg/kg. The extract increased the threshold of maximum electroshock and reduced duration of convulsive episodes, dose dependently. Oral administration of *S. campanulata* ethanol extract did not significantly affect other centrally coordinated behaviours and convulsion-related properties such as position sense, righting reflex, rotarod performance, phenobarbital sleep time, and amphetamine-induced stereotypy in treated animals. The results also showed *S. campanulata* extract was nonsedative, had no antipsychotic properties, and may not affect motor coordination when used as an anticonvulsant.

Antimalarial Activity

The alcoholic extract of *Spathodea campanulata* leaves exhibited antiplasmodial activity (Markinde et al. 1987). Schizontocidal activity of the plant extract in mice blood was determined on both the early and established infections of *Plasmodium berghei berghei.* The plant extract was more effective in treating the early infection than the established one. The study provided scientific data for the use of the aqueous alcoholic decoction of the leaves of *Spathodea campanulata* for the treatment of malaria. The hexane and chloroform extracts of *S. campanulata* stem bark showed blood schizontocidal action in both the 4-day test and Rane test against *berghei berghei* in mice (Makinde et al. 1988). The chloroform extract demonstrated some prophylactic properties while the aqueous extract did not show any significant antimalarial property. Three antimalarial principles isolated from the stem bark, namely, 3β-hydroxyurs-12-en-28-oic acid (ursolic acid) and two of its derivatives; 3β-hydroxyurs-12,19-dien-28-oic acid (tomentosolic acid) and 3β,20β-dihydroxyurs-12-en-28-oic acid suppressed parasitaemia and prolonged survival times of mice infected with *Plasmodium berghei berghei* (Amusan et al. 1996).

Larvicidal Activity

Spathodea campanulata extract exhibited larvicidal activity at 100 ppm against the mosquito *Aedes fluviatilis*, a vector of Rift Valley fever (Consoli et al. 1988). *S. campanulata*

extract had a repulsive effect on female mosquitoes at 100 ppm but at 1 ppm was attractive to females (Consoli et al. 1989). In recent studies, *Spathodea campanulata* extracts were found to have larvicidal and mosquito repellency activity against the malarial vector *Anopheles stephensi* (Aarthi and Murugan 2010). The extracts of *Spathodea campanulata* were found most effective with LC50 value of 1.343, 1.607, 1.981, 2.165 and 2.432 of larval stages I, II, III, IV and pupa, respectively. The smoke toxicity was more effective against *Anopheles stephensi*. Smoke-exposed gravid females oviposited fewer eggs when compared to those that were not exposed.

Nephroprotective Activity

Pretreatment of Wistar albino rats with the ethanol extract of *Spathodea campanulata* bark orally was found to ameliorate the effects of gentamicin on lipid peroxide formation and showed a decrease in serum marker enzymes blood urea nitrogen and serum creatinine (Shanmukha et al. 2010). It also prevented depletion of tissue-reduced glutathione levels. The histopathological studies of the kidney revealed a protective role of the extract in gentamicin-treated rats. The results indicated that the pretreatment with ethanol extract of *Spathodea campanulata* bark may be useful in preventing the damage induced by gentamicin in rat kidneys. Similar nephroprotective effects was observed against paracetamol-induced nephrotoxicity when the 70 % ethanol bark extract was orally administered to Wistar albino rats (Siddiq et al. 2012).

Hypoglycaemic Activity

Spathodea campanulata stem bark decoction exhibited hypoglycaemic activity in Streptozocin-induced diabetic mice (Niyonzima et al. 1990). The decoction decreased blood glucose in glucose tolerance test but no effect was observed on insulin levels. In another paper they reported that the most polar fraction of the stem bark decoction exerted by far the most prominent hypoglycaemic, anticomplement, and anti-HIV activities (Niyonzima et al. 1999).

Analgesic and Antiinflammatory Activities

The ethanol leaf extract of *Spathodea campanulata*, (250–1,000 mg/kg) significantly and dose dependently prolonged the pain reaction times in hot-plate and tail-flick pain models and reduced acetic acid-induced writhing in rats (Ilodigwe and Akah 2009). The extract demonstrated significant antiinflammatory activity against acute inflammation induced by carrageenan in rats. The estimated LD50 of the extract was 4,500 mg/kg. Phytochemical analysis revealed the presence of tannins, saponins, anthraquinone glycosides, and flavonoids. The findings indicated that the leaf extract of *Spathodea campanulata* had both analgesic and antiinflammatory properties and could be beneficial in alleviating painful inflammatory conditions.

Antidiarrhoeal Activity

The antidiarrhoeal activity of *Spathodea campanulata* stem bark extracts was observed in three experimentally induced diarrhoea models, i.e. castor oil-induced diarrhoea, prostaglandin E2 (PG-E2)-induced enteropooling in rats, and charcoal meal test in mice (Rajesh et al. 2009). In castor oil-induced model, both aqueous and alcoholic extracts showed significant dose-dependent reduction of cumulative wet faecal mass. In PG-E2-induced enteropooling model, both extracts inhibited PG-E2-induced secretions. Similarly in charcoal meal test both extracts decreased the movement of charcoal indicating its antimotility activity. It was observed that the aqueous extract had more potent antidiarrhoeal activity than the alcoholic extract. Acute toxicity studies revealed that both the extracts were safe up to 2,000 mg/kg.

Photoprotective Activity

Methanol extract of macerated flowers showed maximum absorbance of UV at 200–240 nm, with good absorbance at 240–325 nm. Moderate absorbance was noted at 310–340 nm (Patil et al. 2009). The results showed that the flower extract had UV absorption ability and has potential as an antisolar agent.

Molluscicidal Activity

The aqueous (macerated and boiled), hexanic, and ethylic extracts of *S. campanulata* was found to be effective in-vitro against *Biomphalaria glabrata* in Brazil (Mendes et al. 1990) Of four plant species, *S. campanulata* was the least effective of all extracts tested against *Bulinus africanus*, the schistosomiasis (bilharzia) vector, although its methanol extract was molluscicidal (Amusan et al. 1995; Bosch 2002).

Toxicity Studies

The acute and subchronic toxicities of ethanol leaf extract of *Spathodea campanulata* was investigated by Ilodigwe et al. (2010b). For the acute toxicity study, 1,000–5,000 mg/kg of the ethanol leaf extract were administered to rats, and obvious toxic symptoms and mortality 24 hours post-administration of the extract were determined. In the subchronic study, 750–3,000 mg/kg of the extract were administered daily for 90 days; food and water consumption and body weight changes, as well as haematological and biochemical parameters, were determined periodically. The estimated LD_{50} of the extract was 4466.84 mg/kg. There was no mortality during the period of study, but the animals showed signs of anorexia, weakness, sluggishness and significant reduction in food and water intake and body weight. The effects on haemoglobin concentration, PCV (packed cell volume), RBC (red blood cells), and WBC (white blood cells) counts were nonsignificant. The extract caused significant increases in serum liver enzymes, aspartate transaminase (AST), alkaline phosphatase (ALP), and alanine transaminase (ALT). These changes showed recovery after 28 days post-treatment.

Traditional Medicinal Uses

Spathodea campanulata has many medicinal uses both in its native range and in areas introduced (Bosch 2002). Extracts of root, bark, leaves, and flowers are used to treat malaria, HIV, diabetes mellitus, oedema, dysentery, constipation, gastrointestinal disorders, ulcers, skin diseases, wounds, fever, urethral inflammation, liver complaints, and used as a poison antidote. *S. campanulata* has astringent properties and is widely used by traditional medicine practitioners as a relief for painful inflammatory conditions (Dalziel 1955; Oliver 1960). In Ivory Coast and Burkina Faso, various decoctions of the bark are used for herpes, impetigo, mycosis, and enema; and in combination with *Cola nitida* fruit or *Aspilia rudis*, it is used to treat Guinea worm infestations (Kerharo and Bouquet 1950). In Togo, decoctions of the bark stem and branches are used for wounds and menses problems (Adjanohoun et al. 1986). In Benin, the decoctions of the stem leaves and bark of underground parts are used for wounds, stomatitis, enteritis, and ulcers (Adjanohoun et al. 1989), and leaf sap is used for baby (Adjanohoun et al. 1988). In the Democratic Republic of Congo, powder of leaves, stem barks, and roots of *Spathodea campanulata* are used for asthma treatment (Disengomoka and Delaveau 1983; Kasonia et al. 1993) and bronchitis (Nyakabwa and Dibaluka 1990). In Yaounde region, Cameroon, fresh bark decoction is used to wash wounds (Tsabang et al. 2001). In Bulamogi, Uganda, a root decoction is used for diarrhoea and flowers and leaves are used in a wash for the body (Tabuti et al. 2003). *S. campanulata* is used in traditional African herbal medicine for the treatment of ulcers, filaria, gonorrhoea, diarrhoea, and fever (Sy et al. 2005). *Commelina diffusa* and *Spathodea campanulata* are used as wound healing agents in Ashanti traditional medicine in Ghana (Mensah et al. 2006). *S. campanulata* was also known in

Cameroon traditional medicine to have a healing activity in burn wounds. *Spathodea campanulata* was one of three plants used by traditional healers for wound healing of stomach ulcers in Bosomtwi-Atwima-Kwanwoma area, Ghana, and decoctions of the leaves and stem bark are used for wounds, skin rashes, and haemorrhoids (Agyare et al. 2009). In Ghana, decoction of the stem and root is used for paludism (Asase and Oppong-Mensah 2009). In Kenya, an infusion of the sap is used to treat colds in children by the Nandi people (Jeruto et al. 2008). *Spathodea campanulata* is popularly used for the treatment of epilepsy in Nigeria (Ilodigwe et al. 2010b).

Other Uses

African Tulip Tree is planted as an ornamental, as wayside tree, and shade tree. It is used for soil improvement, reafforestation, erosion control and land rehabilitation, and as a live fence. Its dense crown does not allow intercropping, but its leaves make a useful mulch. It has been used as a shade tree in coffee plantations. In Singapore, the timber has been reported to be used for making paper. In West Africa, the wood is used to make drums and blacksmith's bellows. The bark, flowers, and leaves are also used in traditional medicine in its native home range (Tan 2001).

The wood is dirty white, very light, soft and fibrous and susceptible to fungal rots. In West Africa, the wood is used for carving but is deemed inferior for other purposes. In Ethiopia, it is used as firewood and to produce charcoal. It is a poor timber and firewood species, although occasionally used as such. The wood is difficult to burn and so the tree can be used in fire-resistant landscaping. In the Philippines, the tree is used for plywood purposes. The flower buds contain a reddish fluid and are used as water pistols by children.

Comments

African Tulip has become an invasive species in the natural ecosystem in Hawaii, Fiji, Guam, Vanuatu, the Cook Islands and Samoa and also poses a potential invader in several other tropical locations.

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Brassica oleracea (Botrytis Group)

Scientific Name

***Brassica oleracea* L. (Botrytis Group)**

Synonyms

Brassica oleracea L. var. *botrytis* (L.) Alef, *Brassica oleracea* L. convar. *botrytis* (L.) Alef. var. *botrytis* f. *botrytis, Brassica oleracea* subsp. *oleracea* convar. *botrytis* var. *botrytis* L., *Brassica botrytis* subsp. *botrytis, Brassica cretica* subsp. *botrytis* var. *cauliflora* (DC.) Schwarz, *Brassica botrytis* var. *cauliflora* Presl, *Brassica cauliflora* subsp. *abortiva* Lizg., *Brassica botrytis* subsp. *botrytis* apud Lizg., *Brassica cretica* subsp. *botrytis* var. *cauliflora* (DC.) Schwarz, *Brassica botrytis* var. *cauliflora* Presl, *Brassica cauliflora* subsp. *abortiva* Lizg.

Family

Brassicaceae

English/Common Names

Cauliflower, Heading Broccoli, Perennial Broccoli

Vernacular Names

Afrikaans: Blomkool, Kool
Arabic: Karnabeet
Burmese: Paan Gor Bi
Chinese: Cai Hua, Gai Lan Hua, Hua Lan Cai, Hua Ye Cai, Ye Cai Hua, Ye Tsoi Fa
Croatian: Cvjetača
Czech: Brukev Květák, Květák
Danish: Blomkål, Blomsterkål
Dutch: Bloemkool
Eastonian: Lillkapsas
Esperanto: Florbrasiko
Finnish: Kukkakaali
French: Chou Brocoli, Chou Fluer, Chou-Fleur Commun, Chou-Fleur D'hiver
German: Blumenkohl, Kopfbrokkoli
Greek: Brókolo, Kounoupídi, Xylokrámvi
Hungarian: Karfiol
Icelandic: Blómkál
India: Phuulgobi (Assamese), Phool Gobi, Phuul Ghobi (Bengali), Fulaver, Phool Gobi, Phulkobi (Gujarati), Ghobi, Phool Gobhi, Phuul Gobhii (Hindi), Hukusu (Kannada), Phulkobi, Pulla Kosu (Konkani), Fulkobi, Phool Ghobi (Marathi), Phul Gobi (Oriya), Baha Kubi (Santhali), Kovippu, Pukosu (Tamil), Ghobi Puvvu, Khosu Povvu (Telugu), Phuul Gobhi (Urdu)
Indonesia: Kobis Bunga, Kol Bunga
Italy: Broccoli, Cavolo Broccolo, Cavolfiore, Cavolo Fiore
Japanese: Hana Kyabetsu, Hana Yana, Hana-Yasai, Kara-Shashin, Karifurawaa
Khmer: Phkaa Spei
Korean: Ja-Ju-Yang-Bae-Chu, Mo Ran Chae
Laos: Kalmapi Dook, Phak Ka Lam Dook
Latvian: Ziedkāposti

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Lithuanian: Kalafioras, Ziedinis Kopūstas
Malaysia: Kobis Bunga, Kol Bunga
Nepali: Kauli
Norwegian: Blomkål, Blomkålhode
Pakistan: Gobhi, Phool Gobhi
Papua New Guinea: Oli Flva
Philippines: Kaliplawer, Koliplor (Tagalog)
Polish: Kalafior
Portuguese: Couve-Flor, Pugliese, Raminhos De Couve-Flor
Romanian: Conopidã
Russian: Kapusta, Kapusta Tsvetnaia
Serbian: Karfiol
Slovak: Karfiol
Spanish: Coliflor
Sri Lanka: Mal Gova (Sinhala)
Thai: Dok Kha Lam
Turkish: Karnabahar, Karnibahar
Ukrainian: Cvitna Kapusta
Vietnamese: Cải Bông, Su Lơ, Súp Lơ
Welsh: Bresychen Wen
Zulu: Ukholifulawa

Origin/Distribution

The primary area of cultivation is in the eastern Mediterranean region; from there it spreads to western and Central Europe before spreading globally, even to tropical countries where it is cultivated in the cooler mountain areas above 1,000 m.

Cauliflower and broccoli are believed to have evolved in Roman times from wild or primitive cultivated forms of *Brassica oleracea* in the eastern Mediterranean region; from there it spreads to western and Central Europe before spreading globally, even to tropical countries where it is cultivated in the cooler mountain areas above 1,000 m. During the last 400 years, white-headed cauliflower spread from Italy to central and northern Europe, which became secondary centres of diversity for annual and biennial types. Cauliflower adapted to hot and humid tropical climates has evolved in India during the last 200 years from biennial cauliflower of mainly British and Central European origin.

The leading cauliflower- and broccoli-producing counties in terms of total production (tonnes) are China 9,030,990, India 6,745,000, Spain 527,500, Mexico 427,884, Italy 420,989, France 334,170, United States 325,180, Poland 297,649, Pakistan 227,591, Egypt 201,200, United Kingdom 180,577, Bangladesh 168,238, Turkey 162,134, Japan 153,305, Germany 144,136, Indonesia 113,492, Belgium 99,660, Morocco 92,925 and Algeria 92,500 (FAO Stat 2012).

Agroecology

Cauliflower requires a cool, moist subtemperate climate, average daily temperatures of 15–20 °C; if temperatures go too high, the plants will not produce flower heads; if too low the plants might button, resulting in small heads. It is cold tolerant but will not survive severe frosts. It thrives best in full sun in well-drained, moist, fertile soil with significant organic matter and a pH of 6–7. As with all Brassicas, seeds germinate best with a soil temperature of around 25 °C.

Edible Plant Parts and Uses

Flowering head (curds) is edible. Cauliflower can be roasted, boiled, fried, steamed or eaten raw. When cooking, the outer leaves and thick stalks are removed, leaving only the florets. The florets should be broken into similar-sized pieces so they are cooked evenly. Cauliflower is often served with a cheese sauce, as in the dish cauliflower cheese, or with a meat gravy. Cauliflower stalks are fermented to produce 'achar tandal' in India. The leaves are also edible but are most often discarded. Low carbohydrate dieters can use cauliflower as a reasonable substitute for potatoes and is often used to produce a potato substitute known as 'fauxtato'. Cauliflower is available as quick-frozen vegetables and processed in dried mixtures of soup vegetables.

Botany

An herbaceous annual with elongated cylindrical, non-fleshy stem base and growing to a height of 50–80 cm and higher to 150 cm when flowering.

Plate 1 Cauliflower leaves and curd

Plate 2 Harvested cauliflowers packaged for transport in an Indonesian market

Basal and lower cauline leaves green, few to several, widely spaced, not grouped into a head, enclosing the compact terminal flowering head called the curd (Plate 1). The leaves are oblong-ovate, light greenish-grey, often simple and no lateral buds developed in the leaf axils. The curd consists of a dome of proliferated floral meristems white to cream or yellow (or purple in cultivars) on numerous fleshy peduncles (Plates 1, 2, 3 and 4). The curd is usually compact, sometimes loose, flattish or globose in shape. Bolting plants have several flower stalks. Inflorescence a raceme, 40–70 cm long with 4 merous bisexual flowers with green sepals, spathulate, yellow petals, 6 stamens—2 short and 4 long and superior ovary. Fruit a silique, 5–10 cm by 0.5 cm with 10–30 globose brown seeds.

Plate 3 Harvested cauliflower curds

Plate 4 A purple cauliflower curd

Nutritive/Medicinal Properties

Inflorescence/Leaf Nutrients and Phytochemicals

The proximate value per 100 g edible portion of raw cauliflower was reported as follows: water 92.07 g, energy 25 kcal (105kJ), protein 1.92g, total lipid 0.28g, ash 0.76g, carbohydrate 4.97g, total dietary fibre 2.0 g, total sugars 1.91g, glucose 0.94g, fructose 0.97 g; minerals, Ca 22 mg, Fe, 0.42 mg, Mg 15 mg, P, 44 mg, K 299 mg, Na 30 mg, Zn 0.27 mg, Cu 0.039 mg, Mn 0.155 mg, F 1 µg, Se 0.6 µg; vitamin C 48.2 mg, thiamine, 0.050 mg, riboflavin 0.060 mg, niacin 0.507 mg,

pantothenic acid 0.667 mg, vitamin B-6 0.184 mg, total folate 57 μg, total choline 44.3 mg, vitamin A 13 IU, vitamin E (α-tocopherol) 0.08 mg, γ-tocopherol 0.2 mg, vitamin K (phylloquinone) 15.5 μg; total saturated fatty acids 0.064 g, 15:0 (pentadecanoic acid) 0.001 g, 16:0 (palmitic acid) 0.046 g, 17:0 (margaric acid) 0.001, 18:0 (stearic acid) 0.004 g, 20:0 (arachidic acid) 0.002 g, 22:0 (behenic acid) 0.001 g, 24:0 (lignoceric acid) 0.001 g, total monounsaturated fatty acids 0.017 g, 14:1: (myristoleic acid) 0.001 g, 16:1c (palmitoleic acid *cis*) 0.002 g, 18:1c (oleic acid cis) 0.014 g, 24:1c (nervonic acid) 0.001 g; and total polyunsaturated fatty acids 0.015 g, 18:2 n-6 c,c (linoleic acid) 0.006 g, 18:2 CLAs 0.002 g, 18:3 n-3 c,c,c (ALA, α-linolenic acid) 0.007 g, phytosterols 18 mg, tryptophan 0.020 g, threonine 0.076 g, isoleucine 0.071 g, leucine 0.106 g, lysine 0.217 g, methionine 0.020 g, cystine 0.020 g, phenylalanine 0.065 g, valine 0.125 g, arginine 0.086 g, histidine 0.056 g, alanine 0.116 g, aspartic acid 0.177 g, glutamic acid 0.257 g, glycine 0.071 g, proline 0.071 g, serine 0.086 g and lutein + zeaxanthin 1 μg (USDA 2012).

During period of cauliflower floral induction (2 weeks under 16 hours of light at 5 °C), there was a significant increase in sugar and starch content compared to that in vegetative plants grown at 20–26 °C (Sadik and Ozbun 1968). Sugar and starch content did not increase and flowering was prevented when light and CO_2 were excluded during growth at 5 °C. A 3-day dark period at 20 °C or a high temperature treatment at 33 °C with light following growth at 5 °C reduced the carbohydrate level and prevented flowering.

Brassica plants (e.g. broccoli and cauliflower) contain substantial quantities of isothiocyanates (mostly in the form of their glucosinolate precursors) some of which (e.g. sulforaphane or 4-methylsulfinylbutyl isothiocyanate) are very potent inducers of phase two enzymes (Fahey et al. 1997). Three-day-old sprouts of cultivars of certain crucifers including broccoli and cauliflower were found to contain 10–100 times higher levels of glucoraphanin (the glucosinolate of sulforaphane) than do the corresponding mature plants. Sicilian cultivars of cauliflower possessing coloured curds displayed a high content of glucosinolates, glucoraphanin in particular, compared to white curd commercial cultivars; also some wild species had a high content of other glucosinolates (Branca et al. 2002). The glucosinolate content of 27 European cauliflower was similar to the American cauliflower cultivars but contained low amount of 2-hydroxy-3-butenyl-glucosinolate which was absent in the latter varieties (Sones et al. 1984). The major glucosinolates in European cauliflowers were identified as prop-2-enyl-glucosinolate, 3-methylsulphinyl propyl-glucosinolate, 3-indolylmethyl-glucosinolate and 1-methoxy-3-indolylmethyl-glucosinolate. Smaller amounts of but-3-enyl-glucosinolate, 2-hydroxybut-3-enyl-glucosinolate, 3-methylthiopropyl-glucosinolate, 4-methylthiobutyl-, 2-phenylethyl-glucosinolate, pent-4-enyl-glucosinolate, 2-hydroxypent-4-enyl-glucosinolate and 5-methylthiopentyl-glucosinolate were also found in some cultivars. Allyl-glucosinolate, 3-(methylthio)propyl-glucosinolate, 3-(methylsulfinyl)propyl-glucosinolate and 3-indolylmethyl-glucosinolate were present in all five American cultivars of cauliflower curd and were the major glucosinolates in their seeds as well (Carlson et al. 1987). Other glucosinolates present included 4-(methylsulfinyl)butyl-glucosinolate, 4-(methylthio)butyl-glucosinolate, 3-butenyl-glucosinolate, 4-pentyl-glucosinolate and 2-phenyl-ethyl-glucosinolate. Glucosinolates found in cauliflower purchased from local Singapore markets were in nmol/g wet weight: glucoraphanin NQ (not quantified), gluconasturtiin NQ, sinigrin 132 nmol, glucobrassicin 2,850 nmol, 4-hydroxy glucobrassicin 75.8 nmol, 4-methoxy glucobrassicin 231 nmol, 1-methoxy glucobrassicin 743 nmol, glucoiberin NQ, progoitrin (or epiprogroitrin) NQ, glucoalyssin 14.1 nmol, gluconapoleiferin NQ, gluconapin NQ, glucobrassicanapin NQ, glucoerucin NQ, 7-methylthioeptyl NQ, 8-methylthioeptyl NQ, total glucosinolates 4,190 nmol and glucobrassicans 93.2 % of total glucosinolates (Hecht et al. 2004). Glucobrassicins (glucobrassicin, 1-methoxyglucobrassicin, 4-methoxyglucobrassicin and 4-hydroxyglucobrassicin), precursors to indole-3-carbinols, were the predominant glucosinolates

in seven of the nine vegetables (including cauliflower and broccoli) studied, accounting for 70.0–93.2 % of all glucosinolates.

The following phenolic compounds and glucosinolates were identified in cauliflower: four sinapic acid derivatives (1,2-disinapoyl-diglucoside; 1-sinapoyl-2-feruloyl-diglucoside; 1,2,2′-trisinapoyl- diglucoside; and 1,2′-disinap oyl-feruloyl-diglucoside), three flavonoids (quercetin-3-diglucoside-7-glucoside; kaempferol-3-diglucoside-7-glucoside;andkaempferol-3-diglucoside-7-diglucoside) and six glucosinolates namely 5-methylsulfinylpentyl glucosinolate (glucoalyssin); n-hexyl/methylpentyl glucosinolate (n-hexyl/methylpentyl-3-methylthiopropyl (glucoiberverin); 3-indolylmethyl glucosinolate (glucobrassicin); N-methoxy-3-indolylmethyl glucosinolate (neoglucobrassicin); 4-hydroxy-3-indolylmethyl glucosinolate (4-hydroxyglucobrassicin); and 4-methoxy-3-indolylmethyl glucosinolate (4-methoxyglucobrassicin)) (Gratacós-Cubarsí et al. 2010). The main hydroxycinnamic acids (sinapic, ferulic, *p*-coumaric and caffeic acids) were isolated from cauliflower by capillary zone electrophoresis (Lee et al. 2011).

The following phenolic compounds were found in cauliflower: quercetin derivatives (quercetin -3-*O*-sophoroside-7-*O*-glucoside and quercetin -3-*O*-(sinapoyl)-sophoroside-7-*O*-glucoside), kaempferol derivatives (kaempferol-3-*O*-sophorotrioside-7-*O*-sophoroside; kaempferol-3-*O*-sohorotrioside-7-*O*-glucoside; kaempferol-3-*O*-sophorotrioside-7-*O*-diglucoside; kaempferol-3-*O*-sophoroside-7-*O*-glucoside; kaempferol-7-*O*-glucoside; kaempferol -3-*O*-(caffeoyl)sophoroside-7-*O*-glucoside; kaempferol-3-*O*-(sinapoyl)-sophoroside-7-*O*-glucoside; and kaempferol-3-*O*-(*p*-coumaroyl)-sophoroside-7-*O*-glucoside) and hydroxycinnamic acids namely 3-caffeoylquinic acid); 1,2-disinapoylgentiobiose; 1-sinapoyl-2-feruloylgentiobiose; 1,2,2′-trisinapoylgentiobiose; and 1,2′-disinapoyl-2-feruloylgentiobiose (Cartea et al. 2011). Eight minor glucosinolates, namely, 1-methylpropyl-glucosinolate, 2-methylpropyl-glucosinolate, 2-methylbutyl-glucosinolate, 3-methylbutyl-glucosinolate, n-pentyl-glucosinolate, 3-methylpentyl-glucosinolate, 4-methylpentyl-glucosinolate and n-hexyl-glucosinolate were identified in crude sample extracts of cauliflower, broccoli and rocket salad (Lelario et al. 2012). The occurrence of these glucosinolates belonging to the saturated aliphatic side chain families C4, C5 and C6, presumably formed by chain elongation of leucine, homoleucine and dihomoleucine as primary amino acid precursors, was described. Isothiocyanate content in cauliflower juice treated by freezing, pasteurization, and high pressure was found to range from 0.79 to 25.92, 2.80 to 16.15,and 1.04 to 10.92 μmol/l, respectively (Totušek et al. 2011). Sulforaphane content in cauliflower juice treated by freezing, pasteurization, and high pressure was found to range from 0.66 to 1.61, 0.69 to 0.98 and 0.64 to 1.29 μg/ml, respectively.

No differences in free sugar (glucose, sucrose and fructose) or glucosinolate profiles in cauliflower were found between air and controlled atmosphere (3 % O_2 and 5 % CO_2 at 0 °C) (Hodges et al. 2006) storage treatments. However, the glucosinolates gluconapin (3-butenyl glucosinolate) and glucobrassicin (3-indolylmethyl glucosinolate) increased for each treatment during storage, albeit later in controlled atmosphere storage. Glucobrassicin was the major glucosinolate component, and the dramatic increase in the concentrations of this compound was reflected in increased total glucosinolate levels of air-stored cauliflower on day 28 of storage. Levels of the other glucosinolates (sinigrin (2-propenyl glucosinolate), progoitrin (2-hydroxy-3-butenyl glucosinolate), epiprogoitrin, 4-OH-glucobrassicin and 4-MeOH-glucobrassicin, as well as an unidentified glucosinolate) did not change during storage; glucoiberin content decreased after day 28. Increases in levels of gluconapin and glucobrassicin may be related to metabolic changes associated with natural and/or stress-induced senescence.

Brassica vegetables including cauliflower contain phytochemicals including glucoraphanin, the precursor of sulforaphane (SFN) and glucobrassicin, the precursor of indole-3-carbinole (I3C) and ascorbigen (ABG) (Wagner et al. 2010). Glucobrassicin was found to be enzymatically hydrolyzed to indole-3-carbinol, which in turn

reacted with L-ascorbic acid to yield ascorbigen (Wagner and Rimbach 2009). The degradation of glucobrassicin was induced by plant tissue disruption. The formation of ascorbigen was dependent on pH and temperature. The degradation of ascorbigen in acidic medium released L-ascorbic acid and a formation of methyldeneindolenine; in more alkaline medium, the degradation of ascorbigen yielded 1-deoxy-1-(3-indolyl)-α-L-sorbopyranose and 1-deoxy-1-(3-indolyl)-α-L-tagatopyranose.

A total of 28 compounds were identified in cauliflower agroindustrial by-products; of these, 22 were produced naturally by the plant (Llorach et al. 2003b). The main compounds found were kaempferol 3-diglucoside-7-glucoside and its combinations with different hydroxycinnamic acids. The new products isolated were identified as kaempferol 3-diglucoside-7-diglucoside, kaempferol 3-triglucoside-7-diglucoside, kaempferol 3-feruloyldiglucoside-7-diglucoside, kaempferol 3-sinapoyltriglucoside-7-glucoside,kaempferol3-disinapoyltriglucoside-7-glucoside, kaempferol 3-sinapoyltriglucoside-7-diglucoside and kaempferol 3-disinapoyltriglucoside-7-diglucoside.

Three indole compounds indole-3-acetonitrile, indole-3-carbinol (I3C) and 3,3′-diindolylmethane (DIM) were identified from three cruciferous vegetables, Brussels sprouts, cabbage and cauliflower (Loub et al. 1975; Wattenberg 1975). Four known (isalexin, S-(-)-spirobrassinin, 1-methoxybrassitin, brassicanal C) and three new (caulilexins A–C) phytoalexins were isolated from cauliflower florets under abiotic (UV light) elicitation, and the first synthesis of brassicanal C was reported (Pedras et al. 2006).

Six organoselenium compounds including selenium analogues of known myrosinase-derived *Brassica* volatiles 4-(methylseleno) butanenitrile, 5-(methylseleno)pentanenitrile, 3-(methylseleno)propylisothiocyanate, 4-(methylseleno)butylisothiocyanate and 5-(methylseleno) pentylisothiocyanate were identified in the pentane/ether extracts of broccoli and cauliflower florets and roots of forage rape, all obtained from plants treated with sodium selenate (Matich et al. 2012). LC–MS analysis of ethanol extracts identified three selenoglucosinolates: 3-(methylseleno) propylglucosinolate (glucoselenoiberverin), 4-(methylseleno)butylglucosinolate (glucoselenoerucin) and 5-(methylseleno)pentylglucosinolate (glucoselenoberteroin).

Serine *trans*-hydroxymethylase, purified 46-fold from cauliflower, was found to be specific to serine (Mazelis and Liu 1967). Polyguanylate polymerase and polyadenylate polymerase were detected in the DNA-dependent RNA polymerase I fraction from cauliflower; poly(G) and poly(A) formed in-vitro by the enzyme fraction had chain length of 25–28 and 84–89 nucleotides (Mizuochi and Fukasawa 1976). Two distinct DNA polymerases, A and B, with molecular weights of 78,000 and 50,000, respectively, were isolated from a rapidly growing apical tissue of cauliflower inflorescence (Fukasawa et al. 1980). Polymerase-A bore strong resemblance to polymerase-alpha from mammalian cells in all properties examined, while polymerase-B was quite similar to polymerase-beta of mammalian cells. An ATP-independent DNA topoisomerase with molecular weight of 54,000 was isolated from chloroplasts of cauliflower leaves (Fukata et al. 1991). Cauliflower chloroplast topoisomerase could relax positive supercoils as well as negative supercoils. From these properties, cauliflower chloroplast topoisomerase could be classified as a eukaryotic type I DNA topoisomerase.

A protein with structure-specific endonuclease activity and a molecular mass of 40 kDa was purified from cauliflower inflorescence (Kimura et al. 1997). A DNA polymerase purified from cauliflower inflorescence-designated cauliflower polymerase 1 was found to be a monopolypeptide with a molecular mass of 100 kDa (Seto et al. 1998). The enzyme was clearly different from cauliflower mitochondrial polymerase. Tonoplast intrinsic proteins of molecular mass 23–29 kDa were detected in the meristematic tissues of cauliflower (Barrieu et al. 1998). Appreciable differences in the degree of methyl-esterification (ME) of pectic polysaccharides were detected in cauliflower stem (Femenia et al. 1998). About 65 % of galacturonic acid (GalpA) residues were methyl esterified in floret tissues. Relative ME

showed a basipetal decrease, from 94 % in the upper stem to 51 % in the lower stem vascular tissues. The decrease was not related to a basipetal increase in glucuronic acid (GlcpA) residues. An acyl-CoA oxidase and a second protein of the plant nucleotide pyrophosphatase family purified from cauliflower inhibited both glutamine synthetase (GS) and nitrate reductase (Moorhead et al. 2003). S-methyl methanethiosulfonate, an antimutagenic compound, was isolated from cauliflower (Nakamura et al. 1993).

Cauliflower was found to accumulate dehydrin-like proteins with molecular weight of 10–100 kDa in the leaf and inflorescence mitochondria during some abiotic (cold) stress (Rurek 2010). A peroxidase, a primer antioxidant enzyme, with molecular weight 44 kDa was purified with 19.3-fold and 0.2 % efficiency from cauliflower buds (Köksal and Gülçin 2008).

Upon treatment with norflurazon, both cauliflower wild type and Or gene calli synthesized significant amounts of phytoene (Li et al. 2006). Phytoene was accumulated at comparable levels, and no major differences in carotenogenic gene expression were observed between the wild-type and Or calli, suggesting Or-induced β-carotene accumulation did not result from an increased capacity of carotenoid biosynthesis.

Studies showed significant differences among broccoli and cauliflower cultivar groups for the glucosinolate proportions as well as the contents of health-promoting and flavour-influencing alkyl, alkenyl and indole glucosinolates (Schonhof et al. 2004). These differences impacted on differences in sensory properties colour, taste properties such as bitter and sweet, flavour such as green/grassy, spicy, broccoli-like, cabbage-like, cauliflower-like, kohlrabi-like, leek-like and mouth-feel pungent. Consumers were seen to prefer cultivars with a bright colour, a lower level of bitter tasting glucosinolates (alkenyl and indole glucosinolates) and a higher sucrose content. Studies showed that neoglucobrassicin and sinigrin were responsible for the bitterness of cooked cauliflower (Engel et al. 2002). Allyl isothiocyanate (AITC), dimethyl trisulphide (DMTS), dimethyl sulphide (DMS) and methanethiol (MT) were the key odorants of cooked cauliflower 'sulphur' odours. They concluded that AITC, DMTS, DMS, MT, sinigrin and neoglucobrassicin were the potential physicochemical determinants of cooked cauliflower acceptance.

Cauliflower and red cabbage showed differences in their anthocyanin profiles: cyanidin-3,5-diglucoside was absent in cauliflower, while it was well represented in red cabbage, together with the characteristic anthocyanin of *Brassica* genus, cyanidin-3-sophoroside-5-glucoside (Scalzo et al. 2008). The *p*-coumaryl and feruloyl esterified forms of cyanidin-3-sophoroside-5-glucoside were predominant in cauliflower, while the sinapyl one was mostly present in red cabbage. All thermal treatments, except microwave heating, drastically reduced total cauliflower anthocyanin content.

From disrupted leaf tissues of cauliflower, the predominant vapour component was *cis*-hex-3-enyl acetate (Wallbank and Wheatley 1976). Apart from isothiocyanates, dimethyl disulphide was detected from cauliflower, particularly in vapour from disrupted curd tissue. From fresh Romanesco cauliflower Navona variety leaves extract, a total of 61 compounds were identified, representing 96.8 % of the oil (Valette et al. 2006). The major constituent was found to be hex-3(*Z*)-enol (61.1 %). From fresh disrupted inflorescence tissues of Romanesco, 35 compounds were detected, representing 97.7 % of the extract. Dimethyl disulphide, dimethyl trisulphide and hex-3(*Z*)-enol were identified as major constituents of the hydrodistillation products, representing, respectively, 30.2, 24.2 and 21.7 % of the volatiles. From ripening and frozen inflorescence tissues, dimethyl disulphide and trisulphide were again detected as predominant components. In the latter, hex-3(*Z*)-enol had almost disappeared (0.8 %) whereas dimethyl trisulphide represented 49.7 % of the oil. The steam distillation compounds present in the leaves and inflorescence tissues of cauliflower included limonene, α-pinene; β-pinene; α-terpineol; terpinene-4-ol; γ-terpinene; 4-methylene-1-(1-methylethyl)-bicyclo[3.1.0]hexane; nonanal; hexanal; camphor; decanal; eugenol; benzeneacetaldehyde; heptanal; 1-hexanol; (*E*)-2-hexenal; (*Z*)-3-hexen-1-ol;

(*E,E*)-2,4-decadienal; *trans*-β-ionone; furfural; pyridine; 2-buten-1-one, 1-(2,6,6-trimethyl-1,3-cyclohexadien-1-yl)-, (*E*)-; methional; pinocarvone; dimethyl disulphide; dimethyl trisulphide; 2-pentyl-furan; acetic acid, hexyl ester; hexadecanoic acid, methyl ester; benzyl benzoate; (*E,Z*)-2,6-nonadienal; (*Z*)-3-hexen-1-ol, acetate; indole; tetradecanal; 2-methoxy-4-vinylphenol; (*E*)-2-Hexen-1-ol-; (*E,E*)-2,4-Heptadienal;2,6-dimethylpyrazine;1-(2-furanyl)-ethanone; pentadecanal; 2,6,6-trimethyl-1-cyclohexene-1-carboxaldehyde; tridecanal; 1-dococene; (*Z*)-3-hexen-1-ol, benzoate; 2-pentadecanone; butanoic acid, 3-hexenyl ester, (*Z*)-; 1-tridecene; dimethyl sulphoxide; dimethyl tetrasulphide; 2-acetylthiazole; 3-ethyl-phenol; (*Z*)-2-penten-1-ol; 2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde; 4-methyl-1-(1-methylethyl)-bicyclo[3.1.0]hex-3-en-2-one; 4-vinylphenol; 2-hexadecanone; (*E*,*E*)-3,5-octadien-2-one; 2,2,6-trimethyl-cyclohexanone; 1,2-dihydro-1,1,6-trimethyl naphthalene; 4-(2,2,6-trimethyl-7-oxabicyclo[4.1.0]hept-1-yl)-3-buten-2-one; methyl (methylthio)methyl disulphide; 1-(methylthio)pentane; β-damascone; *trans*-2-(2-pentenyl)furan; benzenepropanenitrile; 2,6,6-trimethyl-1-cyclohexene-1-acetaldehyde; benzene, (2-isothiocyanatoethyl)-; 4-methylthiobutyl isothiocyanate; 5-(methylthio)pentanenitrile; propane, 1-isothiocyanato-3-(methylthio)-; isobutyl isothiocyanate; 1-(methylthio)-3-pentanone; 4-methylthio butanenitrile; 2,6-dimethyl-3-methoxymethyl-p-benzoquinone; and 1,3,5-trimethyl-2-(1,3-butadienyl)benzene.

Environmental stress affecting harvest time was found to impact on the antioxidant properties and lipidic profile as quality indexes of cauliflower in a 3-year (2001–2003) study (Scalzo et al. 2007). Late harvested cauliflowers in 2002 were found to have a very different composition profile (increase of dry and fatty matter, polyphenols and antioxidant activity, decrease in ascorbic acid content) and a difference in fatty acid composition related to a relative increase in unsaturated fatty acids with respect to saturated ones.

Major volatile components identified in cauliflower included nonanal, octanol, 3-methylthiopropyl cyanide, 3-methylthiobutyl cyanide, 2-phenylethyl cyanide and 2-phenylethyl isothiocyanate (Buttery et al. 1976). Volatiles emitted during blanching of cauliflowers included thiols, sulphides, polysulphides, aldehydes, isothiocyanates, nitriles, furans, esters, terpenes and carbonyl compounds (Van Langenhove et al. 1991). Aldehydes were the most abundant cauliflower volatiles. Blanching of purple, two white and two green varieties of cauliflower, prior to freezing, reduced total aliphatic and indole glucosinolates (GLS) by 31 and 37 %, respectively (Volden et al. 2009). L-ascorbic acid (L-AA), total phenols (TP), anthocyanins, FRAP (ferric reducing ability) and ORAC (oxygen radical absorbance capacity) were on average reduced by 19, 15, 38, 16 and 28 %, respectively. Long-term freezer storage did not markedly affect total aliphatic and indole GLS in cauliflower. Freezer storage did result in an average L-AA decrease of 24 % for all but the purple cultivar; smaller reductions in the TP levels were also found. Reductions in FRAP and ORAC values occurred towards the end of the storage period; the mean reductions were 15 and 37 %, respectively. Long-term freezer storage did not affect the anthocyanin content and only minor effects were found for the colour parameters.

Seed Phytochemicals

Forty-three compounds, representing more than 99.7 % of Romanesco cauliflower seed oil for the Natalino variety, 41 (99.6 %) for the Campidoglio variety and 32 (99.5 %) for the Navona variety, were identified (Valette et al. 2006). The major compounds were cyanides such as 4-(methylthio) butyl cyanide (61.3, 66.3 and 79.6 %, respectively), 3-(methylthio)propyl cyanide (21.7, 21.6 and 10.7 %) and isothiocyanates such as 4-(methylthio)butyl isothiocyanate (5.3, 4.0 and 6.7 %) for the three oils. The majority of identified volatile compounds were obtained by hydrolysis of glucosinolates. The compounds identified included nonanal; hexanal; benzeneacetaldehyde; phenylethyl alcohol; 6 methyl-5-hepten-2-one; (*E,E*)-2,4-decadienal; furfural; (*E*)-2-nonenal; methional; 2-pentyl-furan; indole; 1-hexadecanol; 2-methoxy-4-vinylphenol; 2-furanmethanol;

dihydro-5-pentyl-2(3H)-furanone; benzophenone; 1-octadecanol; 4-methoxy-6-(2-propenyl)-1,3-benzodioxole; benzyl nitrile; hexanenitrile; 6-methyl-5-hepten-2-ol; (*E,E*)-3,5-octadien-2-one; allyl isothiocyanate; benzene, (isothiocyanatomethyl)-; heptanonitrile; 4-isothiocyanato-1-butene; benzenepropanenitrile; isoamyl cyanide; benzene, (2-isothiocyanatoethyl)-; 5-methylhexanenitrile; 1-isothiocyanato-3-(methylthio)-propane; isobutyl isothiocyanate; 4-methylpentyl isothiocyanate; 5-methylthiopentyl isothiocyanate; pent-4-enenitrile; 1-isothiocyanato-3-methyl-butane and 4-(methylthio)-butanenitrile.

As seen from the above, cauliflower is low in fat and high in folate, dietary fibre and vitamin C and a good source of vitamin A, calcium, iron, manganese, riboflavin, niacin, thiamin, pantothenic acid and vitamin B6. It has beneficial antioxidant phenolics and flavonoids and glucosinolates and isothiocyanates with anticancer and other positive biological properties.

Antioxidant Activity

Cauliflower by-product extracts showed significant free radical scavenging activity (DPPH and ABTS radicals), ferric reducing ability (FRAP assay) and capacity to inhibit lipid peroxidation (ferric thiocyanate assay) (Llorach et al. 2003a). Furthermore, the antioxidant activity was linearly correlated with the phenolics content. The water and ethanol extraction of cauliflower yielded a phenolic content of 33.8 mg/g freeze-dried extract and 62.1 mg/g freeze-dried extract, respectively. This percentage increased considerably when the extracts were purified yielding a phenolic content of 186 mg/g freeze-dried extract (water extract) and 311.1 mg/g freeze-dried extract (ethanol extract). The results indicated that the cauliflower by-products are a cheap source of antioxidant phenolics.

Cauliflower glucosinolates and their derivatives were found to have significant antioxidant capacity in the oxygen radical absorbance capacity (ORAC) and superoxide radical scavenging activity (SRSA) assays especially glucobrassicin, followed by glucoiberin and gluconapin (Cabello-Hurtado et al. 2012). In contrast the antioxidant activities of the glucosinolates in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis-(3-ethyl-benzothiazoline-6-sulphonic acid) (ABTS) assays were weak. There was no synergy or antagonism between glucosinolates. Breakdown products of glucosinolates were far more active than the native glucosinolates. The highest increases in antioxidant activity were obtained for enzymatic hydrolysis-derived products (EHDP) from progoitrin, sinigrin and glucoraphanin, progoitrin EHDP being the second most active derivative behind glucobrassicin EHDP. Overall, the contribution of glucosinolates to antioxidant activity of cauliflower appeared low.

Anticancer Activity

In-Vitro Studies

Three indole compounds indole-3-acetonitrile, indole-3-carbinol and 3,3′-diindolylmethane were identified from three cruciferous vegetables, Brussels sprouts, cabbage and cauliflower (Loub et al. 1975; Wattenberg 1975). These indoles were found to be naturally occurring inducers of aryl hydrocarbon hydroxylase (Loub et al. 1975) and microsomal mixed function oxidase system and to exert a protective effect against chemical carcinogens (Wattenberg 1975). Besides these indoles, other naturally occurring inducers include flavones, safrole, isosafrole, β-ionone and oxidized sterols (Wattenberg et al. 1976). Thus, the composition of the diet could play a role in inhibiting the neoplastic response to carcinogenic agents.

Indole-3-carbinol (I3C), a secondary plant metabolite produced in vegetables of the *Brassic*a genus, including cabbage, cauliflower and Brussels sprouts, could be both an anti-initiator and a promoter of carcinogenesis (Bjeldanes et al. 1991). Consumption of I3C by humans and rodents could lead to marked increases in activities of cytochrome P-450-dependent monooxygenases and in a variety of phase II drug-metabolizing enzymes. They reported previously that the enzyme-inducing activity of I3C was mediated through a mechanism requiring exposure of the

compound to the low-pH environment of the stomach. They found that indolo[3,2-b]carbazole (ICZ), a major acid condensation product generated from I3C in the order of 0.01 % in-vitro and, after oral intubation, in-vivo to be an aromatic hydrocarbon responsiveness-receptor agonist and to induce cytochrome P4501A1 activity in murine hepatoma Hepa 1c1c7 cells. Isothiocyanates and indoles (e.g. indole-3-carbinol) from *Brassica* vegetables (e.g. broccoli, cauliflower) induce phase I and phase II enzymes responsible for the oxidation, reduction and metabolism of endogenous and exogenous carcinogens (Fowke et al. 2006). Oral administration of indole-3-carbinol (I3C) had been shown to manipulate oestrogen metabolism in humans in a possibly beneficial manner (Brignall 2001). I3C increased the 2/16-hydroxyestrone ratio, a ratio found to be predictive of breast cancer risk in some prospective studies. Animal and in-vitro studies had identified a number of other possibly beneficial effects of I3C and its metabolites, including inhibition of oestrogen binding and modulation of oncogene expression. A chemopreventive effect of I3C had been demonstrated in a number of animal models. Some chemical carcinogenesis models had found a tumour-promoting effect of I3C, however. Ascorbigen, a derivative of indole-3-carbinol may partly mediate the known anticarcinogenic effect of diets rich in Brassicaceae (Wagner and Rimbach 2009). Further, ascorbigen could induce phase I and II enzymes centrally involved in the detoxification of xenobiotics.

Both indole-3-carbinol (I3C) and diindolylmethane (DIM) from *Brassica* vegetables were found to be partial aryl hydrocarbon (Ah) receptor antagonists in the T47D human breast cancer cell line (Chen et al. 1996). In aryl hydrocarbon (Ah)-responsive T47D human breast cancer cells, I3C and DIM did not induce significantly CYP1A1-dependent ethoxyresorufin O-deethylase (EROD) activity or CYP1A1 mRNA levels at concentrations as high as 125 or 31 μM, respectively. In T47D cells co-treated with 5 nM [3H] TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) alone or in combination with 250 μM I3C or 31 μM DIM, there was a 37 and 73 % decrease, respectively, in formation of the nuclear Ah receptor. The more effective inhibition of induced EROD activity by I3C and DIM was due to in-vitro inhibition of enzyme activity. Firestone and Bjeldanes (2003) found that indole-3-carbinol and 3-3′-diindolylmethane antiproliferative signalling pathways controlled cell-cycle gene transcription in human MCF-7 breast cancer cells by regulating nuclear promoter-Sp1 transcription factor interactions.

Following ingestion of *Brassica* vegetables, indole-3-carbinol (I3C) is converted to a series of oligomeric products that presumably are responsible for the in-vivo effects of I3C; tumour-promoting effects of high doses of I3C may be due to activation of aryl hydrocarbon receptor (AhR)-mediated pathways (Riby et al. 2000). Hong et al. (2002) found that 3,3′-diindolylmethane (DIM), a major in-vivo derivative of the putative anticancer agent indole-3-carbinol, could induce apoptosis in breast cancer cells independent of oestrogen receptor status by a process mediated by the modulated expression of the Bax/Bcl-2 family of apoptotic regulatory factors. Degner et al. (2009) found that co-treatment of MCF-7 breast cancer cells with 3,3′-diindolylmethane (DIM) (10 μmol/l) abrogated the xenobiotic 2,3,7,8 tetrachlorodibenzo (p)dioxin (TCDD)-induced recruitment of the aryl hydrocarbon receptor and acetylated histone H4 to the acetylated histone H4 promoter and the induction of COX-2 mRNA and protein levels. The data suggested that naturally occurring modulators of the aryl hydrocarbon receptor such as DIM may be effective agents for dietary strategies against epigenetic activation of COX-2 expression by aryl hydrocarbon receptor agonists. In another study, 3,3′-diindolylmethane (DIM), a putative anticarcinogenic agent formed in the acidic environment of the stomach following consumption of indole-3-carbinol (I3C), inhibited the proliferation of three human breast cancer cell lines, MCF-7, MDA-MB-231 and SKBr-3 and concomitantly inhibited the expression of transcription factor Sp1 and fatty acid synthase (FAS) but not in nontumorigenic human breast epithelial cell line MCF-10A (Saati and Archer 2011).

A major trimeric product of I3C, 5,6,11,12,17,18-hexahydrocyclonona[1,2-b:4,5-b′:7,8-b″]triindole (CTr) was found to be a strong agonist of the oestrogen receptor signalling pathway (Riby et al. 2000; Xue et al. 2005). CTr stimulated the proliferation of oestrogen-responsive MCF-7 cells to a level similar to that produced by estradiol (E(2)) but did not affect the growth of the oestrogen-independent cell line, MDA-MD-231. CTr failed to activate AhR-mediated pathways, consistent with the low-binding affinity of CTr for the AhR reported previously. CTr increased proliferation of oestrogen-dependent breast tumour cells, bound with strong affinity for the oestrogen receptor-alpha (ERalpha) and activated expression of oestrogen (E(2))-dependent genes (Xue et al. 2005). Analysis of growth and cell-cycle arrest of indole-treated human breast cancer cells revealed a striking increase in efficacy of the N-alkoxy indole-3-carbinol (I3C) derivatives that was significantly enhanced by the presence of increasing carbon lengths of the N-alkoxy substituents (Jump et al. 2008). Compared to I3C, the half maximal growth arrest responses occurred at 23-fold lower indole concentration for N-methoxy I3C, 50-fold lower concentration for N-ethoxy I3C, 217-fold lower concentration for N-propoxy I3C and 470-fold lower concentration for N-butoxy I3C. At these lower concentrations, each of the N-alkoxy substituted compounds induced the characteristic I3C response in CDK6 gene expression, CDK6 promoter activity and CDK2-specific enzymatic activity for its retinoblastoma protein substrate and was strongly downregulated. 3-Methoxymethylindole and 3-ethoxymethylindole were approximately as bioactive as I3C, whereas both tryptophol and melatonin failed to induce the cell-cycle arrest, showing the importance of the C-3 hydroxy methyl substituent on the indole ring. The results indicated I3C-based N-alkoxy derivatives to be a novel class of potentially more potent experimental therapeutics for breast cancer.

Indole-3-carbinol was found to inhibit the expression of cyclin-dependent kinase-6 (CDK6) and induced a G1 cell-cycle arrest of human MCF7 breast cancer cells independent of oestrogen receptor signalling (Cover et al. 1998). The antioestrogen tamoxifen also suppressed MCF7 cell DNA synthesis but had no effect on CDK6 expression. Combinations of indole-3-carbinol (I3C) and the antioestrogen tamoxifen inhibited the growth of the oestrogen-dependent human MCF-7 breast cancer cell line more effectively than either agent alone (Cover et al. 1999). This more stringent growth arrest was demonstrated by a decrease in adherent and anchorage-independent growth, reduced DNA synthesis and a shift into the G1 phase of the cell cycle. A combination of I3C and tamoxifen also caused a more pronounced decrease in cyclin-dependent kinase (CDK) 2-specific enzymatic activity than either compound alone but had no effect on CDK2 protein expression. Also, treatment with I3C and tamoxifen eroded expression of the phosphorylated retinoblastoma protein (Rb), an endogenous substrate for the G1 CDKs, whereas either agent alone only partially inhibited endogenous Rb phosphorylation.

Indole-3-carbinol (I3C) could induce a G(1) cell-cycle arrest of human MCF-7 breast cancer cells through inhibition of cyclin-dependent kinase 6 (CDK6) expression by disrupting Sp1 transcription factor interactions with DNA composite element in CDK6 gene promoter (Cram et al. 2001). Sarkar et al. (2003) found that translocation of Bax to the mitochondria followed by mitochondrial depolarization and cytochrome C release was necessary and important that may be responsible for selective induction of apoptosis cell death by indole-3-carbinol (I3C) treatment of breast cancer cells. Matsuzaki et al. (2004) demonstrated that I3C activated the cyclin-dependent kinase (CDK) inhibitor p15INK4b gene through its promoter, accompanied by cell growth inhibition in human adult keratinocyte HaCaT cells. Studies showed that one mechanism by which indole-3-carbinol (I3C)-mediated anticancer effects was by stimulating expression of the interferon IFN-gammaR1 and augmenting the IFN-gamma response in MCF-7 human breast cancer cells (Chatterji et al. 2004).

Treatment of highly invasive MDA-MB-231 breast cancer cells with indole-3-carbinol (I3C) shifted the stable accumulation of cyclin E protein from the hyperactive lower-molecular-mass 35-kDa form associated with cancer cell

proliferation and poor clinical outcomes to the 50-kDa cyclin E form typically expressed in normal mammary tissue (Nguyen et al. 2008). It was demonstrated that I3C, but not its natural dimer, 3,3′-diindolylmethane, disrupted proteolytic processing of the 50-kDa cyclin E into the lower-molecular-mass forms by direct inhibition of human neutrophil elastase enzymatic activity. The results suggested that the direct I3C inhibition of elastase enzymatic activity implicated the potential use of this indole, or related compounds, in targeted therapies of human breast cancers where high elastase levels were correlated with poor prognosis.

Both indole-3-carbinol (I3C) and genistein induced the expression of both breast cancer susceptibility genes (BRCA1 and BRCA2) in breast (MCF-7 and T47D) and prostate (DU-145 and LNCaP) cancer cell types, in a time- and dose-dependent fashion (Fan et al. 2006). Induction of the BRCA genes occurred at low doses of I3C (20 μM) and genistein (0.5–1.0 μM), suggesting potential relevance to cancer prevention. A combination of I3C and genistein afforded greater than expected induction of BRCA expression. Studies using small interfering RNAs (siRNAs) and BRCA expression vectors suggested that the phytochemical induction of BRCA2 was due, partly to BRCA1. Functional studies suggested that I3C-mediated cytotoxicity was, in part, dependent upon BRCA1 and BRCA2. It was also shown that the phytochemical induction of BRCA1 expression was due, in part, to endoplasmic reticulum stress response signalling. Oestrogen receptor (ER)alpha is a critical target of therapeutic strategies to control the proliferation of hormone-dependent breast cancers, and studies had shown that indole-3-carbinol (I3C) eroded ERalpha expression (Marconett et al. 2010). It was found that I3C-dependent activation of the aryl hydrocarbon receptor (AhR) initiated Rbx-1 E3 ligase-mediated ubiquitination and proteasomal degradation of ERalpha protein. I3C inhibited endogenous binding of ERalpha with the 3′-enhancer region of GATA3 and disrupted endogenous GATA3 interactions with the ERalpha promoter, leading to a loss of GATA3 and ERalpha expression. The preclinical results implicated I3C to be a novel anticancer agent in human cancers that coexpress ERalpha, GATA3 and AhR, a combination found in a large percentage of breast cancers but not in other critical ERalpha target tissues essential to patient health. In-vitro and in-vivo studies in a mouse xenograft model showed that indole-3-carbinol (I3C)-induced activation of the ATM-Chk2 pathway and degradation of cell division cycle 25A (Cdc25A) phosphatase represented a novel molecular mechanism of I3C in arresting the G(1) cell cycle and inhibiting the growth of breast cancer cells (Wu et al. 2010). The finding that I3C induced Cdc25A degradation suggested the potential use of this agent for preventing and treating cancers and other human diseases with Cdc25A overexpression.

Isothiocyanates (ITCs) and indoles derived from cruciferous vegetables had been reported to possess growth-inhibiting and apoptosis-inducing activities in cancer cell lines in-vitro (Pappa et al. 2007). ITCs like sulforaphane (SFN) were cytotoxic, whereas indoles including indole-3-carbinol or its condensation product 3,3′-diindolylmethane (DIM) acted by cytostatic mechanisms in human colon cancer cell lines. In cultured 40–16 colon carcinoma cells, at a total drug concentration of 2.5 microM, all combinations of SFN and DIM were antagonistic. SFN (10 μM) in combination with DIM (10 μM) resulted in strong G(2)/M cell-cycle arrest, which was not observed with either compound alone. The results indicated that cytotoxic concentrations of SFN:DIM combinations affected cell proliferation colon cancer cell synergistically.

Indole-3-carbinol (I3C) inhibited the growth of PC-3 prostate cancer cells in-vitro by inducing G1 cell-cycle arrest leading to apoptosis and regulating the expression of apoptosis-related genes (Chinni et al. 2001). They found that I3C-induced apoptosis was partly mediated by the inhibition of Akt kinase activation, resulting in the alterations in the downstream regulatory molecules of Akt/PI3K cell survival pathway, Bcl-x(L) and BAD proteins in PC-3 prostate cancer cells (Chinni and Sarkar 2002). Additionally, I3C abolished epidermal growth factor (EGF)-induced activation of Akt in PC-3 cells.

Zhang et al. (2003) reported that I3C suppressed the growth of LNCaP prostate carcinoma cells in a dose-dependent manner by inducing a G1 block in cell-cycle progression. I3C selectively inhibited the expression of CDK6 protein and transcripts and strongly stimulated the production of the p16 CDK inhibitor. In LNCaP prostate carcinoma cells, I3C treatment inhibited production of PSA, whereas combinations of I3C and the androgen antagonist flutamide more effectively inhibited DNA synthesis and PSA levels compared with either agent alone. In another study, I3C was shown to induce a G(1) cell-cycle arrest in the cells of human lymph node carcinoma of prostate (LNCaP) through regulation of specific G(1)-acting cell-cycle components and to inhibit androgen receptor expression and downregulation of androgen responsiveness in human prostate cancer cells as a part of its antiproliferative mechanism (Hsu et al. 2005). Further, they found that indole-3-carbinol induced G1 arrest of LNCaP human prostate cancer cells necessitating the induced production of the activated phosphorylated forms of p53 tumour suppressor protein, which stimulated transcription of the cyclin-dependent kinase (CDK) 2 inhibitor p21 (Hsu et al. 2006). Wang et al. (2012) found that indole-3-carbinol (I3C) and 3,3′-diindolylmethane (DIM) exerted concentration-dependent pleiotropic effects on prostate cancer cells via signalling pathways that included proliferation, cell cycle and nuclear receptors-mediated pathways. However, the efficacies and mechanisms of these compounds varied according to differences in effective concentrations, a differential effect on androgen receptor binding and a differential effect on xenobiotic metabolic pathway through aryl hydrocarbon receptor-dependent and receptor-independent mechanism. Both compounds inhibited androgen and oestrogen-mediated pathways and induced xenobiotic metabolism pathway at 1–5 μM. In contrast-induced cyclin inhibitors, indicators of stress/DNA damage only at ≥25 μM.

In-vitro studies by Takada et al. (2005) demonstrated that indole-3-carbinol (I3C) suppressed nuclear factor-kappaB (NF-kappaB) and IkappaBalpha kinase activation, inhibited expression of NF-kappaB-regulated antiapoptotic and metastatic gene products and enhanced apoptosis in myeloid and leukaemia cells. I3C suppressed IkappaBalpha kinase, IkappaBalpha phosphorylation, IkappaBalpha ubiquitination, IkappaBalpha degradation, p65 phosphorylation, p65 nuclear translocation, p65 acetylation and NF-kappaB-dependent reporter gene expression. The NF-kappaB-regulated gene products cyclin D1, cyclooxygenase-2 (COX-2), matrix metalloproteinase-9 (MMP-9), survivin, inhibitor of apoptosis protein 1 (IAP1), IAP2, X chromosome-linked IAP (XIAP), Bcl-2, Bfl-1/A1, TNF receptor-associated factor-1 (TRAF1) and Fas-associated death domain protein-like interleukin-1-beta-converting enzyme inhibitory protein (FLIP) were all downregulated by indole-3-carbinol. Another in-vitro study showed that indole-3-carbinol (I3C) inhibited cell viability of human T-cell leukaemia virus type-infected T-cell lines and adult T-cell leukaemia/lymphoma cells in a dose-dependent manner but not uninfected T-cell lines and normal peripheral blood mononuclear cells (Machijima et al. 2009). I3C prevented the G1/S transition by reducing the expression of cyclin D1, cyclin D2, Cdk4 and Cdk6 and induced apoptosis by reducing the expression of XIAP, survivin and Bcl-2 and by upregulating the expression of Bak. The induced apoptosis was associated with activation of caspase-3, -8 and -9 and poly(ADP-ribose) polymerase cleavage. I3C also suppressed IkappaBalpha phosphorylation and JunD expression, resulting in inactivation of NF-kappaB and AP-1.

In-vitro, indole-3-carbinol (I3C) had been shown to suppress the proliferation of various tumour cells including breast cancer, prostate cancer, endometrial cancer, colon cancer and leukaemic cells; induce G1/S arrest of the cell cycle; and induce apoptosis (Aggarwal and Ichikawa 2005). The cell-cycle arrest involved downregulation of cyclin D1, cyclin E, cyclin-dependent kinase (CDK) 2, CDK4 and CDK6 and upregulation of p15, p21 and p27. Apoptosis by I3C involved downregulation of antiapoptotic gene products, including Bcl-2, Bcl-xL, survivin, inhibitor of apoptosis protein (IAP), X

chromosome-linked IAP (XIAP) and Fas-associated death domain protein-like interleukin-1-beta-converting enzyme inhibitory protein (FLIP); upregulation of proapoptotic protein Bax; release of mitochondrial cytochrome C; and activation of caspase-9 and caspase-3. Under acidic conditions, 13C had been reported to be converted to a series of oligomeric products (e.g. 3,3′-diindolylmethane a major component) thought to be responsible for its biological effects in-vivo.

In-Vivo Studies

In-vivo, I3C was found to be a potent chemopreventive agent for hormonal-dependent cancers such as breast and cervical cancer (Aggarwal and Ichikawa 2005). These effects were found to be mediated through its ability to induce apoptosis, inhibit DNA-carcinogen adduct formation and suppress free radical production, stimulate 2-hydroxylation of estradiol and inhibit invasion and angiogenesis. Numerous studies had indicated that I3C also had a strong hepatoprotective activity against various carcinogens. Initial clinical trials in women had shown I3C to be a promising agent against breast and cervical cancers.

Indole-3-carbinol (I3C) was found to be an inhibitor in several experimental animal models of carcinogenesis by polynuclear aromatic hydrocarbons or aflatoxin B1 (AFB1) when administered prior to or during carcinogen exposure (Bailey et al. 1987). Pre-initiation exposure to I3C reduced AFB1-initiated hepatocellular carcinomas in trout, but post-initiation I3C exposure strongly enhanced the tumour incidence above the positive AFB1 control.

Studies showed that feeding of rats with S-methyl methanethiosulfonate (MMTS) isolated from cauliflower prevented azoxymethane-induced colon carcinogenesis (Kawamori et al. 1995). In experiment 1, feeding of 100 ppm MMTS for 5 weeks significantly decreased the number of aberrant crypt foci/colon. Colonic mucosal ornithine decarboxylase activity and the number of silver-stained nucleolar organizer regions per nucleus in colonic epithelium were significantly decreased by MMTS treatment compared with those of azoxymethane alone. In experiment 2, incidence of intestinal neoplasms of rats fed MMTS-containing diets after azoxymethane exposure was reduced in a dose-dependent manner. Feeding of MMTS during the post-initiation phase decreased the number of aberrant crypt foci/colon, colonic ornithine decarboxylase activity, 5-bromodeoxyuridine-labelling index in colonic epithelium and polyamine level in blood compared with those of azoxymethane alone. In another study, compared with control rats given the carcinogen, 2-amino-3-methylimidazo[4,5-f]quinoline (IQ) alone, 0.1 % indole-3-carbinol (I3C) treatment suppressed the multiplicity of IQ-induced colon tumours in male F344 rats and chlorophyllin, a water-soluble derivative of chlorophyll in leafy vegetables, inhibited in a dose-related manner the incidence of IQ-induced liver tumours (Xu et al. 2001). However, 0.001 % chlorophyllin increased significantly the multiplicity of 1,2-dimethylhydrazine-induced colon tumours while having no effect on the colon tumours induced by IQ. The results indicated that both the choice of carcinogen and the dose of the tumour modulator could be important determinants of the events that occur during post-initiation exposure to chlorophyllin or I3C. Based on the present findings and data in the literature, chlorophyllin and I3C could act as tumour promoters or anticarcinogens, depending upon the test species, initiating agent and exposure protocol.

The results of in-vitro studies by Rahman et al. (2006) suggested that indole-3-carbinol (I3C) could be a promising agent for the prevention and/or treatment of breast cancer bone metastasis. In the severe combined immunodeficient (SCID)-human mouse model of experimental bone metastasis with MDA-MB-231 breast cancer cell line, I3C significantly inhibited MDA-MB-231 bone tumour growth. The results were correlated with the downregulation of NF-kappaB. Further, I3C significantly inhibited the expression of multiple genes involved in the control of metastasis and invasion in-vitro and in-vivo, especially the expression of chemokine receptor CXCR4 and matrix metalloproteinases MMP-9 along with pro-MMP-9, with concomitant

decrease in Bcl-2 and increase in the proapoptotic protein Bax. They concluded that the CXCR4/NF-kappaB pathway was critical during I3C-induced inhibition of experimental breast cancer bone metastasis. 3′-Diindolylmethane (DIM), a major in-vivo acid-catalyzed condensation product of I3C, also showed some benefit in breast cancer (Rahman and Sarkar 2005). DIM was found to induce apoptotic processes in MCF10A-derived malignant (MCF10CA1a) cell lines but not in nontumorigenic parental MCF10A cells. DIM specifically inhibited Akt kinase activity and abrogated the epidermal growth factor-induced activation of Akt in breast cancer cells, similar to those observed for I3C. Also DIM reduced phosphorylation of IkappaBalpha, an inhibitor of NF-kappaB. In-vitro and in-vivo studies in a mouse xenograft model showed that indole-3-carbinol (I3C)-induced activation of the ATM-Chk2 pathway degradation of cell division cycle 25A (Cdc25A) phosphatase arrested the G(1) cell cycle and inhibited the growth of breast cancer cells (Wu et al. 2010). The authors suggested that I3C had potential for preventing and treating cancers and other human diseases with Cdc25A overexpression.

Intragastric administration of indole-3-carbinol (I3C) and phenethyl isothiocyanate (PEITC), from *Brassica* plants (cauliflower, broccoli, cabbage, etc.) to male Fischer rats for 5 days, was found to significantly increase bile excretion and γ-glutamyl transpeptidase (γ-GTP) activity compared to control rats, but no difference was observed in the pancreatic juice (Ishibashi et al. 2012). Increases of bile excretion and γ-GTP activity in bile might be a factor involved in the anticancer effect of I3C and PEITC.

Indole-3-carbinol suppressed growth of murine WEHI-3 leukaemia cells in-vitro and caused morphological changes (DNA fragmentation and chromatin condensation) in a concentration- and time-dependent manner (Lu et al. 2012). It elicited G0/G1 phase arrest and the levels of cyclin A, cyclin D and CDK2 and increased the levels of p21, cytochrome C, FADD, GADD153, GRP78 and caspase-12 as well as induced activities of caspase-3, -8 and -9. In vivo, I3C increased the level of T cells and decreased the level of macrophages in WEHI-3 leukaemia mice. I3C also reduced the weights of liver and spleen, and it promoted phagocytosis by macrophages as compared to the non-treated leukaemia mice group.

Studies showed that supplementation of the diet of carcinogen (a mixture of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and benzo[a]pyrene (BaP))-treated mice with indole-3-carbinol (I3C) reduced the elevated levels of pulmonary surfactant-associated protein C (SP-C), L-plastin, annexin A1 and haptoglobin to that of untreated controls (Kassie et al. 2007). The results suggested that the lung tumour chemopreventive activity of I3C might be related to modulation of carcinogen-induced alterations in protein levels.

Preliminary human trials had demonstrated that I3C was well tolerated and had a sustained oestrogen-modifying effect and to be a good candidate for clinical trial in women at increased risk of developing breast cancer (Brignall 2001). *Brassica* intake has been associated with reduced risk of colon, lung, bladder, breast, prostate and other cancers (Fowke et al. 2006). In a randomized crossover trial ($n=20$) comparing the effects of a *Brassica* vegetable supplementation intervention against a micronutrient and fibre (M+F) supplementation, *Brassica* intervention was found to significantly decrease urinary F2-isoprostane levels (F2-iP), a stable biomarker of systemic oxidative stress by 21 % compared to baseline and (M+F) intervention (Fowke et al. 2006). Their results suggested that *Brassica* consumption reduces systemic oxidative stress independent of the vitamin and mineral content of these vegetables.

Hecht et al. (2004) investigated the effects of cruciferous vegetable (including cauliflower, broccoli) consumption on the metabolism of the tobacco-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in 84 smokers. They found that glucobrassicins, which release indole-3-carbinols on chewing, were the major glucosinolates in seven of the nine cruciferous vegetables, accounting for 70.0–93.2 % of all glucosinolates in these vegetables. There was a significant correlation ($P=0.01$) between increased consumption of glucobrassicins and decreased levels of metabolites of NNK:

4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronides (NNAL-Glucs) in urine after adjustment for number of cigarettes smoked per day. Their results were consistent with those of previous studies, which demonstrated that indole-3-carbinol decreased levels of urinary NNAL probably by inducing hepatic metabolism of NNK.

In a prospective study of fruit and vegetable intake and risk of prostate cancer, involving 1,338 patients with prostate cancer among 29,361 men (average follow-up = 4.2 years) in the screening arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, Kirsh et al. (2007) found that a high intake of cruciferous vegetables, including broccoli and cauliflower, may be associated with reduced risk of aggressive prostate cancer, particularly extraprostatic disease.

Review Studies

The results of 7 cohort studies and 87 case-control studies on the association between *Brassica* consumption and cancer risk showed inverse associations between the consumption of cabbage, cauliflower and broccoli and risk of lung cancer; between the consumption of Brassicas and risk of stomach cancer; between broccoli consumption and risk of all cancers taken together; and between *Brassica* consumption and the occurrence of second primary cancers (Verhoeven et al. 1996). Of the case-control studies, 67 % showed an inverse association between consumption of total *Brassica* vegetables and risk of cancer at various sites. For cabbage, broccoli, cauliflower and Brussels sprouts, these percentages were 70, 56, 67 and 29 %, respectively. Although the measured effects might have been distorted by various types of bias, it was concluded that a high consumption of *Brassica* vegetables was associated with a decreased risk of cancer.

Hepatoprotective Activity

Indole-3-carbinol did not show an enhancement effect on quinone reductase activity (associated with anticarcinogenic processes), but its acidic derivative, indolo[3.2-b]carbazole (ICZ), increased the expression of quinone reductase mRNA, which then caused the augmentation of quinone reductase activity in murine Hepa-1 and human (HepG2) hepatoma cells (Chen and Yang 2002). Indole-3-carbinol (I3C) was found to have protective effect in-vitro on acute ethanol-induced hepatotoxicity and acetaldehyde-stimulated hepatic stellate cells (HSC) activation using precision-cut liver slices (Guo et al. 2010). It was found that the hepatoprotective effect may be associated with the regulation of ethanol metabolic enzymes, attenuation of oxidative injury and acceleration of collagen degradation. Ping et al. (2011b) found that I3C could significantly inhibit hepatic stellate cell proliferation during the course of liver fibrosis, in a concentration-dependent manner with or without platelet-derived growth factor-BB (PDGF-BB) stimulation. I3C could also block hepatic stellate cell in the G(0)/G(1) phase from entering the S phase. They concluded that I3C could inhibit the proliferation of hepatic stellate cell by blocking the NADPH oxidase/reactive oxygen species/p38 MAPK signal pathway. The results suggested that dietary I3C might play a novel role in prevention and treatment of chronic liver disease. Studies showed that indole-3-carbinol (I3C) treatment significantly reduced the number of activated hepatic stellate cells (HSC) in the livers of rats with liver fibrosis (Ping et al. 2011a). I3C significantly increased the HSC-T6 apoptosis rate and the expression ratio of Bax to Bcl-2 by the inhibitor of κB kinase α/inhibitor of κB-α/nuclear factor-κB pathway. Administration of cauliflower extract for 5, 10 and 15 days was found to reduce the level of alanine transaminase and improved the microscopic appearance of hepatic cells in Wistar rats given a single dose of theophylline (Sunarsih et al. 2012). Ethanol extract of cauliflower exhibited cytotoxic effect against hepatic carcinoma induced by diethylnitrosamine (DEN) (1 µl/100 g b.wt.) in rats (Hamed et al. 2012). The extract elicited 33.30 % inhibition of carcinogenic hepatic cells.

Hypolipidaemic Activity

Indole-3-carbinol (I3C) was found to dose-dependently inhibit apolipoprotein B-100 (apoB) production in HepG2 cells and to have beneficial effects on lipid synthesis that could contribute to their potential cardioprotective effects (Maiyoh et al. 2007). Significant decreases in cellular lipid synthesis, including triglycerides and cholesterol esters, were observed in HepG2 cells treated with I3C, indicating limited lipid availability to be a major factor in the regulation of apoB secretion. The decrease in triglycerides synthesis was associated with significantly decreased diacylglycerol acyltransferase-1 and -2 activity and reduced fatty acid synthase (FASN) gene expression. The decreased cholesterol esters synthesis was associated with significantly decreased acyl CoA:cholesterol acyltransferase gene expression and activity.

In-vitro studies showed that indole-3-carbinol (I3C) ameliorated adipogenesis by activating SIRT1 (silent mating type information regulation 2 homolog 1), a NAD(+)-dependent deacetylase sirtuin in 3T3-L1 (adipose-like) cells (Choi et al. 2012b). I3C treatment reduced mRNA levels of adipogenic genes that encode for C/EBPα, PPARγ2, FAS and aP2 in 3T3-L1 cells but not in SIRT1 knockdown cells. Indole-3-carbinol supplementation significantly ameliorated 40 % energy, high fat diet (HFD)-induced increases in mice body weight gain, visceral fat pad weights and plasma lipid levels (Choi et al. 2012a). It was found that indole-3-carbinol prevented obesity and metabolic disorders in mice through multiple mechanisms including decreased adipogenesis and inflammation, along with activated thermogenesis.

Antimutagenic Activity

S-methyl methanethiosulfonate isolated from cauliflower was found to have antimutagenic activity to *Escherichia coli* B/r WP2 (Nakamura et al. 1993). High pressure or freezing treatment of cauliflower juice exerted positive AFTB1 (aflatoxinB1) mutagen inhibition. In the Ames mutagenic test using *Salmonella typhimurium* TA 100, high pressure or freezing treatment of cauliflower juice exerted strongly positive test MNU (2-nitroso-2-methylurea) mutagen inhibition (Totušek et al. 2011). In the Ames mutagenic test using *Salmonella typhimurium* TA 98, high pressure or freezing treatment of cauliflower juice exerted strongly positive test on IQ (2-amino-3-methyl-3H-imi-dazo-[4,5-*f*]quinoline) mutagen inhibition.

Antiinflammatory Activity

In-vitro studies showed that 2-phenylethyl isothiocyanate (PEITC) and indole-3-carbinol (I3C), from *Brassica* vegetables, inhibited lipopolysaccharide (LPS)- and interferon-gamma (IFN-gamma)-induced NO production in RAW 264.7 cells, and this inhibition was associated with lowering the expression of iNOS protein and mRNA (Chen et al. 2003). In contrast, indolo[3,2- b]carbazole (ICZ), a derivative of I3C, had no significant effect on the stimulated NO production. Inhibition of iNOS expression or activity is an important therapeutic goal.

In vitro studies showed that indole-3-carbinol (I3C), a natural hydrolysis product of glucobrassicin, inhibited LPS-induced inflammatory response by blocking TRIF-dependent signalling pathway Raw264.7 cells and THP-1 cells (Jiang et al. 2013). Further, I3C suppressed the infiltration of immune cells into the lung and proinflammatory cytokine production such as IL-6, TNF-α in broncho-alveolar lavage fluid (BALF) in the LPS-induced acute lung injury mouse model and also suppressed IL-1β secretion in nigericin treated in-vivo model. The results suggested that indole-3-carbinol may provide a valuable therapeutic strategy in treating various inflammatory diseases.

Antiplatelet and Antithrombotic Activity

The results of in-vitro and in-vivo studies suggested that indole-3-carbinol, present in cauliflower, could be a potent antithrombotic agent with antiplatelet activity through the inhibition of GP IIb/IIIa receptor and thromboxane B2 formation (Park

et al. 2008). Indole-3-carbinol significantly and dose-dependently inhibited collagen-induced platelet aggregation in human platelet-rich plasma and fibrinogen binding to the platelet surface glycoprotein IIb/IIIa (GP IIb/IIIa) receptor. Further, the levels of thromboxane B2 and prostaglandin E2 (PGE2) in collagen-stimulated human platelet-rich plasma were significantly inhibited. In-vivo, it dose-dependently suppressed the death of mice with pulmonary thrombosis induced by intravenous injection of collagen and epinephrine.

Antihyperglycaemic Activity

Cauliflower extract was found to decrease the hyperglycaemic but not the area under the glucose tolerance curve (Roman-Ramos et al. 1995).

Microbial Activity

Fresh cauliflower juice was found to be effective both in inhibiting the growth of blastoconidia and reducing the appearance of *C. albicans* germ tubes (Sisti et al. 2003). The juice also inhibited the growth of some pathogenic, filamentous fungi.

Blood Labelling Studies

The cauliflower leaf extract did not alter the labelling of blood elements with technetium-99 m; however, it abolished the lethal effect of SnCl(2) on the *Escherichia coli* culture (Lima et al. 2002). It was suggested that the oxidant action of the substances of the extract would not be strong enough to oxidize the stannous ions altering the 99mTc-labelling. However, the referred substances could oxidize these ions sufficiently to protect the *E. coli* culture against the lethal effect of the stannous ion.

Antiulcerogenic Activity

Oral administration of indole-3-carbinol alone or in combination with omeprazole to aspirin-ulcerated rats for 7 days produced a profound protection to the gastric mucosa from injury induced by aspirin (El-Shinnawy et al. 2012).

Skin Protective Activity

Brassica degradation products of sulforaphane (SFN) and glucobrassicin, the precursor of indole-3-carbinole (I3C) and ascorbigen (ABG), was tested on their efficacy in inducing cytoprotective genes in the skin, namely, Nrf2-dependent gene expression in human keratinocytes in culture (Wagner et al. 2010). They found SFN but not ABG, and its precursors I3C and ascorbic acid induced Nrf2-dependent gene expression at a relatively low concentration (5 μmol/l). This induction was accompanied by an increase in mRNA and protein levels of NADPH quinone oxidoreductase 1, heme oxygenase 1 and gamma-glutamylcysteine synthetase. Also SFN elevated cellular glutathione levels and antagonized tumour necrosis factor-alpha-induced NF-kappaB transactivation. They concluded that sulforaphane treatment may present a strategy for enhancing the cellular defence mechanisms in skin.

Adverse Immunotoxic Activity

Studies found that oral administration of 3,3′-diindolylmethane (DIM) to neonatal mouse induced multiple immunotoxic effects including decreases in various immune cells (F4/80(+), CD11c(+), CD19(+) and CD3(+) cells) in the spleen, induction of splenic white pulp atrophy, an increase in immune cell apoptosis and decreased expression of various toll-like receptors (TLRs) in the spleen and small intestine (Roh et al. 2011). Also DIM administration led to deterioration of rotavirus-induced intestinal disease and delayed viral clearance in the intestine.

Allergy Problems

Work-related symptoms such as rhinitis, conjunctivitis, asthma and urticaria caused by broccoli

and cauliflower pollen were reported by 44 % of the participants (24/54), of whom all but one had positive skin prick tests for cauliflower- and/or broccoli-pollen/flower extracts, and 58 % (14/24) had positive radioallergosorbent test (RAST) results (Hermanides et al. 2006). Symptoms had developed within the first 2 years in 33 % of the patients. Six patients had to stop or change work.

Other Uses

The antifungal activity of phytoalexins caulilexins A–C against the economically important phytopathogenic fungi *Leptosphaeria maculans, Rhizoctonia solani* and *Sclerotinia sclerotiorum* was reported (Pedras et al. 2006).

Comments

Refer also to notes under broccoli—*Brassica oleracea* (Italica Group).

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Brassica oleracea (Italica Group)

Scientific Name

***Brassica oleracea* L. (Italica Group)**

Synonyms

Brassica oleracea L. var. *italica* Plenck, *Brassica botrytis* subsp. *italica* Lizg., *Brassica cauliflora* subsp. *simplex* Lizg., *Brassica oleracea* var. *asparagoides* Gmel., *Brassica oleracea* var. *botrytis* subvar. *cymosa* Thell.

Family

Brassicaceae

Common/English Names

Asparagus Broccoli, Broccoli, Calabrese, Cape Broccoli, Heading Broccoli, Green Heading Broccoli, Purple Heading Broccoli, Sprouting Broccoli, Winter Cauliflower

Vernacular Names

Afrikaans: Spruitjes, Spruitkool, Winterblomkool, Winterkool
Albanian: Brokoli
Arabic: Brokli
Brazil: Arroz De Brócolis, Brócolis Americano, Brócolos (Portuguese)
Breton: Brouskaolenn
Bulgarian: Vid Cvetno Sele
Catalan: Broquil
Chinese: Gaai Choi Fa, Qing Hua Cai, Sai Lan Fa (Cantonese), Jie Cai Hua, Lu Hua Cai, Nen Jing Hua Ye Cai, Yang Ye Cai Hua, Yi Da Li Jie Lan, Ying Hua Gan Lan (Mandarin)
Croatian: Kelj-Pupčar, Prokula, Prokulica
Czech: Brokolice, Brukev Brokolice
Danish: Broccoli, Brokkoli
Dhivehi: Burokol
Dutch: Broccoli, Broccolikiemen, Broccolispruiten
Eastonian: Asparkapsas
Esperanto: Brokolo
Finnish: Parsakaali
French: Brocoli Asperge, Brocoli Branchu, Chou Broccoli
Frisian: Brokolli
Gaelic: Callish Rangagh
German: Braunkohl, Brokkoli, Spargelkohl, Sprossenbrokkoli
Greek: Brókola
Haitian: Bwokoli (Creole)
Hungarian: Brokkoli
Icelandic: Spergilkál
India: Phulagobhi, Phoolagobhee, Fulagobhi (Hindi), Brēākkeāḷi (Malayalam), Brōkalī (Marathi)
Indonesian: Brokali
Italian: Broccolo, Cavolo Broccoli, Cavolo Broccolo, Cavolo Romano

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Japanese: Burokkorii, Italia-Kanran, Karifurawaa
Korean: Beu Ro Kol Li, Nok-Saek-Kkoch-Yang-Bae-Chu
Latvian: Brokoli
Lithuanian: Brokolis
Macedonian: Brokoli
Malaysia: Brokaoli
Maltese: Brokkli
Norwegian: Bróculo, Brokkoli
Philippines: Brokoli (Cebuano), Broccoli (Illoko)
Polish: Brokul, Brokuly, Kapusta Szparagowa
Portuguese: Brócolis, Brócos, Brócolos, Bróculos
Russian: Brokoli
Serbian: Brokoli
Sicilian: Bròcculu, Ciurettu
Slováščina: Brokolica
Slovenčina: Brokolica
Romanian: Broccoli
Provencale: Brokoli
Spanish: Brécol, Brecolera, Brócoli, Bróculi
Swedish: Sparriskål
Thai: Bř̀xkh Kho Lì̀, Sêung Kláai Gà Hŏr
Turkish: Brokoli, Italya Lahanasi
Ukrainian: Brokoli
Vietnamese: Cải Bông Xanh

Origin/Distribution

Broccoli and cauliflower are thought to have evolved in Roman times from wild or primitive cultivated forms of *Brassica oleracea* in the eastern Mediterranean region. A remarkable diversity of cauliflower and broccoli-like vegetables has been developed in Italy.

The leading cauliflower- and broccoli-producing countries in terms of total production (tonnes) are as follows: China, 8,935,000; India, 6,745,000; Spain, 513,783; Mexico, 427,884; Italy, 420,989; France, 364,558; United States, 301,590; Poland, 297, 649; Pakistan, 227,591; Egypt, 201,200; United Kingdom, 180,577; Bangladesh, 168,238; Turkey, 162,134; Japan, 152,400; Germany, 144,136; Indonesia, 113,492; Algeria, 105,829; Morocco, 104,569; and Belgium, 99,660 (FAO 2012).

Agroecology

Broccoli requires a cool, moist subtemperate climate, with average daily temperatures of 15–20 °C. Higher temperatures result in no flower-head production, and too low temperature results in small button heads. The plant is cold tolerant, but is not frost hardy. It thrives best in well-drained, moist, fertile loamy, sandy loam or loamy clay soils, rich organic matter and an alkaline pH of 6–7 with sufficient soil boron. Boron deficiency results in blackened hollow stem.

Edible Plant Parts and Uses

Flowering head consisting of unopened flower buds and fleshy upper portion of the stem is consumed as vegetables. Flower head is divided into smaller bits and can be eaten raw or lightly cooked, steam, microwave and stir-fry and eaten as mixed salads or in pickles. The stems need to be cooked longer. Broccoli is available as quick-frozen vegetables and processed in dried mixtures of soup vegetables.

Botany

Erect, glabrous, annual or biennial herb up to 80 cm tall at the mature vegetative stage, up to 130 cm when flowering with unbranched, waxy stem thickening upwards; a shallow, strongly branched tap root system. Leaves are thick, somewhat leathery, smooth oblong, simple, alternate, lamina blade ovate to oblong, up to 80 cm × 40 cm, undulate or irregularly incised to almost entire, greyish blue to green, shortly petiolate and exstipulate (Plate 1). Inflorescence a terminal paniculate raceme up to 70 cm long, the thick, fleshy branched inflorescence begins as a compact slightly dome-shaped head up to 40 cm across (Plates 1, 2 and 3) and loses it compactness as the flower stalk enlarges and flowers open. The inflorescence produces bisexual cross-shaped, tetramerous flowers on 1–2 cm pedicel, with four erect, oblong sepals; four yellow

Plate 1 Broccoli leaves and flower head

Plate 2 Harvested broccoli

Plate 3 Close-up of broccoli flower head

obovate, clawed petals; six stamens; superior ovary-2-loculed; and a globose stigma. Fruit a slender, linear silique 5–10 cm × 0.5 cm, with a tapering beak 5–15 mm long, dehiscent when dry, 20–40 seeded. Seeds globose, 2–4 mm in diameter, finely reticulate, brown.

Nutritive/Medicinal Properties

Nutrients and Phytochemicals

Nestle (1997) listed the following potentially anticarcinogenic attributes and components of broccoli and other cruciferous vegetables: low fat, low energy, macronutrients, micronutrients, vitamin A, vitamin C, vitamin E, folic acid, selenium, fibre, carotenoids, coumarins, dithiolthiones, flavonoids, glucosinolates, indoles, isothiocyanates, phenols and terpenes.

The proximate nutrient value per 100 g edible portion of raw broccoli (USDA 2012) was reported as follows: water, 89.30 g; energy, 34 kcal (141 kJ); protein, 2.82 g; total lipid, 0.37 g; ash, 0.87 g; carbohydrate, 6.64 g; total dietary fibre, 2.6 g; total sugars, 1.7 g; sucrose, 0.10 g; glucose, 0.49 g; fructose, 0.68 g; lactose, 0.21 g; maltose, 0.21 g; minerals Ca, 47 mg; Fe, 0.73 mg; Mg, 21 mg; P, 66 mg; K, 316 mg; Na, 33 g; Zn, 0.41 mg; Cu, 0.049 mg; Mn, 0.210 mg; Se, 2.5 µg); vitamins vitamin C, 89.2; thiamine, 0.071 mg; riboflavin, 0.117 mg; niacin, 0.639 mg; pantothenic acid, 0.573 mg; vitamin B 6, 0.175 mg; total folate, 63 µg; total choline, 18.7 mg; betaine, 0.1 mg; vitamin A, 623 IU; vitamin A, 31 µg RAE; β-carotene, 361 µg; lutein + zeaxanthin, 1,403 µg; vitamin E (α-tocopherol), 0.78 mg; β-tocopherol, 0.01 mg; γ-tocopherol, 0.17 mg; vitamin K (phylloquinone), 101.6 µg; total saturated fatty acids, 0.039 g; 14:0 (myristic acid), 0.001 g; 16:0 (palmitic acid), 0.029 g; 18:0 (stearic acid), 0.006 g; 20:0 (arachidic acid), 0.002 g; 22:0 (behenic acid), 0.002 g; total monounsaturated fatty acids, 0.011 g; 17:1 (heptadecenoic acid), 0.001 g; 18:1 undifferentiated, 0.010 g; total polyunsaturated fatty acids, 0.038 g; 18:2 undifferentiated (oleic acid), 0.017 g; 18:3 undifferentiated (linolenic acid), 0.021 g; and amino acids tryptophan, 0.033 g; threonine, 0.088 g; isoleucine, 0.079 g; leucine, 0.129 g; methionine, 0.038 g; cystine, 0.028 g; phenylalanine, 0.117 g; tyrosine, 0.050 g; valine, 0.125 g; arginine, 0.191 g; histidine, 0.059 g; alanine, 0.104 g; aspartic acid, 0.325 g; glutamic acid, 0.542 g;

glycine, 0.089 g; proline, 0.110 g; and serine, 0.121 g.

Maximum mean vitamin C (52.9 mg/100 g), β-carotene (0.81 mg/100 g), lutein (0.68 mg/100 g), dl-α-tocopherol content (0.47 mg/100 g) and phenol content (63.4 mg/100 g) were recorded in broccoli (Singh et al. 2007). The following carotenoids were found in broccoli: neoxanthin, neochrome, violaxanthin, luteoxanthin, auroxanthin, lutein-5,6-epoxide, flavoxanthin, lutein and β-carotene (Khachik et al. 1986, 1991). Studies found substantial variation in α-carotene, β-carotene, α-tocopherol, γ-tocopherol and ascorbate contents within and between subspecies of *Brassica oleracea* (50 broccoli and 13 cabbage, kale, cauliflower and Brussels sprouts accessions) (Kurilich et al. 1999). Kale had the highest levels of vitamins, followed by broccoli and Brussels sprouts with intermediate levels and then by cabbage and cauliflower, with comparatively low concentrations. Variability in vitamin content among the broccoli accessions suggested potential health benefits associated with consumption were genotype dependent. Broccoli and other vegetables and fruit were found to contain glucaric acid, the content of which varied from a low of 1.12–1.73 mg/100 g for broccoli and potatoes to a high of 4.53 mg/100 g for oranges (Dwivedi et al. 1990). The predominant glucosinolates in broccoli were 4-methylsulphinylbutyl glucosinolate (glucoraphanin), 3-butenyl glucosinolate (gluconapin) and 3-indolylmethyl glucosinolate (glucobrassicin) (Kushad et al. 1999). Glucoraphanin concentration in broccoli ranged from 0.8 μmol/g^{-} DW in cv. EV6-1 to 21.7 μmol/g DW in cv. Brigadier. Concentrations of the other glucosinolates in broccoli varied similarly over a wide range.

Glucosinolates identified in broccoli inflorescences included the following: 3-methylsulphinylpropyl-glucosinolate (glucoiberin), 2-hydroxy-3-butenyl-glucosinolate (progoitrin), 4-methylsul phinylbutyl-glucosinolate (glucoraphanin), 5-methylsulphinylpentyl-glucosinolate (glucoalyssin), 3-butenyl-glucosinolate (gluconapin), 4-hydroxy-3-indolylmethyl-glucosinolate (4-hydroglucobrassicin), 4-pentenyl-glucosinolate (glucobrassicanapin), 3-indolylmethyl-glucosinolate (glucobrassicin), 2-phenylethyl-glucosinolate (gluconasturtin), 4-methoxy-3-indolylmethyl-glucosinolate (4-methoxyglucobrassicin) and 1-methoxy-3-indolylmethy-glucosinolate (neoglucobrassicin) (Rosa and Rodrigues 2001; Vallejo et al. 2003a, b; Moreno et al. 2006). The predominant glucosinolates in all broccoli cultivars were 4-methylsulphinylbutyl-glucosinolate (glucoraphanin), 3-indolylmethyl-glucosinolate (glucobrassicin) and 1-methoxy-3-indolylmethyl-glucosinolate (neoglucobrassicin) (Rosa and Rodrigues 2001; Vallejo et al. 2003a). A new glucosinolate cinnamoyl derivative 6′-*O*-trans-(4″- hydroxy cinnamoyl)-4-(methylsulphinyl) butyl glucosinolate was isolated from broccoli florets (Survay et al. 2010). Two glucosinolates, glucoiberin and 3-hydroxy, 4(α-L-rhamnopyranosyloxy) benzyl glucosinolate, were identified in aqueous Broccoli extract (Hashem et al. 2012b). Further, two compounds were isolated after enzymatic hydrolysis of the aqueous extract by myrosinase; one of them was identified as 4-vinyl-3-pyrazolidinone and the second compound (sulphoraphane) 1-isothiocyanate-4-methyl-sulphinyl butane was converted to the most stable form of thiourea (sulphoraphane thiourea).

Total and individual glucosinolate levels varied significantly between seasons, among cultivars and between inflorescences. The cv. 'Shogun' contained the highest total glucosinolate levels (between 35.2 mmol/kg dry weight in primary inflorescences of the early crop and 47.9 mmol/kg in secondary inflorescences of the late crop) (Rosa and Rodrigues 2001). Total and individual glucosinolate levels were generally higher in the late than in the early crop. Similarly total glucosinolates were detected more significantly in the late than in the early season and all broccoli cultivars showed a higher content of indolic glucosinolates than aliphatic glucosinolates (Vallejo et al. 2003a). Broccoli florets were characterized by particularly high glucoraphanin content, 17.95 μmol/g dry weight on average, which comprised about 50 % of total glucosinolates (Borowski et al. 2008). High individual variation was observed for several bioactive compounds, as well as for DPPH$^{\bullet}$

and OH• radical-scavenging activity. Among glucosinolates, the highest coefficient of variation (CVs) was noted for progoitrin (34.22 %), 4-hydroxyglucobrassicin (27.32 %) and neoglucobrassicin (24.44 %). High CVs were also observed for vitamin C (29.11 %), including dehydroascorbic acid (26.72 %), and for OH• (25.76 %) and DPPH (21.77 %) radical-scavenging activities. Smaller variations were found for glucoraphanin (CV = 14.84 %) and polyphenols (CV = 14.95 %). The highest concentration of glucoraphanin occurred in young broccoli seedlings and seeds (Rangkadilok et al. 2002a). The glucoraphanin concentration decreased from the start of seed germination to the flowering stages. The lowest concentration was also found at the flowering stage. A higher concentration of glucoraphanin was detected in the green broccoli heads and flower heads than in other reproductive tissues. Each kilogram of extracted broccoli seed yielded approximately 4.8 g of sulforaphane and 3.8 g of sulforaphane nitrile (Matusheski et al. 2001). Vitamin C was not detected in dormant broccoli seeds, and its content increased with the germination, reaching values ranging from 53 (cv. Nubia) to 64 (cv. Marathon) mg/100 g FW, at the end of the monitored period (14 days) (Pérez-Balibrea et al. 2011). The total glucosinolate content in seeds and 3-day-old sprouts was higher in cv. Marathon (1,005 and 556 mg/100 g FW, respectively); however, cv. Viola sprouts registered the highest glucosinolate content 7 and 14 days after sowing (235 and 208 mg/100 g FW, respectively). Glucoraphanin was the predominant glucosinolate in cv. Nubia and cv. Marathon, whereas glucoiberin was the major glucosinolate in cv. Viola. The flavonoid and total phenolic content was significantly higher in cv. Viola. Also, seeds of this cultivar showed the highest antioxidant capacity (2.7 mg Trolox/g FW) .

Broccoli cvs. was found to have a predominance of 4-(methylsulfinyl)butyl-glucosinolate and 4-(methylthio)butyl-glucosinolate in the head and 2-hydroxy-3-butenyl-glucosinolate as secondary component; other glucosinolates present included allyl-glucosinolate, 3-(methylthio)propyl-glucosinolate, 3-(methylsulfinyl)-propyl- glucosinolate, 3-butenyl- glucosinolate, 4-pentyl- glucosinolate, 2-phenyl-ethyl- glucosinolate and 3-indolylmethyl- glucosinolate (Carlson et al. 1987). Eight aliphatic glucosinolates, four indole glucosinolates and one aromatic glucosinolate were identified and quantified in the florets of 5 main Chinese broccoli and 143 parent materials (Wang et al. 2012b). Glucoraphanin, glucobrassicin, 4-methoxyglucobrassicin and neoglucobrassicin were present in all samples. The anticancer glucoraphanin concentration ranged from 0.06 to 24.17 μmol/g in pure lines and from 1.57 to 5.95 μmol/g in commercial cultivars. The progoitrin concentration in commercial cultivars varied from 1.77 to 6.07 μmol/g with a mean value of 3.20 μmol/g. Significant variations were observed in the concentration of individual glucosinolates and in each class of glucosinolates among broccoli populations.

Phenolics found in broccoli inflorescences included: caffeoylquinic derivatives (3-*O*-caffeoylquinic (neochlorogenic acid), 5-*O*-caffeoylquinic (chlorogenic acid)); sinapic derivatives (1,2-disinapoylgentiobiose, 1-sinapoyl-2-feruloylgentiobiose, 1,2,2-trisinapoylgentiobiose, 1,2-disinapoyl-2-feruloylgentiobiose, 1-sinapoyl-2,2-diferuloylgentiobiose, 1,2,2-trisinapoylgentiobiose); and feruloyl acid derivatives (1,2-diferuloylgentiobiose) (Vallejo et al. 2003b). The main hydroxycinnamic acids (sinapic, ferulic, *p*-coumaric and caffeic acids) were isolated from broccoli and broccolini by capillary zone electrophoresis (Lee et al. 2011). Eight minor glucosinolates, viz., 1-methylpropyl-glucosinolate, 2-methylpropyl-glucosinolate, 2-methylbutyl-glucosinolate, 3-methylbutyl-glucosinolate, n-pentyl-glucosinolate, 3-methylpentyl-glucosinolate, 4-methylpentyl-glucosinolate and n-hexyl-glucosinolate, were identified in crude sample extracts of broccoli, cauliflower and rocket salad (Lelario et al. 2012). The occurrence of these glucosinolates belonging to the saturated aliphatic side chain families C4, C5 and C6, presumably formed by chain elongation of leucine, homoleucine and dihomoleucine as primary amino acid precursors, was described. Two nitrogenous compounds were uridine and uridine 9-acetate isolated from the ethyl acetate broccoli extract (Hashem et al. 2012a).

A large number of hydroxycinnamic acid esters of kaempferol and quercetin glucosides were characterized in broccoli inflorescences (Vallejo et al. 2004b) The structures of the flavonoid glycosides were analyzed after alkaline hydrolysis and were identified as 3-sophoroside/sophorotrioside-7-glucoside/sophoroside of kaempferol, quercetin and isorhamnetin. Additionally, several less complex glucosides based on the same aglycones were identified. Flavonoids acylated with hydroxycinnamic acid derivatives included sinapoyl/feruloyl gentiobioside compounds; 1,2-disinapoylgentiobiose; 1-sinapoyl-2-feruloylgentiobiose; 1,2-diferuloylgentiobiose; 1,2,2′-trisinapoylgentiobiose; 1,2′-disinapoyl-2-feruloylgentiobiose; 1-sinapoyl-2,2′-diferuloylgentiobiose; 1,2,2′-trisinapoylgentiobiose; and 1,2,2′-triferuloylgentiobiose. Some of the flavonoids identified included: quercetin-3-*O*-sophorotrioside-7-*O*-glucoside; quercetin-3-*O*-sophoroside-7-*O*-glucoside; quercetin-3-*O*-sophorotrioside-7-*O*-sophoroside; kaempferol-3-*O*-sophorotrioside-7-*O*-glucoside; kaempferol-3-*O*-sophorotrioside-7-*O*-sophoroside; kaempferol-3-*O*-sophoroside-7-*O*-glucoside; isorhamnetin-3-*O*-sophorotrioside-7-*O*-glucoside; kaempferol-3-*O*-sophoroside-7-*O*-sophoroside; isorhamnetin-3-*O*-sophorotrioside-7-*O*-sophoroside; quercetin-3,7-di-*O*-glucoside; quercetin-3-*O*-glucoside-7-*O*-sophoroside; kaempferol-3,7-di-*O*-glucoside; kaempferol-3-*O*-glucoside-7-*O*-sophoroside; isorhamnetin-3,7-di-*O*-glucoside; isorhamnetin-3-*O*-glucoside-7-*O*-sophoroside; quercetin-3-*O*-sophoroside; kaempferol-3-*O*-sophoroside; quercetin-3-*O*-glucoside; kaempferol-3-*O*-glucoside; quercetin-3-*O*-(feruloyl/sinapoyl)-sophorotrioside-7-*O*-glucoside; and kaempferol-3-*O*-(caffeoyl/sinapoyl)-sophorotrioside-7-*O*-sophoroside. Using liquid chromatography-photodiode array-solid-phase extraction-nuclear magnetic resonance/mass spectrometry, five related glycosylated phenolic acids were identified in broccoli: 1,2-di-*O*-*E*-sinapoyl-β-gentiobiose; 1-*O*-*E*-sinapoyl-2-*O*-*E*-feruloyl-β-gentiobiose; 1,2-di-*O*-*E*-feruloyl-β-gentiobiose; 1,2,2′-tri-*O*-*E*-sinapoyl-β-gentiobiose; and 1,2′-di-*O*-*E*-sinapoyl-2-*O*-*E*-feruloyl-β-gentiobiose (Moco and Vervoort 2012).

Major volatile components identified in broccoli included nonanal, octanol, 3-methylthiobutyl cyanide, 2-phenylethyl cyanide and 2-phenylethyl isothiocyanate (Buttery et al. 1976). The major volatiles identified in blanched, cooked broccoli florets were: n-pentanal, 3-methyl-2-pentanone, n-hexanal, n-heptanal, ethyl acetate, cyclopentanecarboxaldehyde, 3-methylbutanal, 3-butenenitrile, 2-methylbutanal, dimethyl trisulfide and dimethy disulfide (Kallio et al. 1999). In broccoli and cabbage, exogenous methyl jasmonate induced the emission of the volatiles sesquiterpene (*E,E*)-α-farnesene, the homoterpene (*E*)-4,8-dimethyl-1,3,7-nonatriene (DMNT) and green leaf volatiles (*Z*)-3-hexenyl acetate and octanal (Ibrahim et al. 2005). Volatiles produced by the action of endogenous cystine lyase on S-methyl-cysteine sulphoxide present in Broccoli florets showed three sulphur components: dimethyl disulphide, dimethyl trisulphide and 3,5-dimethyl-1,2,4-trithiolane (Motawea et al. 2010). Four isothiocyanate compounds were also present. Cystine lyase enzymatic fission of endogenous myrosinase yielded the unsaturated glucosinolates ethenyl isothiocyanate and allyl isothiocyanate, together with the saturated 4-methylthiobutyl isothiocyanate (erucin) and the aromatic 2-phenylethyl isothiocyanate (PEITC).

Glucosinolates found in broccoli purchased from local Singapore markets were in nmol/g wet weight: glucoraphanin, 522 nmol; gluconasturtin, NQ (not quantified); sinigrin, NQ; glucobrassicin, 4,250 nmol; 4-hydroxy glucobrassicin, 198 nmol; 4-methoxy glucobrassicin, 432 nmol; 1-methoxy glucobrassicin, 1,100 nmol; glucoiberin, 40.9; progoitrin (or epiprogrotrin), NQ; glucoalyssin, 18.4 nmol; gluconapoleiferin, NQ; gluconapin, NQ; glucobrassicanapin, NQ; glucoerucin, NQ; 7-methylthioeptyl, NQ; 8-methylthioeptyl, NQ; total glucosinolates, 6,570 nmol; and glucobrassicans, 91 % of total glucosinolates (Hecht et al. 2004). Glucobrassicins (glucobrassicin, 1-methoxyglucobrassicin, 4-methoxyglucobrassicin and 4-hydroxyglucobrassicin), precursors to indole-3-carbinols, were the predominant glucosinolates in seven of the nine vegetables (including cauliflower and broccoli) studied, accounting for 70.0–93.2 % of

all glucosinolates. Six individual desulfo-glucosinolates, including progoitrin, glucoraphanin, sinigrin, gluconapin, glucobrassicanapin and glucobrassicin, were commonly identified in the flower head of 95 Korean broccoli assessions (Lee et al. 2012). The total glucosinolate contents varied from 4.2 to 29 μmol/g DW, and the glucoraphanin (1.6–13.9 μmol/g DW) was confirmed as a major constituent in the total glucosinolate profile; in contrast, progoitrin was only detected in 13 accessions. Glucobrassicanapin, glucoraphanin, glucobrassicin, and gluconapin were the major glucosinolates.

Two novel glucosinolates identified as 2-mercaptomethyl sulfinyl glucosinolate [(*Z*)-4-(methylsulfinyl)-*N*-(sulfooxy)-2-((2′S,3′R,4′S,5′S,6′R)-3′,4′,5′-trihydroxy-6′(hydroxylmethyl)-2′-mercapto tetrahydro-2H-pyran-2-yl) butane amide] and (*Z*)-1-((2S,5S)-5-hydroxytetrahydro-2H-pyran-2-ylthio)-2-(1H-indol-3-yl) ethylidene amino sulfate along with one known cinnamoyl [6′-*O*-trans-(4″-hydroxy cinnamoyl)4-(methylsulphinyl)butyl glucosinolate] were isolated from broccoli florets (Survay et al. 2012).

Six organoselenium compounds including selenium analogues of known myrosinase-derived *Brassica* volatiles, 4-(methylseleno)butanenitrile, 5-(methylseleno) pentanenitrile, 3-(methylseleno)propylisothiocyanate, 4-(methylseleno) butylisothiocyanate and 5-(methylseleno) pentylisothiocyanate, were identified in the pentane/ether extracts of broccoli and cauliflower florets and roots of forage rape, all obtained from plants treated with sodium selenate (Matich et al. 2012). LC–MS analysis of ethanolic extracts identified three selenoglucosinolates: 3-(methylseleno) propylglucosinolate (glucoselenoiberverin), 4-(methylseleno) butylglucosinolate (glucoselenoerucin) and 5-(methylseleno)pentylglucosinolate (glucoselenoberteroin). In broccoli, concentrations of the selenoglucosinolates and their aglycones (mainly nitriles) were up to 60 and 1,300 %, respectively, of their sulphur analogues.

A DNA topoisomerase I with an 80 kDa monomer was isolated from broccoli (Kieber et al. 1992). Three isoforms (a, b and c) of cystine lyase were found in broccoli inflorescence tissues (Ukai and Sekiya 1999). Cystine lyase b, the most abundant isoform, had a molecular weight of 160,000 and composed of four identical subunits with a molecular weight of 40,000. The purified cystine lyase b utilized l-cystine and *S*-alkyl l-cysteine sulfoxide as substrates. Cystine lyase a and b were localized in cytosolic and/or vacuole fraction. Three peroxidase (POD) isoenzymes were purified from a soluble extract of broccoli stems (Thongsook and Barrett 2005). The neutral and basic PODs had molecular masses of approximately 43 kDa, and the acidic POD had a molecular mass of 48 kDa. All three of the purified isoenzymes were glycosylated. Two cDNAs encoding proteins with homocysteine S-methyltransferase (HMT) activity were isolated from broccoli and functionally characterized (Lyi et al. 2007). While one gene product exhibited only HMT activity, the other displayed both HMT and selenocysteine Se-methyltransferase (SMT) activities, indicating the gene had evolved to include an additional function in sulfur/selenium accumulating species. The presence of acidic metalloproteases, serine proteases and cysteine proteases was found in broccoli florets (Rossano et al. 2011). Post-harvest senescence of broccoli florets was characterized by decrease in protein and chlorophyll contents and increase of protease activity, particularly cysteine protease. Pheophytinase (PPH) activity in broccoli florets increased concomitantly with a decline in chlorophyll *a* and *b*, suggesting that PPH may be involved in chlorophyll degradation (Aiamla-or et al. 2012). PPH activity in broccoli flowers treated with a UVB dose of 19 kJ/m^2 was repressed for the first 2 days of storage at 15 °C, whereas it increased gradually with senescence of broccoli florets. UVB treatment delayed upregulation of chlorophyll-degrading enzyme chlorophyllase genes resulting in the suppression of floret yellowing in stored broccoli.

Brassica plants (e.g., broccoli and cauliflower) contain substantial quantities of isothiocyanates (mostly in the form of their glucosinolate precursors), some of which (e.g., sulforaphane or 4-methylsulfinylbutyl isothiocyanate) are very potent inducers of phase 2 enzymes (Fahey et al. 1997). Three-day-old sprouts of cultivars of

certain crucifers including broccoli and cauliflower were found to contain 10–100 times higher levels of glucoraphanin (the glucosinolate of sulforaphane) than do the corresponding mature plants. Broccoli seedlings cultivated using a 30/15 °C (day/night) temperature regime had significantly higher glucosinolate levels (measured at six consecutive days postemergence) than did sprouts cultivated at lower temperatures (22/15 and 18/12 °C). Both higher (33.1 °C) and lower (11.3 °C) constant temperatures induced higher glucosinolate levels in sprouts grown to a uniform size (Pereira et al. 2002). Glucosinolate levels were highest in cotyledons and lowest in roots of sprouts dissected both early and late in the 11-day developmental span investigated. Nongerminated seeds have the highest glucosinolate levels and concordantly greater induction of mammalian phase 2 detoxication enzymes. Levels declined as sprouts germinated and developed, with consistently higher glucosinolate content in younger developmental stages, independent of the temperature regime. Temperature stress or its associated developmental anomalies induced higher glucosinolate levels, specific elevations in glucoraphanin content and parallel induction of phase 2 chemoprotective enzymes. Pérez-Balibrea et al. (2008) found broccoli (flower head) to be a rich source of phytochemicals (glucosinolates and phenolic compounds) and micronutrients (vitamins and minerals), but germinated broccoli sprouts were found to contain much higher levels (10–100 times) of aliphatic (glucoraphanin) and indolic glucosinolates than the inflorescences. Broccoli sprouts grown in the light were found to have much higher concentrations of vitamin C (by 83 %), glucosinolates (by 33 %) and phenolic compounds (by 61 %) than those grown in the dark. Among the different organs studied (seeds, cotyledons, stems and roots), the cotyledons contained the highest levels of bioactive compounds, while the roots contained the lowest. Glucosinolate concentration in broccoli sprouts was strongly influenced by germination, causing a rapid increase during the first 3 days after sowing, and decreasing afterwards (Pérez-Balibrea et al. 2010). Fertilization with potassium sulphate 15, 30 and 60 mg/l at 9 and 12 days after sowing enhanced glucosinolate content.

Using liquid chromatography–mass spectrometry, Maldini et al. (2012) validated the presence of eight glucosinolates: glucobrassicin, glucoraphanin, glucoiberin, glucoerucin, progoitrin, gluconapin, sinigrin and glucocheirolin in broccoli sprouts with an overall recovery of 99 % for the eight glucosinolates. Using high-performance liquid chromatography–electrospray ionization–tandem mass spectrometry, Tian et al. (2005) quantified ten individual glucosinolates in broccoli, broccoli sprouts, Brussels sprouts and cauliflower. Detection limits for glucoiberin, sinigrin, progoitrin, glucoerucin and glucotropaeolin were 1.75, 1.38, 1.36, 0.6 and 0.63 pmol, respectively. Aliphatic glucosinolates (glucoraphanin, glucoiberin and glucoerucin) and a group of indole glucosinolates including 4-hydroxy-glucobrassicin and folates preformed in broccoli seeds were detected in broccoli sprouts (Rychlik and Adam 2008). In the early stage of sprouting, a reduction (approx. 20 %) of the aliphatic glucosinolates was determined, and levelling off up to the 12th day while 4-hydroxy-glucobrassicin declined continuously, three minor indole derivatives increased steadily, but remained at a comparatively low level. During germination, the contents of total folates increased to 72 µg/100 g fresh mass and 546 µg/100 g dry mass on the 4th day decreased again to 13 µg/100 g fresh mass until the 8th day of germination and remained at this low level. 5-Methyltetrahydrofolate was found as the predominant vitamer at each stage. Vitamin C, phenolic compounds, and glucosinolates in these purple sprouting varieties, EEP (Extra Early), EP (Early) and LP (Late) grown in Spain, were higher than in traditionally grown green broccolis and other purple broccolis grown under different climate conditions (Rodríguez-Hernández et al. 2012).

The following acylated anthocyanins were identified in broccoli sprouts: cyanidin-3-*O*-diglucoside-5-*O*-glucoside acylated and double acylated with *p*-coumaric, sinapic, caffeic, ferulic or sinapic acids, with at least three predominant anthocyanins isomers of cyanidin 3-*O*-(acyl) diglucoside-5-*O*-glucoside, cyanidin 3-*O*-(acyl 1)

(acyl 2)diglucoside-5-*O*-glucoside and cyanidin 3-*O*-(acyl 1)(acyl 2)diglucoside-5-*O*-(malonyl) glucoside (Moreno et al. 2010). The early purple sprouting broccoli sprouts ('Viola') showed significantly higher concentrations of cyanidin 3-*O*-(sinapoyl) diglucoside-5-*O*-glucoside, cyanidin 3-*O*-(feruloyl) diglucoside-5-*O*-glucoside, cyanidin 3-*O*-(sinapoyl) (sinapoyl) diglucoside-5-*O*-glucoside and cyanidin 3-*O*-(sinapoyl) (feruloyl) diglucoside-5-*O*-(malonyl) glucoside. The total concentration of anthocyanins identified in 'green head' broccoli cultivars (Marathon, Nubia) and the green variety-for-sprouts (Intersemillas) was similar (0.23–0.29 mg/100 g) and significantly lower than that in cv. 'Viola' (0.64 mg/100 g).

Processing/Storage and Broccoli Phytochemicals

Broccoli offers many health-promoting properties owing to its content of antioxidant and anticarcinogenic compounds (Mahn and Reyes 2012). The concentration and bioavailability of polyphenols, glucosinolates, sulforaphane and selenium depend on plant biochemistry, cultivation strategy and type of processing. Steaming and drying had been reported to result in an apparent increment of sulforaphane content as well as antioxidant activity, most likely due to an increase of the extractability of antioxidants and sulforaphane. Freezing and boiling were found to diminish polyphenols concentration, mainly due to volatilization and leaching into the cooking water. The two main flavonol glycosides quercetin 3-*O*-sophoroside and kaempferol 3-*O*-sophoroside and three minor glucosides of quercetin and kaempferol, namely, isoquercitrin, kaempferol 3-*O*-glucoside and a kaempferol diglucoside, were identified in broccoli florets (Price et al. 1998). The sophorosides of quercetin and kaempferol were present in raw florets at a level of 65 and 166 mg/kg fresh weight, respectively. The total content of quercetin and kaempferol glycosides expressed as aglycone was 43 and 94 μg/g fresh weight, respectively, and these agree with other recently published data. During the cooking process, only 14–28 % of the individual glucosides were retained in the cooked tissue, the remainder being largely leached into the cooking water with only a small loss attributed to the formation of the respective aglycones. Studies showed a general decrease in the levels of glucosinolates, phenolic compounds, and vitamin C compounds except for mineral nutrients which were stable under all microwave cooking conditions (López-Berenguer et al. 2007). Vitamin C showed the greatest losses mainly because of degradation and leaching, whereas losses for phenolic compounds and glucosinolates were mainly due to leaching into water. In general, the longest microwave cooking time and the higher volume of cooking water should be avoided to minimize losses of nutrients. Studies showed that during stir-frying of broccoli, phenolics and vitamin C were more affected than glucosinolates and minerals (Moreno et al. 2007). Stir-fry cooking with extra virgin olive, soybean, peanut or safflower oil did not reduce the total glucosinolate content of the cooked broccoli compared with that of the uncooked sample. The vitamin C content of broccoli stir-fried with extra virgin olive or sunflower oil was similar to that of the uncooked sample, but greater than those samples stir-fried with other oils.

The predominant sinapic acid derivatives in broccoli inflorescence after cooking were identified as 1,2,2′-trisinapoylgentiobiose and 1,2′-disinapoyl-2-feruloylgentiobiose; 1,2-diferuloylgentiobiose and 1-sinapoyl-2,2′-diferuloylgentiobiose were also identified (Vallejo et al. 2003c). The results showed large differences in flavonoid and hydroxycinnamoyl derivative contents in broccoli among the four cooking treatments. Clear disadvantages were detected when broccoli was microwaved, namely, high losses of flavonoids (97 %), sinapic acid derivatives (74 %) and caffeoylquinic acid derivatives (87 %). Conventional boiling led to a significant loss of flavonoids (66 %) from fresh raw broccoli, while high-pressure boiling caused considerable leaching (47 %) of caffeoylquinic acid derivatives into the cooking water. In contrast, steaming had minimal effects, in terms of loss, on both flavonoid and hydroxycinnamoyl derivative contents.

Isothiocyanate content in broccoli juice treated by freezing, pasteurization and high pressure was found to range from 1.45 to 10.68, 1.94 to 5.54 and 1.87 to 11.27 µmol/l, respectively (Totušek et al. 2011). Sulforaphane content in broccoli juice treated by freezing, pasteurization and high pressure was found to range from 7.77 to 14.25, 8.87 to 15.67 and 8.24 to 14.64 µg/ml, respectively.

Production of nitrile during hydrolysis of unheated broccoli cultivars varied among cultivars from 91 to 52 % of hydrolysis products (Pinnacle > Marathon > Patriot > Brigadier) (Wang et al. 2012a). Boiling and microwave heating caused an initial loss of nitrile, with a concomitant increase in sulforaphane, followed by loss of sulforaphane, all within a minute. In contrast, steaming enhanced sulforaphane yield between 1 and 3 minutes in all but cv. Brigadier. The data indicated that steaming for 1–3 minutes provided less nitrile and more sulforaphane yield from a broccoli meal. Processing was found to reduce the glucosinolate content of broccoli, among other aspects due to thermally induced degradation (Hanschen et al. 2012). In broccoli sprouts, methylsulfanylalkyl glucosinolates were more susceptible to degradation at high temperatures, whereas methylsulfinylalkyl glucosinolates were revealed to be more affected in aqueous medium under alkaline conditions. Besides small amounts of isothiocyanates, the main thermally induced breakdown products of sulfur-containing aliphatic glucosinolates were nitriles. Although nitriles were most rapidly formed at comparatively high temperatures under dry heat conditions, their highest concentrations were found after cooking in acidic medium, conditions being typical for domestic processing.

The highest content of glucoraphanin and quinone reductase activity was found in broccoli florets stored under controlled atmosphere storage of 21 % O_2 + 10 % CO_2 at 5 °C (Xu et al. 2006). These conditions were able to maintain the visual quality, glucoraphanin content and quinone reductase activity of the broccoli florets for 20 days.

Vapor cooking of fresh broccoli did not generate 2,3,5-trithiahexane (TTH), but cutting broccoli into pieces followed by cooking in water allowed the detection of this odorant (Spadone et al. 2006). Cutting broccoli activates cysteine sulfoxide lyase transforming methylcysteine sulfoxide into methylsulfenic acid, which upon heating gives rise to dimethylsulfide and dimethyl trisulfide that react to TTH. The formation of TTH was enhanced upon frozen storage of cut broccoli pieces for a few weeks. Visual quality of broccoli heads declined significantly with increasing temperature and length of storage, caused primarily by increasing yellowing and loss of turgor (Winkler et al. 2007). Glucoraphanin, quercetin and kaempferol contents were not significantly affected by storage and marketing temperature and time. The results suggested that current transport and marketing practices were not likely to have a deleterious effect on the levels of aliphatic glucosinolates and flavonols in broccoli.

Studies showed significant differences among broccoli and cauliflower cultivar groups for the glucosinolate proportions as well as the contents of health-promoting and flavour-influencing alkyl, alkenyl and indole glucosinolates (Schonhof et al. 2004). These differences impacted on differences in sensory properties such as colour; taste properties such as bitter and sweet; and flavour such as green/grassy, spicy, broccoli-like, cabbage-like, cauliflower-like, kohlrabi-like, leek-like and mouthfeel pungent. Consumers were seen to prefer cultivars with a bright colour, a lower level of bitter-tasting glucosinolates (alkenyl and indole glucosinolates) and a higher sucrose content.

Endogenous folate poly-γ-glutamates in broccoli florets were found predominantly as hepta- and hexa-γ-glutamates (Munyaka et al. 2009). Crushing raw broccoli, acidification and LTLT (low temperature long time, 60 °C/40 minutes) blanching enhanced folate deconjugation, resulting in monoglutamate, di- and tri-γ-glutamates. Compared to other treatments, HTST (high temperature short time, 90 °C/4 minutes) blanching preformed prior to crushing resulted in the highest concentration of long-chain poly-γ-glutamates. Acidification combined with LTLT blanching decreased folate poly-γ-glutamates stability, whereas HTST blanching combined

with different sequences of blanching and crushing did not affect folate poly-γ-glutamates stability. It was concluded that crushing (prior to heating), acidification and blanching could be strategically applied to increase the folate monoglutamate content of broccoli. Crushing of raw broccoli resulted in significant poly-γ-glutamate profile changes in broccoli, indicating γ-glutamyl hydrolase catalyzed hydrolysis (Munyaka et al. 2010). During treatments at 25–140 °C, folate retention was higher at 80 and 100 °C than at the other temperatures. A similar trend in thermal stability was observed for folates, vitamin C, total phenols and Trolox equivalent antioxidant capacity (TEAC) value, an indication that conditions that resulted in endogenous antioxidants degradation might also result in folate degradation.

Green colour of broccoli florets was retained under N_2 flow (<0.01 % O_2 and <0.25 % CO_2) and no flow (down to 1.3 % O_2 and up to 30 % CO_2), but these same conditions led to increased sour and sulfurous odors of the fresh product (Hansen et al. 1993). The relative concentration of ethanol, 3-hydroxy-2-butanone, and 2,3-butanediol increased, and C_5–C_7 aldehydes and alcohols decreased in the cooked broccoli which was stored fresh under N_2 or no flow conditions as compared to fresh samples and samples stored under air flow (20.5 % O_2 and <0.5 % CO_2), or restricted air flow (down to 17.2 % O_2 and up to 3.7 % CO_2). Schonhof et al. (2007) found elevated atmospheric CO_2 concentration had a differing effect on individual glucosinolates and glucosinolate groups in broccoli grown in the green house. Total glucosinolate content increased at elevated atmospheric CO_2 concentration as a result of a strong increase in both methylsulphinylalkyl glucosinolates glucoraphanin and glucoiberin. In contrast, indole glucosinolates simultaneously decreased, predominantly because of a reduction of glucobrassicin and 4-methoxy-glucobrassicin contents. Elevated CO_2 concentration increased photochemical quenching coefficient values in broccoli leaves by up to 100 and 89 % in heads, while glucose and sucrose in leaves increased by about 60 % (Krumbein et al. 2010). Further, in broccoli heads, elevated CO_2 concentration induced approximately a twofold increase in concentrations of three fatty acid-derived C(7) aldehydes ((*E*)-2-heptenal, (*E*,*Z*)-2,4-heptadienal and (*E*,*E*)-2,4-heptadienal), two fatty acid-derived C(5) alcohols (1-penten-3-ol, (*Z*)-2-pentenol), and two amino acid-derived nitriles (phenyl propanenitrile, 3-methyl butanenitrile). Contrariwise, concentrations of the sulfur-containing compound 2-ethylthiophene and C(6) alcohol (*E*)-2-hexenol decreased. Finally, elevated CO_2 concentration increased soluble sugar concentrations due to enhanced photochemical activity in leaves and heads, which may account for the increased synthesis of volatiles. Both applied modified atmospheres (1 % O_2 + 21 % CO_2; 8 % O_2 + 14 % CO_2) provided by two different microperforated biaxial-oriented polypropylene films maintained aliphatic glucosinolates in cauliflower florets, whereas in broccoli florets, the aliphatic glucosinolate concentration decreased slightly in each modified atmosphere (Schreiner et al. 2007). In addition, total indole glucosinolate concentration for both broccoli and cauliflower florets was maintained. Thus, to simultaneously maintain glucosinolates and external appearance as well as to prevent off-odor, a modified atmosphere of 1 % O_2 + 21 % CO_2 provided a suitable environment for storage of *Brassica* floret medley for up to 7 days at 8 °C. Rangkadilok et al. (2002b) found the best method for preserving glucoraphanin concentration in broccoli heads after harvest was storage of broccoli in modified atmosphere packaging treatments and refrigeration at 4 °C. Such condition maintained the glucoraphanin concentration for at least 10 days and also maintained the visual quality of the broccoli heads.

The organosulfur chemicals, namely, glucosinolates and the S-methyl cysteine sulphoxide, found in broccoli (Stoewsand 1995; Vasanthi et al. 2009) in concert with other constituents such as vitamins E, C and K and the minerals such as iron, zinc and selenium and the polyphenols, namely, kaempferol, quercetin glucosides and isorhamnetin, were reported to be responsible for various health benefits of broccoli (Vasanthi et al. 2009). Thus, broccoli consumption had been reported to mediate a variety of functions including providing

antioxidants, regulating enzymes and controlling apoptosis and cell cycle. Thus, the cancer chemopreventive effects of *Brassica* vegetables (like broccoli) that had been shown in human and animal studies may be due to the presence of both types of sulfur-containing phytochemicals (i.e., certain glucosinolates and S-methyl cysteine sulfoxide) (Stoewsand 1995). The cancer protective effect of cruciferous vegetables had been attributed to the presence of isothiocyanates, and sulforaphane, present in broccoli and broccoli sprouts, was by far the most extensively studied (Juge et al. 2007; Clarke et al. 2008). Sulforaphane had proved to be an effective chemoprotective agent in cell culture, carcinogen-induced, and genetic animal cancer models, as well as in xenograft models of cancer. These protective effects of sulforaphane involved multiple mechanisms activated in response to sulforaphane, including suppression of cytochrome P450 enzymes, induction of apoptotic pathways, suppression of cell cycle progression and inhibition of angiogenesis and antiinflammatory activity. Sulforaphane from broccoli had been reported to be an important potent inducer of cytoprotective proteins (also known as phase 2 enzymes) and to act as antioxidants with a dual protective role by (i) scavenging hazardous oxidants directly and instantaneously and (ii) inducing cytoprotective enzymes involved in the detoxification of carcinogens in carcinogenesis (Dinkova-Kostova and Talalay 2008).

Antioxidant Activity

Studies found that the antioxidant capacity of hydrophilic extracts of eight broccoli genotypes ranged from 65.8 to 121.6 μmol Trolox equivalents (TE)/g of tissue and the capacity of lipophilic extracts ranged from 3.9 to 17.5 μmol TE/g using the oxygen radical absorbance capacity (ORAC) assay (Kurilich et al. 2002). Ascorbic acid and flavonoid content of the hydrophilic extracts did not account for the total variation in antioxidant capacity of those extracts, suggesting either the presence of other antioxidant components that have yet to be identified or that the known antioxidants are producing synergistic effects. The carotenoids did correlate with antioxidant capacity of the lipophilic extracts and accounted for the majority of the variability in that fraction. Studies in noncellular assay systems indicated that broccoli extracts possessed a high capacity for scavenging free radicals or interrupting free radical reactions (Kurilich et al. 2003). Broccoli extracts were also found to protect against reactive oxygen species in HepG2 cells using the dichlorofluorescein–diacetate assay. In HepG2 cells, the level of protection against AAPH (2,2′-azobis (2-amidinopropane) dihydrochloride)-induced reactive oxygen species differed among broccoli genotypes tested. It was concluded that the HepG2 cell assay provided more information about the antioxidative lipid-soluble fraction than the commonly reported ORAC assay. Total antioxidant activity (as determined by ferric reducing antioxidant power) of North Indian broccoli cultivars ranged from 2.05 to 3.56 μmol Trolox/g fresh weight (Kaur et al. 2007). Free radical scavenging activity, as estimated by 2, 2-diphenyl-1-picrylhydrazyl, ranged from 57 to 74 %. Free phenolics ranged from 19.60 to 41.40 mg/100 g fresh weight and on an average constituted 73 % of total extractable phenolics. There was strong positive correlation between free phenolics and antioxidant activity.

For lipophilic broccoli extracts, oxygen radical absorbance capacity (ORAC-L) correlated with inhibition of cellular oxidation of dichlorofluorescein (dichlorofluorescein-L, $R^2 = 0.596$) (Eberhardt et al. 2005). Also, DNA damage in the presence of the lipophilic extract was negatively correlated with both chemical and cellular measures of antioxidant activity as measured by ORAC-L ($R^2 = -0.705$) and dichlorofluorescein-L ($R^2 = -0.671$), respectively. However, no correlations were observed for hydrophilic (–H) broccoli extracts, except between polyphenol content and ORAC (ORAC-H; $R^2 = 0.778$,). Inhibition of cellular oxidation by hydrophilic extracts (dichlorofluorescein-H) and ORAC-H was approximately 8- and 4-fold greater than dichlorofluorescein-L and ORAC-L, respectively. Studies showed that steam processing of broccoli elevated the total ORAC (hydrophilic, lipophilic)

value by 2.3-fold (Roy et al. 2009). The hydrophilic part of a steam-processed broccoli had a significant reduction of 2,2′-azobis [2-amidinopropane] dihydrochloride (AAPH)-induced intracellular ROS level in comparison to that of fresh counterpart. Total phenolic content and total flavonoid content also increased in steam-processed broccoli.

The chloroform and ethanol extracts of broccoli florets showed 100 % antioxidant activity in the DPPH assay at 10 mg/1 ml concentration resembling that of vitamin C (ascorbic acid), and the crude extract gave 90.7 % (Motawea et al. 2010). Two novel glucosinolates identified as 2-mercaptomethyl sulfinyl glucosinolate (1) and (*Z*)-1-((2S,5S)-5-hydroxytetra-hydro-2H-pyran-2-ylthio)-2-(1H-indol-3-yl) ethylidene amino sulfate (2) and a known cinnamoyl [6′-*O*-trans-(4″-hydroxy cinnamoyl)4-(methylsulphinyl)butyl glucosinolate] (3) isolated from broccoli florets exhibited antioxidant activity (Survay et al. 2012). Compound 1 exhibited scavenging activity against DPPH with an inhibitory concentration IC_{50} of 20 mM, whereas compound 3 was a weak antioxidant when compared to the standard quercetin (5 mM) as a positive control. Total phenolic content (TPC), total flavonoid content (TFC) and total glucosinolate content (TGsC) were almost higher in Calabrese cultivar than Southern star cultivar (Naguib et al. 2012). Calabrese cultivar showed higher 1, 1-diphenyl-2-picrylhydrazyl DPPH scavenging activity with IC_{50} value of 16.56 μg/ml compared to Southern star 19.42 μg/ml. Additionally, Calabrese showed higher chelating power (75.36 μg/ml) than Southern star (72.43 μg/ml) at 30 μg/ml when the organic fertilizer was applied. The results indicated that there is a good margin for enhancing antioxidant compounds of broccoli for economic production using organic fertilization. Studies showed that combined hot air and UVC treatment of minimally processed broccoli may enhance protection against oxidative molecules not only by increasing levels of phenolics and ascorbic acid but also by enhancing the activity of enzymes (catalase and ascorbate peroxidase) involved in removing reactive oxygen species (Lemoine et al. 2010).

The major phenolic compounds in broccoli, two flavonol glycosides (quercetin 3-*O*-sophoroside and kaempferol 3-*O*-sophoroside) and four hydroxycinnamic acid esters (1,2′-disinapoyl-2-feruloyl gentiobiose, 1-sinapoyl-2-feruloyl gentiobiose, 1,2,2′-trisinapoyl gentiobiose and 1,2-disinapoyl gentiobiose), were exhibited antioxidant activity in the Trolox C equivalent antioxidant capacity (TEAC) and inhibition of iron/ascorbate-induced lipid peroxidation of phosphatidyl choline vesicle assays (Plumb et al. 1997). In the aqueous phase TEAC assay, the two flavonol glycosides were less active than their respective aglycones. TEAC values for the hydroxycinnamic acid esters were less than the sum of their constituent hydroxycinnamic acids on a molar basis. Quercetin 3-*O*-sophoroside was a potent inhibitor of lipid peroxidation, in contrast to kaempferol 3-*O*-sophoroside. The hydroxycinnamic acid esters were highly effective at preventing lipid damage with the exception of 1,2,2′-trisinapoyl gentiobiose.

Anticancer Activity (Refer Also to Notes Under B. oleracea *(Botrytis Group))*

Organic isothiocyanates occurring in *Brassica* vegetables had been reported to block the production of tumours induced in rodents by diverse carcinogens (polycyclic aromatic hydrocarbons, azo dyes, ethionine, N-2-fluorenylacetamide and nitrosamines) (Zhang and Talalay 1994). Protection had been reported to be afforded by α-naphthyl-, β-naphthyl-, phenyl-, benzyl-, phenethyl- and other arylalkyl isothiocyanates against tumour development in liver, lung, mammary gland, forestomach and esophagus. The anticarcinogenic effects of isothiocyanates appeared to be mediated by tandem and cooperating mechanisms: (a) suppression of carcinogen activation by cytochrome P450, probably by a combination of downregulation of enzyme levels and direct inhibition of their catalytic activities, which thereby lower the levels of ultimate carcinogens formed, and (b) induction of phase 2 enzymes such as glutathione transferases and NAD(P)H: quinone reductase, which detoxify

any residual electrophilic metabolites generated by phase 1 enzymes and thereby destroy their ability to damage DNA. Among isothiocyanates sulforaphane had received a great deal of attention because of its ability to simultaneously modulate multiple cellular targets involved in cancer development, including (i) DNA protection by modulating carcinogen-metabolizing enzymes and blocking the action of mutagens; (ii) inhibition of cell proliferation and induction of apoptosis, thereby retarding or eliminating clonal expansion of initiated, transformed and/or neoplastic cells; and (iii) inhibition of neoangiogenesis, progression of benign tumours to malignant tumours and metastasis formation (Fimognari and Hrelia 2007). Sulforaphane had been reported to prevent, delay or reverse preneoplastic lesions, as well as to act on cancer cells as a therapeutic agent. Isothiocyanates and indoles (e.g., indole-3-carbinol) from *Brassica* vegetables (e.g., broccoli) induce phase I and phase II enzymes responsible for the oxidation, reduction and metabolism of endogenous and exogenous carcinogens (Fowke et al. 2006). *Brassica* intake had been associated with reduced risk of colon, lung, bladder, breast, prostate and other cancers.

Numerous epidemiological studies indicated that *Brassica* vegetables in general and broccoli in particular being rich sources of glucosinolates as well as possessing a high content of flavonoids, vitamins and mineral nutrients could protect humans against cancers (Moreno et al. 2006).

In-Vitro Studies

Broccoli contained selenium in the form of methylated selenium compounds (e.g., Se-methylselenocysteine), which can readily be converted into the methylselenol (Keck and Finley 2004). In-vitro studies showed that methylselenol inhibited the migration and invasive potential of HT1080 fibrosarcoma tumour cells (Zeng et al. 2009).

By monitoring quinone reductase induction in cultured murine hepatoma cells as the biological assay, Zhang et al. (1992) isolated and identified (−)-1-isothiocyanato-(4R)-(methylsulphinyl) butane [CH3-SO-(CH2)4-NCS, sulforaphane] as a major and very potent phase II enzyme inducer in SAGA broccoli. Sulforaphane was found to be a monofunctional inducer, like other anticarcinogenic isothiocyanates and induced phase II enzymes selectively without the induction of aryl hydrocarbon receptor-dependent cytochrome P450 (phase I enzymes). In murine hepatoma cells, sulforaphane was the most potent inducer. Sulforaphane and its sulfide and sulfone analogues induced both quinone reductase and glutathione transferase activities in several mouse tissues. The induction of detoxication enzymes by sulforaphane may be a significant component of the anticarcinogenic action of broccoli. Steam-processed broccoli gave significant cytoprotection in PC-12 (rat adrenal pheochromocytoma) cell line, and the authors asserted that this neuroprotective efficacy warranted further investigation (Roy et al. 2009).

Indole-3-carbinol (I3C) significantly inhibited cell adhesion, spreading and invasion associated with an upregulation of PTEN (a tumour suppressor gene) and E-cadherin (a regulator of cell–cell adhesion) expression in T47-D human breast cancer cells (Meng et al. 2000). Thus, I3C exhibited anticancer activities by suppressing breast tumour cell growth and metastatic spread. Studies demonstrated that extracts of broccoli and water cress suppressed TPA(12-*O*-tetradecanoylphorbol-13-acetate)-induced matrix metalloproteinase-9 activity and invasiveness of human MDA-MB-231 breast cancer cells in a concentration-dependent manner (Rose et al. 2005). The inhibitory effects of each vegetable were associated with the presence of 4-methysulfinylbutyl (sulforaphane) and 7-methylsulphinylheptyl isothiocyanates. Sulforaphane and 2-oxohexyl isothiocyanate were found to be potent inducers of detoxication phase 2 enzymes in mouse tissues and murine hepatoma cells in culture (Misiewicz et al. 2003). Sulforaphane was shown to induce cell growth arrest of murine leukemia L-1210 and human melanoma ME-18 cells in a dose-dependent manner, followed by cell death via an apoptotic process. The mammary MCF-7cancer suppressive action of sulforaphane was found to involve mitotic cell cycle arrest and disruption of normal tubulin polymerization (Jackson and Singletary 2004).

Moon et al. (2009) found that sulforaphane suppressed that tumour necrosis factor-alpha (TNF-alpha)-induced NF-kappaB activity and induced apoptosis through activation of reactive oxygen species S-dependent caspase-3 in TNF-alpha-resistant leukemia cells (THP-1, HL60, U937 and K562). Studies showed that the anti-proliferative effects of benzyl and phenethyl isothiocyanates (PEITC) towards Caco-2 cells were due at least in part to the activation of the G_2/M DNA damage checkpoint and that sustained G_2/M phase cell cycle arrest in response to benzyl and phenethyl isothiocyanates may be maintained through upregulation of p21 (Visanji et al. 2004). The crude extract (80 % alcohol extract) of broccoli florets showed good inhibition of colon cancer (IC_{50} 3.88 µg/ml) (Hashem et al. 2012b). In contrast each of the successive extracts (petroleum ether, chloroform, ethyl acetate and ethanol) showed no significant cytotoxic activity. When myrosinase hydrolysate was tested for cytotoxic activity on the colon cancer cell line, it showed very high activity—95 % lethality up to 0.78 µg/ml.

Zhang et al. (2003) reported that indole-3-carbinol (I3C) suppressed the growth of LNCaP prostate carcinoma cells in a dose-dependent manner by inducing a G1 block in cell cycle progression. I3C selectively inhibited the expression of CDK6 protein and transcripts and strongly stimulated the production of the p16 CDK inhibitor. In LNCaP prostate carcinoma cells, I3C treatment inhibited production of PSA, whereas combinations of I3C and the androgen antagonist flutamide more effectively inhibited DNA synthesis and PSA levels compared with either agent alone.

Animal Studies

Dietary supplementation of calcium-D-glucarate, the calcium salt of glucaric acid, contained in broccoli, had been shown to inhibit β-glucuronidase, an enzyme produced by colonic bacterial flora and involved in phase II liver detoxification (Dwivedi et al. 1990). A 4 % calcium glucarate-supplemented diet inhibited β-glucuronidase activity by 70 and 54 % of the bacterial flora obtained from proximal (small intestine) and distal (colon) segments of intestine, respectively. Elevated β-glucuronidase activity had been found to be associated with an increased risk for various cancers, particularly hormone-dependent cancers such as breast, prostate and colon cancers. One of glucaric acid derivatives, the potent β-glucuronidase inhibitor D-glucaro-1,4-lactone (1,4-GL), had been found to increase detoxification of carcinogens and tumour promoters/progressors by inhibiting β-glucuronidase and preventing hydrolysis of their glucuronides (Walaszek et al. 1997). 1,4-GL and its precursors, such as potassium hydrogen D-glucarate and calcium D-glucarate, may exert their anticancer action, in part, through alterations in steroidogenesis accompanied by changes in the hormonal environment and the proliferative status of the target organ. Thus, GA and its derivatives may be useful as new or adjuvant cancer preventive and therapeutic agents. Other potential clinical applications of oral calcium-D-glucarate include regulation of estrogen metabolism and as a lipid-lowering agent (Anonymous 2002).

Talalay et al. (1995) reported that phase 2 enzymes (e.g., glutathione transferase, NAD(P)H–quinone reductase, UDP-glucuronosyltransferases) and high intracellular levels of glutathione in mammalian cells played a prominent role in providing protection against the toxic and neoplastic effects of electrophilic metabolites of carcinogens and reactive oxygen species. Phase 2 enzymes are transcriptionally induced by low concentrations of a wide variety of chemical agents such as phenolic antioxidants, Michael reaction acceptors, isothiocyanates, 1,2-dithiole-3-thiones, trivalent arsenicals, HgCl2 and organomercurials, hydroperoxides and vicinal dimercaptans. Such induction suppressed chemical carcinogenesis via the antioxidant/electrophile response element (ARE/EpRE). Search for such inducer activity in broccoli afforded the isolation of sulforaphane, an isothiocyanate, as a very potent phase 2 enzyme inducer that suppressed mammary tumour formation in rats (Talalay et al. 1995). Studies confirmed that sulforaphane and three synthetic norbornyl isothiocyanates acted as norbornyl isothiocyanates in blocking the formation of mammary tumours in Sprague–Dawley

rats treated with single doses of 9,10-dimethyl-1,2-benzanthracene (Zhang et al. 1994).

Studies found that extracts of 3-day-old broccoli sprouts (containing either glucoraphanin or sulforaphane as the principal enzyme inducer) were highly effective in reducing the incidence, multiplicity and rate of development of mammary tumours in dimethylbenz(*a*)anthracene-treated rats (Fahey et al. 1997). Hence, small quantities of crucifer sprouts may protect against the risk of cancer as effectively as much larger quantities of mature vegetables of the same variety.

Studies in male F344 rats showed that phenethyl isothiocyanate (PEITC), a broccoli component, selectively inhibited lung metabolic activation of carcinogens, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), a major metabolite of NNK (Staretz et al. 1997). The results supported the hypothesis that PEITC inhibited NNK-induced lung tumours by inhibiting metabolic activation of NNK in the lung. This study also demonstrated that PEITC inhibited lung alpha-hydroxylation of NNAL; this may play a role in PEITC inhibition of lung tumorigenesis by NNK. Boysen et al. (2003) demonstrated that dietary 2-phenethyl isothiocyanate (PEITC), or a dietary mixture of benzyl isothiocyanate (BITC) plus PEITC, inhibited the formation of 4-hydroxy-1-(3-pyridyl)-1-butanone (HPB) releasing adducts of benzo[a]pyrene (B[a]P) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in the lung of A/J mice, leading to inhibition of lung tumorigenesis induced by NNK. Oral administration of sulforaphane (SFN) to benzo(a)pyrene [B(a)P]-induced lung cancer in Swiss albino mice mitigated the damaging effects of B(a)P in mice by upholding the GSH redox cycle and stabilizing the thiol status (Kalpana et al. 2011). SFN was also found to prevent formation of leaky membranes by boosting the antioxidant status, leading to maintenance of ATPase activity in B(a)P-treated animal and reduced carcinogen-associated morphological changes in the lung tissue. Further, they found that sulforaphane treatment decreased hydrogen peroxide production in benzo(a)pyrene [B(a)P]-induced lung cancer in Swiss albino mice, confirming its antioxidant potential (Kalpana et al. 2013). Apoptosis was induced by increasing the release of cytochrome c from mitochondria, decreasing expression of Bcl-2 and increasing expression of Bax. Caspase-3 activity was also enhanced leading to DNA fragmentation in SFN-treated groups.

Sulforaphane blocked benzo[a]pyrene-evoked forestomach tumours in ICR mice (Fahey et al. 2002). This protection resulted from induction of phase 2 detoxication and antioxidant enzymes and was abrogated in mice lacking the nrf2 gene, which regulated phase 2 enzymes. Studies demonstrated that ApcMin/+ mice fed with sulforaphane-supplemented diet developed significantly less and smaller polyps with higher apoptotic and lower proliferative indices in their small intestine in a dose-dependent manner (Hu et al. 2006). Immunohistochemical staining of the adenomas indicated that sulforaphane significantly suppressed the expression of phosphorylated c-Jun N-terminal kinase (p-JNK), phosphorylated extracellular signal-regulated kinases (p-ERK) and phosphorylated-Akt (p-Akt), which were found to be highly expressed in the adenomas of ApcMin/+ mice. It was found that the concentrations between 3 and 30 nmol/g of sulforaphane and its metabolite sulforaphane-GSH were required to prevent, or retard, adenoma formation in the gastrointestinal tract of ApcMin/+ mice.

Administration of sulforaphane (SFN) and phenethyl isothiocyanate (PEITC), major ITCs in broccoli and watercress, respectively, and their corresponding N:-acetylcysteine (NAC) conjugates showed chemopreventive activity towards azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) in F344 rats (Chung et al. 2000). SFN, SFN–NAC, PEITC and PEITC–NAC all significantly reduced the formation of total ACF from 153 to 100–116 and multicrypt foci from 52 to 27–38 (more than four crypts/focus) during the post-initiation treatment. However, only SFN and PEITC were effective during the initiation phase, reducing the total ACF from 153 to 109–115 and multicrypt foci from 52 to 35 (more than four crypts/focus). The NAC conjugates were inactive as anti-initiators against AOM-induced ACF. The results indicated a potential role of sulforaphane

and phenethyl isothiocyanate in the protection against colon cancer. Recent studies demonstrated that the chemopreventive effects of sulforaphane on human colon cancer Caco-2 cells may have been partly attributed to Nrf2-mediated UDP-glucuronosyltransferase 1A (UGT1A) induction and apoptosis induction, providing experimental basis for clinical application of sulforaphane to human colon cancer prevention (Wang et al. 2012c).

A broccoli sprout isothiocyanate-rich extract significantly induced both glutathione S-transferase (GST) or NAD(P)H–quinone oxidoreductase 1 (NQO1) in cultured bladder cells in-vitro and in rat bladder tissues in-vivo (Zhang et al. 2006). Deficiency GST or (NQO1) in humans had been reported to be associated with increased risk of urothelial bladder cancer. The study showed broccoli sprout ITC extract to be a potent inducer of GST and NQO1 in the bladder and to be a promising agent for prevention of bladder cancer. Studies showed that combinations of tomato and broccoli enhanced antitumour activity in dunning r3327-h prostate adenocarcinomas in rats (Canene-Adams et al. 2007). Broccoli decreased tumour weights by 42 %, whereas the 10:10 combination with tomato caused a 52 % decrease. Lycopene at 23 or 224 nmol/g of the diet insignificantly reduced tumour weights by 7 or 18 %, respectively, whereas tomato reduced tumour weight by 34 %.

Broccoli and broccoli sprout extracts and pure isothiocyanates were found to inhibit normal, noninvasive (RT4) and invasive (J82, UMUC3 bladder cancer cells) human urothelial cell viability (Abbaoui et al. 2012). Sulforaphane (IC_{50} = 5.66 μM) and erucin (IC_{50} = 8.79 μM) were found to be the most potent inhibitors, and normal cells were least sensitive. This inhibition was associated with downregulation of survivin, epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2/neu), G_2/M cell cycle accumulation and apoptosis. In a murine UMUC3 xenograft model, feeding semipurified diets containing 4 % broccoli sprouts or 2 % broccoli sprout isothiocyanate extract, or gavaged pure sulforaphane or erucin (each at 295 μmol/kg, similar to dietary exposure) elicited report tumour weight reduction of 42, 42, 33, and 58 %, respectively. Sulforaphane and erucin metabolites were present in mouse plasma (micromolar range) and tumour tissue, with *N*-acetylcysteine conjugates as the most abundant. Interconversion of sulforaphane and erucin metabolites was observed.

Clinical Studies

In both men and women, oral ingestion of dietary indole-3-carbinol (I3C), which is present in cruciferous vegetables (e.g., cabbage, cauliflower and broccoli), significantly increased the urinary excretion of C-2 estrogens (Michnovicz et al. 1997). The urinary concentrations of nearly all other estrogen metabolites, including levels of estradiol, estrone, estriol and 16alpha-hydroxyestrone, were lower after I3C treatment. The results confirmed the hypothesis that I3C induced estrogen 2-hydroxylation, resulting in decreased concentrations of several metabolites known to activate the estrogen receptor. This effect may have a beneficial effect on estrogen metabolism and may lower estrogenic stimulation in women. I3C may have chemopreventive activity against breast cancer in humans.

Hecht et al. (2004) investigated the effects of cruciferous vegetable (including cauliflower, broccoli) consumption on the metabolism of the tobacco-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in 84 smokers. They found that glucobrassicins, which release indole-3-carbinols on chewing, were the major glucosinolates in seven of the nine cruciferous vegetables, accounting for 70.0–93.2 % of all glucosinolates in these vegetables. There was a significant correlation (P = 0.01) between increased consumption of glucobrassicins and decreased levels of metabolites of NNK: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronides (NNAL-Glucs) in urine after adjustment for number of cigarettes smoked per day. Their results were consistent with those of previous studies, which demonstrated that indole-3-carbinol decreased levels of urinary NNAL probably by inducing hepatic metabolism of NNK. In a randomized crossover trial (n = 20) comparing the effects of a *Brassica* vegetable supplementation intervention against a

micronutrient and fibre (M + F) supplementation, *Brassica* intervention was found to significantly decreased urinary F2-isoprostane levels (F2-iP), a stable biomarker of systemic oxidative stress by 21 % compared to baseline and (M + F) intervention (Fowke et al. 2006). Their results suggested that brassica consumption reduces systemic oxidative stress independent of the vitamin and mineral content of these vegetables.

Sulforaphane (SFN), an anticarcinogenic isothiocyanate found in cruciferous vegetables such as broccoli and cauliflower, was first identified as a potent inducer of phase 2 enzyme (Myzak et al. 2007). They found that when consumed in the diet at an average daily dose of 7.5 µmol per animal for 21 days, SFN suppressed the growth of human PC-3 prostate cancer cells by 40 % in male nude mice. There was a significant decrease in histone deacetylase (HDAC) C activity in the xenografts, as well as in the prostates and mononuclear blood cells (MBC), of mice treated with SFN, compared to controls. There also was a trend towards increased global histone acetylation in the xenografts, prostates and MBC. In human subjects, a single dose of 68 g Brocco Sprouts inhibited HDAC activity significantly in peripheral blood mononuclear cells (PBMC) 3 and 6 hours following consumption. These findings provided evidence that one mechanism through which SFN acted as a cancer chemopreventive agent in-vivo was through the inhibition of HDAC activity. A study on a group of Jordanians men and women found that dietary consumption of broccoli induced the activities of cytochromes CYP1A2 and CYP2A6 (Hakooz and Hamdan 2007). Induction or inhibition of cytochrome P450 (CYP) enzyme activities, enzymes that activate or detoxify xenobiotics, is one mechanism by which vegetables may alter cancer risk.

In a study of 628 men diagnosed with prostate cancer, conducted at the Fred Hutchinson Cancer Research Center in Seattle, WA, those eating 28 or more servings of vegetables per week showed a 35 % decreased risk for prostate cancer when compared with those eating fewer than 14 servings per week (Cohen et al. 2000). There was also a 41 % decreased risk among men eating three or more servings of cruciferous vegetables (broccoli, cabbage, Brussels sprouts, cauliflower) per week compared with those eating less than one serving per week, even after controlling for total vegetable intake. In a prospective study of fruit and vegetable intake and risk of prostate cancer, involving 1,338 patients with prostate cancer among 29,361 men (average follow-up = 4.2 years) in the screening arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, Kirsh et al. (2007) found that a high intake of cruciferous vegetables, including broccoli and cauliflower, may be associated with reduced risk of aggressive prostate cancer, particularly extraprostatic disease.

The results of 7 cohort studies and 87 case–control studies on the association between brassica consumption and cancer risk showed inverse associations between the consumption of cabbage, cauliflower and broccoli and risk of lung cancer; between the consumption of brassicas and risk of stomach cancer; between broccoli consumption and risk of all cancers taken together; and between brassica consumption and the occurrence of second primary cancers (Verhoeven et al. 1996). Of the case–control studies, 67 % showed an inverse association between consumption of total brassica vegetables and risk of cancer at various sites. For cabbage, broccoli, cauliflower and Brussels sprouts, these percentages were 70, 56, 67 and 29 %, respectively. Although the measured effects might had been distorted by various types of bias, it was concluded that a high consumption of brassica vegetables was associated with a decreased risk of cancer.

Antimutagenic/Anticlastogenic Activities

Studies found that glucosinolate-rich broccoli seed extracts inhibited mutagenesis induced by the S9-dependent mutagen (2-aminofluorene) more significantly than direct-acting mutagens (Rampal et al. 2010). Out of the four extracts tested, 0.1 mol/l of HCl extract was found to be the most effective in inhibiting mutagenesis with both TA 98 and TA 100 strains of *Salmonella*

typhimurium. All other extracts also showed pronounced antimutagenic potential. The results of this study indicated the presence of potent antigenotoxic factors in broccoli. In the Ames mutagenic test using *Salmonella typhimurium* TA 100, high pressure or freezing treatment of broccoli juice exerted strongly positive test MNU (2-nitroso-2-methylurea) mutagen inhibition (Totušek et al. 2011). In the Ames mutagenic test using *Salmonella typhimurium* TA 98, high pressure or freezing treatment of broccoli juice exerted strongly positive test on IQ (2-amino-3-methyl-3H-imi-dazo-[4,5-*f*]quinoline) mutagen inhibition. In the clastogenicity test assessed using the micronucleus test animals administered broccoli juice and MNU or broccoli and IQ, a statistically significant reduction in micronuclei number was found compared to MNU- or IQ-treated animals, both with high micronuclei numbers. The results indicated the suppressive action of broccoli juice on clastogenic effects of MNU.

Antiviral Activity

Sulforaphane was found to inhibit Epstein–Barr virus (EBV) reactivation in nasopharyngeal carcinoma cells, thereby decreasing virus production (Wu et al. 2012). It was found that sulforaphane inhibited transactivation activity of the EBV immediate-early gene Rta but not Zta and had the capability to inhibit EBV lytic cycle.

Antimicrobial Activity

It was found that 23 out of 28 different microbial species were inhibited in-vitro by sulforaphane (found abundantly in broccoli) with a minimal inhibitory concentration (MIC) ranging from 1 to 4 μg/ml (Johansson et al. 2008). Five pathogens—*Pseudomonas aeruginosa*, three methicillin-resistant *Staphylococcus aureus* (MRSA) isolates and *Candida albicans*—were considered resistant to sulforaphane having MICs ≥ 16–32 μg/ml.

Two novel glucosinolates identified as 2-mercaptomethyl sulfinyl glucosinolate (1) and (*Z*)-1-((2S,5S)-5-hydroxytetra-hydro-2H-pyran-2-ylthio)-2-(1H-indol-3-yl) ethylidene amino sulfate (2) and a known cinnamoyl [6′-*O*-trans-(4″-hydroxy cinnamoyl)4-(methylsulphinyl)butyl glucosinolate] (3) isolated from broccoli florets exhibited antimicrobial activity (Survay et al. 2012). Both compounds 1 and 3 showed a significant and similar antimicrobial activity against *Staphylococcus aureus* with an IC_{50} of <625 μg/ml when compared to antibiotic Duricef. Against *Salmonella typhimurium*, the IC_{50} of 1 and 3 was determined as <625 and <1,250 μg/ml, respectively, when compared to ampicillin ($IC_{50} \leq 39$ μg/mL) as a positive control. Ethyl acetate and chloroform extracts of broccoli were found to be effective against Gram-positive bacteria *Bacillus cereus* and *Bacillus subtilis* and *Candida albicans* (Hashem et al. 2012a). The ethyl acetate and ethanol extracts were highly active against *E. coli* (Gram negative). Sulforaphane and erucin, two natural isothiocyanates highly abundant in broccoli, were found to strongly inhibit quorum sensing and virulence in *Pseudomonas aeruginosa* (Ganin et al. 2013). Mechanistic evaluations of these effects suggested that these isothiocyanates were antagonists of the transcriptional activator LasR.

Gastroprotective Activity

Studies found that sulforaphane, a component in broccoli and broccoli sprouts, exhibited potent bacteriostatic activity against 3 reference strains and 45 clinical isolates of *Helicobacter pylori* with MIC_{90} value of <4 g/ml (Fahey et al. 2002). *H. pylori* was completely eradicated in 8 of the 11 sulforaphane-treated human gastric xenografts implanted in nude mice, suggesting that sulforaphane might be beneficial in the treatment of *H. pylori*-infected individuals (Haristoy et al. 2003). Twelve isothiocyanates (ITC) including sulphoraphane exerted antibacterial activity against 25 strains of *H. pylori* in-vitro (Haristoy et al. 2005). The MIC_{90} values for these ITCs ranged between 4 and 32 μg/ml, and 4 of the most potent compounds exhibited bactericidal activity against both extra- and intracellular bacteria.

Nine *Helicobacter pylori*-positive patients completed the oral treatment with broccoli sprouts (14, 28 or 56 g) twice daily for 7 days (Galan et al. 2004). Seven of nine (78 %) patients were stool antigen negative immediately after the completion of therapy, and 6 remained negative at day 35. Urea breath testing was completed on six patients. Two patients were negative, two positive and two indeterminate. Six patients rated the taste of broccoli sprouts from okay to very good; one patient stated they were "not good." Consumption of oral broccoli sprouts was temporally associated with eradication of *H. pylori* infection in three of nine patients. Most patients found broccoli sprouts palatable.

Dietary treatment of C57BL/6 female mice infected with *H. pylori* Sydney strain 1 with sulforaphane-rich broccoli sprouts reduced gastric bacterial colonization, attenuated mucosal expression of tumour necrosis factor-alpha and interleukin-1 beta, mitigated corpus inflammation and prevented expression of high salt-induced gastric corpus atrophy (Yanaka et al. 2009). This therapeutic effect was not observed in mice in which the nrf2 gene was deleted, strongly implicating the important role of Nrf2-dependent antioxidant and antiinflammatory proteins in sulforaphane F-dependent protection. In a randomized, placebo-controlled study of 48 patients, 8-week dietary intervention with broccoli sprouts, but not with placebo, decreased the levels of urease and *H. pylori* stool antigen (both biomarkers of *H. pylori* colonization) and serum pepsinogens I and II (biomarkers of gastric inflammation). Daily intake of sulforaphane-rich broccoli sprouts for 2 months reduced *H. pylori* colonization in mice and improved the sequelae of infection in infected mice and in humans. This treatment appeared to enhance chemoprotection of the gastric mucosa against *H. pylori*-induced oxidative stress.

Cardiovascular Protective (Antihypertensive/Antihypercholesterolemic) Activities

An in-vivo study in rats showed that dietary intake of broccoli sprouts containing glucoraphanin, which metabolized into the phase 2 protein inducer sulforaphane, resulted in significantly decreased oxidative stress in cardiovascular and kidney tissues, as shown by increased glutathione (GSH) content and decreased oxidized GSH, decreased protein nitrosylation, as well as increased GSH reductase and GSH peroxidase activities (Wu et al. 2004). Decreased oxidative stress correlated with better endothelial-dependent relaxation of the aorta and significantly lowered (20 mmHg) blood pressure. Thus, consuming broccoli containing phase 2 protein inducers reduces the risk of developing cardiovascular problems of hypertension and atherosclerosis.

Studies showed that consumption of broccoli sprouts containing 20 μmol of glucoraphanin (BS10X) had more marked effects on cholesterol homeostasis than glucoraphanin-rich broccoli sprout (GRE) and sulforaphane-rich broccoli sprout (SFE) extracts in Syrian hamsters with dietary-induced hypercholesterolemia (Rodríguez-Cantú et al. 2011). Hepatic cholesterol was reduced by BS10X and SFE treatments in all animals. This correlated with a downregulation of gene expression of sterol regulatory element-binding proteins (SREBP-1 and SREBP-2) and fatty acid synthase caused by GRE and SFE diets. BS10X caused changes in gene expression in a gender-specific manner; additionally, it increased coprostanol excretion in females.

In a phase 1 study of 12 subjects, it was found that consuming broccoli sprouts 100 g daily for a week showed a reduction in total cholesterol, LDL cholesterol and an increase in HDL cholesterol (Murashima et al. 2004). All subjects showed decreased plasma cysteine, plasma PCOOH (phosphatidylcholine hydroperoxide), urinary 8-isoprostane and urinary 8-OHdG (8-hydroxydeoxyguanosine) and increased serum coenzyme Q(10). There was improved cholesterol metabolism and decrease in oxidative stress markers.

Photoprotective Activity

The UV radiation-induced skin carcinogenesis in "initiated high-risk mice" was substantially inhibited by broccoli sprout extracts containing sulforaphane (Dinkova-Kostova et al. 2006).

After completion of the UV irradiation schedule (30 mJ/cm^2/session twice a week for 20 weeks), mice treated topically with broccoli sprout extract containing 1.0 μmol (high-dose) sulforaphane for 5 days a week for 11 weeks had their tumour burden, incidence and multiplicity reduced by 50 % compared to 100 % tumour incidence in untreated control mice. Sulforaphane inhibited cytokine-dependent (gamma-interferon or lipopolysaccharide) induction of iNOS in RAW 264.7 macrophages. The results showed topical application of sulforaphane-containing broccoli sprout extracts to be a promising strategy. Treatment of murine and human keratinocytes with the isothiocyanate sulforaphane elevated phase 2 enzymes and glutathione and protected against oxidant toxicity. Topical application of sulforaphane-containing broccoli sprouts extracts induced the phase 2 response in mouse skin in-vivo. Topical application of broccoli sprout extract delivering 100 nmol sulforaphane/cm(2) increased the protein levels of NAD(P)H–quinone oxidoreductase 1 (NQO1), glutathione S-transferase A1 and heme oxygenase 1, three representative phase 2 enzymes, in mouse skin epidermis (Dinkova-Kostova et al. 2007). Quantitative assessment of the activity of NQO1 24 hours after dosing showed increases of 1.5- and 2.7-fold after application of single and multiple (thrice, every 24 hours) doses, respectively. A dose-escalation safety study in healthy human subjects revealed no adverse reactions when doses as high as 340 nmol of sulforaphane in the form of broccoli sprout extracts were applied topically to the center of a 1 cm diameter circle drawn on the volar forearm. The enzyme activity of NQO1 in homogenates of 3 mm full thickness skin punch biopsies increased in a dose-dependent manner, with maximum increases of 1.5- and 4.5-fold after application of 150 nmol doses, once or three times (at 24-hours intervals), respectively, thus providing direct evidence for induction of the phase 2 response in humans. Further they found that feeding broccoli sprout extracts (providing daily doses of 10 μmol of glucoraphanin) to SKH-1 hairless mice with prior chronic exposure to UV radiation (30 mJ/cm^2) of UVB, twice a week, for 17 weeks) inhibited the development of skin tumours during the subsequent 13 weeks (Dinkova-Kostova et al. 2010). Compared to the controls, tumour incidence, multiplicity and volume were reduced by 25, 47 and 70 %, respectively, in the animals that received the protective agent.

Studies showed that topical application of sulforaphane-rich extracts of 3-day-old broccoli sprouts stimulated phase 2 enzymes in the mouse and human skin, protected against UV radiation-induced inflammation and edema in mice, and reduced susceptibility to erythema arising from narrowband 311-nm UVR in humans (Talalay et al. 2007). Mean erythema reduction in six human subjects was 37.7 %, and protection was catalytic and long-lasting.

Anticataract Activity

After treatment of human adult retinal pigment epithelial cells for 24 hours with 0–5 μM concentrations of sulforaphane (a potent phase 2 enzyme inducer isolated from broccoli), the toxicities of the oxidants (menadione, tert-butyl hydroperoxide, 4-hydroxynonenal and peroxynitrite) were markedly reduced as shown by 1.5- to 3-fold increases in D(m) values (Gao et al. 2001). Protection was prolonged and persisted for several days after removal of sulforaphane before returning to control levels. The sulforaphane-dependent increases in specific activities of cytosolic quinone reductase and the glutathione levels were highly significantly correlated with the degree of protection as measured by D(m) values. Antioxidant protection was also demonstrated for human HaCaT keratinocytes and L1210 murine leukemia cells. Significant protection of retinal pigment epithelial cells against UV light (320–400 nm) photooxidative cytotoxicity was obtained by prior treatment with phase 2 gene inducers, such as the isothiocyanate sulforaphane or a bis-2-hydroxybenzylideneacetone Michael reaction acceptor (Gao and Talalay 2004). The degree of protection was correlated with the potencies of these inducers in elevating cytoprotective glutathione levels and activities of NAD(P)H–quinone oxidoreductase.

The flavonoid fraction of broccoli was found to prevent selenite-induced cataractogenesis in Sprague–Dawley albino rat pups, possibly by maintaining antioxidant status and ionic balance through Ca^{2+} ATPase pump, inhibition of lipid peroxidation, calpain activation and protein insolubilization (Vibin et al. 2010).

In a prospective cohort study of 36,644 men (45–75 years), it was found that men who consumed specific foods high in carotenoids, lutein and zeaxanthin, like broccoli and spinach, twice a week, had a modestly lower risk of cataract (Brown et al. 1999).

Immunomodulatory Activity

Administration of allyl isothiocyanate (AITC) and phenyl isothiocyanate (PITC) was found to stimulate the immunological response in Balb/c mice (Manesh and Kuttan 2003). Both isothiocyanates augmented total WBC count and alpha-esterase positive cell number. Treatment with AITC and PITC along with the antigen sheep red blood cells (SRBC) produced an enhancement in the circulating antibody titer and the number of plaque-forming cells in the spleen. Similarly intraperitoneal administration of sulforaphane to Balb/c mice enhanced total WBC count and alpha-esterase positive cell number (Thejass and Kuttan 2007a). Treatment with sulforaphane along with the antigen, sheep red blood cells (SRBC), produced an enhancement in the circulating antibody titre and the number of plaque-forming cells in the spleen and in the phagocytic activity of peritoneal macrophages. Also sulforaphane significantly reduced the elevated level of TNF-alpha production by LPS-stimulated macrophages. They also found that administration of sulforaphane significantly enhanced natural killer cell activity and antibody-dependent cellular cytotoxicity in B16F-10 melanoma-induced metastasis-bearing C57BL/6 mice (Thejass and Kuttan 2007b). Administration of sulforaphane significantly enhanced the production of IL-2 and IFN-gamma in metastatic tumour-bearing animals and sulforaphane significantly downregulated the serum levels of proinflammatory cytokines such as IL-1beta, IL-6, TNF-alpha and GM-CSF during metastasis. The results suggested that sulforaphane effectively inhibited the spread of metastatic tumour cells through the stimulation of cell-mediated immune response, upregulation of IL-2 and IFN-gamma and downregulation of proinflammatory cytokines IL-1beta, IL-6, TNF-alpha and GM-CSF.

Antiinflammatory Activity

Heiss et al. (2001) found a potent decrease in lipopolysaccharide (LPS)-induced secretion of proinflammatory and pro-carcinogenic signaling factors (NO, prostaglandin E(2) and tumour necrosis factor alpha) in cultured Raw 264.7 macrophages after sulforaphane treatment. Sulforaphane selectively reduced DNA binding of NF-kappa B, a pivotal transcription factor in LPS-stimulated proinflammatory response, without interfering with LPS-induced degradation of the inhibitor of NF-kappa B nor with nuclear translocation of NF-kappaB. Their data indicated that antiinflammatory mechanisms contribute to sulforaphane-mediated cancer chemoprevention.

In animal studies, dietary intake of dried broccoli sprouts containing high amounts of glucoraphanin that afforded phase 2 protein-inducing isothiocyanate sulforaphane was found to decrease aging-associated degenerative and inflammatory changes in spontaneously hypertensive rat stroke-prone rat central nervous system (Noyan-Ashraf et al. 2005). Recent animal studies showed that treatment of rats under noninflamed conditions with broccoli extract and the essential oils of turmeric, thyme and rosemary promoted intestinal health by reducing the proinflammatory adhesion molecule VCAM-1 and by increasing the tight junction marker Cldn3, leading to an improved gut barrier (Mueller et al. 2013). These phytogenic additives also exhibited antiinflammatory properties as indicated by the reduction of the dextran sulphate sodium-induced increase in proinflammatory mediators like NFκB, VCAM-1, MCP-1 and COX2 to varying degree in rats.

Weight Loss Activity

The chloroform extract, the combined ethyl acetate and ethanol extracts and the crude extract of broccoli florets at 5 and 1 % of diet elicited significant body weight loss in female rats, 180, 85 and 75 g total loss in body weight, respectively (Motawea et al. 2010). When these results were compared with the water extract of green tea (117 g loss), the chloroform broccoli extract was more active. No toxicity was observed in the crude broccoli extract up to 10 g/kg body weight in rats in the LD_{50} test.

Pharmacokinetic Studies

The gastric digestion (in-vitro) of broccoli caused high losses in glucosinolates (69 % loss), whereas phenolics and vitamin C presented higher stability under these conditions (Vallejo et al. 2004a). There were no losses in flavonoids, a 7 % loss of vitamin C and a variable rate of loss (6–25 %) in hydroxycinnamic acid derivatives were observed. Under in-vitro intestinal conditions, flavonoids and hydroxycinnamoyl acid derivatives were of low availability, due to their significant losses (84 and 80 % loss, respectively) under these conditions, at the end of the experiment. Vitamin C showed greater decrease after intestinal digestion (91 % loss). Regarding the remaining glucosinolates, these compounds presented higher stability under intestinal conditions, rendering an availability similar to that found for phenolics (75 % loss). The study showed glucosinolates were mainly degraded by gastric conditions, whereas phenolic compounds and vitamin C were degraded by intestinal conditions.

In a crossover study of healthy volunteers, urinary dithiocarbamate excretion increased sharply after administration of broccoli sprout glucosinolates or isothiocyanates (Shapiro et al. 2001). Cumulative excretion of dithiocarbamates following 111-μmol doses of isothiocyanates was greater than that after glucosinolates. In subjects fed four repeated 50 μmol doses of isothiocyanates, the intra- and intersubject variation in dithiocarbamate excretion was very small, and after escalating doses, excretion was linear over a 25–200 μmol dose range. Dithiocarbamate excretion was higher when intact sprouts were chewed thoroughly rather than swallowed whole. The studies indicated that isothiocyanates were about six times more bioavailable than glucosinolates, which must first be hydrolyzed. Thorough chewing of fresh sprouts exposed the glucosinolates to plant myrosinase and significantly increased dithiocarbamate excretion. In another crossover study of 12 subjects, the bioavailability of sulforaphane and erucin (two important isothiocyanates from broccoli) was dramatically lower when subjects consumed broccoli supplements compared to fresh broccoli sprouts (Clarke et al. 2011). The peaks in plasma concentrations and urinary excretion were also delayed when subjects consumed the broccoli supplement. Interconversion of sulforaphane and erucin metabolites was observed. The study confirmed that consumption of broccoli supplements devoid of myrosinase activity did not produce equivalent plasma concentrations of the bioactive isothiocyanate metabolites compared to broccoli sprouts.

Food Safety Studies

Putrescine, cadaverine, histamine, tyramine, spermidine and spermine increased during broccoli and radish sprout production although these levels were below those permitted by legislation (5 mg/100 g of edible food) (Martínez-Villaluenga et al. 2008). Broccoli and radish sprouts demonstrated no toxic effects on proliferation and viability of human promyelocytic leukemia cells and should be included in diets as healthy and safe fresh foods. Owing to the effect of broccoli constituents on the cytochrome P450 system, involved in the metabolism of various medicines, interactions could occur with these medicines (Fahey et al. 2001). Isothiocyanates had been reported to have a goitrogenic effects, but Fahey et al. (2001) asserted that there was no reason to assume that consumption of (isothiocyanates from) *Brassica* varieties should have a negative effect on the thyroid in people who do not have

a thyroid condition, particularly where iodine intake was adequate.

Allergy Problems

Work-related symptoms such as rhinitis, conjunctivitis, asthma and urticaria caused by broccoli and cauliflower pollen were reported by 44 % of the participants (24/54), of whom all but one had positive skin-prick tests for cauliflower- and/or broccoli-pollen/flower extracts, and 58 % (14/24) had positive radioallergosorbent test (RAST) results (Hermanides et al. 2006). Symptoms had developed within the first 2 years in 33 % of the patients. Six patients had to stop or change work.

Traditional Medicinal Uses

One unusual phytotherapeutic role of broccoli is for skin diseases—the juice of the leaves is used to treat warts (Moreno et al. 2006).

Other Uses

Broccoli by-products (harvest remains) resulting from greenhouse cultivation still contained bioactive compounds (glucosinolates, phenolic acids and flavonoids), and nutrients (vitamin C, minerals and trace elements), with radical-scavenging capacity, and may be useful as sources of nutrients and potentially functional ingredients, giving the opportunity to obtain added-value products and reduce agrowaste costs and environmental problems (Domínguez-Perles et al. 2010).

Comments

Cauliflower and broccoli have been classified in convar. *botrytis* (L.) Alef. as *Brassica oleracea* var. *botrytis* L. and var. *italica* Plenck, respectively (Tjeertes 2004). They can best be considered as cultivar groups and as such have been called *B. oleracea* (Cauliflower Group) and (Broccoli Group) (Van der Vossen 1994; Tjeertes 2004) or *B. oleracea* (Botrytis Group) or *B. oleracea* (Italica Group) (Porcher et al. 1995–2020). However, most scientific papers use the name *B. oleracea* var. *botrytis* and *B. oleracea* var. *italica* for cauliflower and broccoli, respectively.

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Brassica oleracea italica x alboglabra

Scientific Name

Brassica oleracea italica* x *alboglabra

Synonyms

Brassica oleracea (Italica x Alboglabra Group)

Family

Brassicaceae

Common/English Names

Asparation, Asparations, Baby Broccoli, Bimi, Broccolette, Broccoletti, Broccolini, Sweet Baby Broccoli, Tenderstem, Tenderstem Broccoli

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Vernacular Name

Brazil: broccolis

Origin/Distribution

The hybrid cultivar was developed by the Sakata Seed Company of Yokohama, Japan, in 1993 and named 'aspabroc'. In 1994, Sakata Seed Company in partnership with Sanbon Incorporated began growing 'aspabroc' commercially in Mexico under the name Asparation®. Asparation® first appeared in US markets in 1996. In 1998, Mann Packing Company in collaboration with Sakata Seed Company began marketing 'Aspabroc' throughout the United States under the name Broccolini.

Agroecology

Broccolini is a cool climate crop, sharing the same agroecological requirements as broccoli. It is intolerant of temperature extremes and is more sensitive to cold temperatures than broccoli and is more tolerant of slightly higher temperatures than broccoli.

Edible Plant Parts and Uses

The entire vegetable (leaves, tender young stems, unopened flowering shoots and flowers) is consumable. Broccolini is usually sold as the young tender unopened flowering shoot of 15–20 cm length; some supermarket chains allow a maximum of four opened flowers in the unopened flowering shoot product. Broccolini's flavour is sweet, with notes of both broccoli and asparagus. Broccolini can be sauteed, steamed, boiled, roasted, grilled and stir-fried. Broccolini makes a great appetizer, pasta or risotto ingredient and pizza topping. Broccolini's flavour goes well with butter, olive oil, light-bodied vinegars, lemon, lime, garlic, tomatoes, chillies, cured meats such as pancetta and prosciutto, barbecued meat, flaky white fish, hard cheeses (parmesan and pecorino) or fresh cheeses (chevre and feta).

Botany

The plant has a structure similar to the sprouting type of broccoli. It is erect, annual or biennial, herbaceous and glabrous up to 80 cm high with an elongated slender, green stem, 15–30 cm long, branching at the top with relatively small, loosely arranged racemose heads. Leaves alternate, petiolate, simple, ovate to ovate-oblong, 40–50 × 30–40 cm, pinnatipartite or lobed with undulating, shallowly dentate margin, grey-green or blue green. The racemose flower heads are fully exposed from an early stage on slender rachis and peduncles unlike the heading or calabrese broccoli with larger compact head and thick peduncle and rachis. Flowers tetramerous; bisexual; four green sepals; four yellow, spatulate petals; six stamens, four long and two short; superior, two-loculed ovary. Fruit a slender silique with 10–30 subglobose seeds.

Nutritive/Medicinal Properties

Broccolini was reported to have the following nutrient composition: energy 35 kcal, protein 2.98 g carbohydrate 6.04 g, total dietary fibre 1 g, total sugars 2.04 g, calcium 60 mg, iron 0.68 mg, sodium 25 mg, vitamin C 78 mg and vitamin A 1,500 IU (Anonymous 2012).

The main hydroxycinnamic acids (sinapic, ferulic, *p*-coumaric and caffeic acids) were isolated from broccoli and broccolini by capillary zone electrophoresis (Lee et al. 2011).

Sixteen volatile constituents were identified from the ethanolic extract of broccolini leaves (Wang et al. 2012). The major components were 5-phenyl-undecane (11 %), n-hexadecanoic acid (9.34 %), octadecanoic acid (6.39 %), 1,1,3-trimethyl-3-phenyl-indan (4.0 %), 3-(2-phenylethyl)benzonitrile (3.48 %) and phytol (3.37 %). Three purified fractions (BLF1, BLF2 and BLF3) were obtained from broccolini leaves by extraction of solvents (petroleum ether, ethyl acetate and

n-butanol), and polyamid resin chromatography and the flavonoids content of purified product increased from 10.2 to 41.6 % (Wang and Zhang 2012b). BLF1 was primarily consisted of quercetin (content up to 85.4), BLF2 was primarily composed of kaempferol (content up to 78.5 %), and BLF3 contains two major constituents kaempferol and apigenin (contents up to 82.6 %).

The following isothiocyanates were isolated and identified from broccolini seeds: 3-BITC (3-benzyl-isothiocyanate) (10.8 %), 4-methyl-pentyl-isothiocyanate (0.5 %), 1-isothiocyanato-butane (26.8 %), PEITC (phenethyl-isothiocyanate) (22.6 %) and sulforaphane (19.2 %) (Zhang et al. 2011). The glucosinolates contents of broccolini, broccoli and Chinese broccoli seeds were determined to be 39.96, 37.77 and 37.25 μmol/g, respectively (Yang and Zhang 2012). Six, eight and four major glucosinolates were identified in broccolini, broccoli and Chinese broccoli seeds, respectively. The common glucosinolates in the three vegetables included 4-methylsuphinylbutyl, 3-butenyl and 4-methylthiobutyl glucosinolates. However, three glucosinolates were different for broccolini and broccoli, one glucosinolate was different for broccolini and Chinese broccoli, and six glucosinolates were different for broccoli and Chinese broccoli.

Anticancer Activity

Studies showed that broccolini leaf flavonoids exhibited a dose-dependent antiproliferative effects in-vitro on four human cancer cell lines (SW480, HepG2, Hela and A549) and induce apoptosis in SW480 cell line (Wang and Zhang 2012a). Studies showed that the crude broccolini Leaf crude extract and the purified flavonoid extracts (BLF1, BLF2 and BLF3) all exhibited an inhibitory effect on the growth of human colon cancer SW480 cell line; the IC_{50} values were estimated to be 88.14, 65.06, 72.62 and 79.42 μg/ml, respectively (Wang and Zhang 2012b). The antiproliferative activities on SW480 cells were increased by 10–26 % after purification. Broccolini seed extract exhibited antiproliferative effects on human lung A549 and ovarian OVCAR-3cancer cells in a dose-dependent manner by using MTT assay, giving IC_{50} values of 81.49 and 78.6 μg/ml, respectively (Yang and Zhang 2011). Further, at high dosage (90–120 μg/ml), the morphology structure of OVCAR-3 cells became irregular and exhibited characteristics of apoptosis such as cell membrane shrinkage, condensation and fragmentation of nuclear chromatin, as well as formation of apoptotic bodies. Isothiocyanates from broccolini seeds induced apoptosis in human colon cancer SW480 cells in a dose-dependent manner in the MTT assay, and the IC_{50} was calculated to be 77.72 μg/ml, superior to the chemotherapeutical drug 5-fluorouracil (Yang et al. 2011).

Other Uses

See notes under broccoli.

Comments

There is a purple broccolini sold under the registered name peacock broccolini. This purple broccolini has small beautifully purple racemose loose flower heads, purple stem and side shoots and large flamboyant purple-tinged edible leaves.

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Lobularia maritima

Scientific Name

***Lobularia maritima* (L.) Desv.**

Synonyms

Adyseton halimifolium Link, *Adyseton maritimum* (L.) Link, *Adyseton orbiculare* Bubani, *Alyssum halimifolium* L., *Alyssum halimifolium* (All.) Willd. (illeg.), *Alyssum maritimum* (L.) Lam., *Alyssum odoratum* Voss, *Anodontea halimifolia* (DC.) Sweet, *Clypeola halimifolia* Link, *Clypeola maritima* Link, *Clypeola maritima* Link, *Draba maritima* (L.) Lam., *Glyce maritima* (L.) Lindl., *Koniga maritima* (L.) R. Br., *Octadenia maritima* (L.) Fisch. & C.A.Mey.

Family

Brassicaceae

Common/English Names

Alyssum, carpet of snow, sea alyssum, Seaside Lobularia, snowdrift, Sweet Alice, Sweet Alison, Sweet Alyssum

Vernacular Names

Chinese: Xiang Xue Qiu
Czech: Lobularie Přímořská, Laločnice Přímořská, Tařicovka Přímořská
Danish: Biblomme
Dutch: Zilverschildzaad
Esperanto: Aliso Mara, Lobulario Mara
Finnish: Tuoksupielus, Valkopielus
French: Alysse Corbeille D'argent, Lobulaire Maritime
German: Duft-Steinrich, Strand-Silberkraut, Strandkresse, Weisses Schildkraut
Maltese: Buttuniera
Norwegian: Silkedodre
Peru: Lágrimas De La Virgin
Polish: Smagliczka Nadmorska
Portuguese: Açafate-De-Prata/Escudinha
Slovencina: Lobulária Prímorská
Spanish: Panalillo
Swedish: Strandkrassing
Turkey: Kuduzotu
Welsh: Alyswm Pêr, Cuddlin, Cyddlin, Cydlyn

Origin/Distribution

Alyssum is native to southern Europe (France, Portugal, Spain, Italy, Albania and Greece), northern Africa (northern Algeria, Egypt, northern Libya, Morocco and Tunisia), the Azores, the Madeira Islands and the Canary Islands. It has naturalized in other areas in the world, including the United States, Australia, China and Taiwan and some Pacific Islands, e.g. Hawaii and New Caledonia. In Australia, it has widely naturalized in the coastal and subcoastal districts of southeastern

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Australia (in eastern New South Wales, southern Victoria, Tasmania, southeastern South Australia and southwest Western Australia) and in south-eastern Queensland, on Norfolk and Lord Howe Islands.

Agroecology

Alyssum does best in areas with a Mediterranean climate where temperatures are mild in winter and warmer in summer and with autumn and spring rainfall and drier periods in summer. It is common on sandy beaches and dunes but can also grow in cultivated fields, stony areas, yards, walls, slopes and waste ground, preferably on calcareous soil, from sea level to 300 m (−2,000 m) altitude. It does well on free-draining sandy and sandy loam soils in full sun but will also grow in partial shade.

Edible Plant Parts and Uses

The young leaves, stems and flowers are used to flavour salads and other dishes where pungency is required (Facciola 1990).

Botany

An erect, ascending or procumbent, pubescent, annual to short-lived perennial herb, 10–30 cm (−40 cm) high with basal branching. Leaves are sessile, simple, linear-lanceolate to lanceolate, 1.5–5 cm long by 0.2–0.4 cm wide, pubescent, green, margin entire, base attenuated and apex acute to subacute (Plates 1, 2, 3 and 4). Inflorescence corymbose-globose, many-flowered and lax when fruiting. Flowers small, fragrant; sepals 1.5–2 mm long, pubescent; petals obovate or suborbicular, 2–3 by 1.5–2.5(−3) mm, clawed, white, pink, apricot, purple to deep purple; stamens short and long with nectar glands at the base and ovate anthers (Plates 1, 2, 3 and 4). Silicula obovate to suborbicular, 2.5–3.5 mm long, sparsely pubescent. Seeds one per locule, ellipsoidal, light to reddish brown, 1–1.5 mm.

Plate 1 White flower Alyssum and leaves

Plate 2 Close view of Alyssum flowers

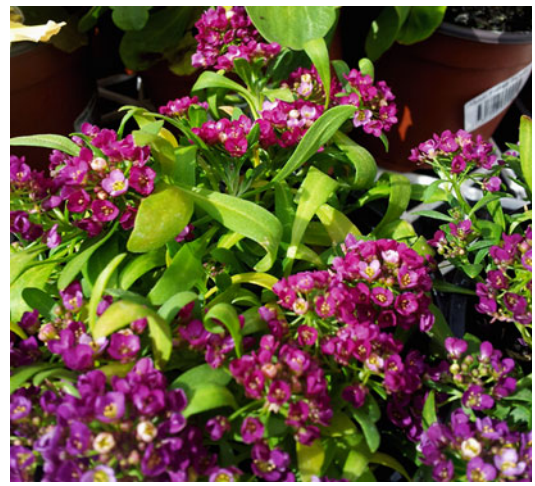

Plate 3 Red flower Alyssum and leaves

Plate 4 Purple flower Alyssum and leaves

Nutritive/Medicinal Properties

Five nucleosides (deoxycytidine, 5-methyldeoxycytidine, deoxyadenosine, deoxyguanosine and thymidine) in the amount of 18.5 % were found in the DNA of *Lobularia maritima* (Wagner and Capesius 1981). The following flavonoids were isolated from the plant: kaempferol, kaempferol 7-rhamnoside, kaempferol 3-glucoside-7-rhamnoside, kaempferol 3-diglucoside and *E*-quercetin 7-glucoside (Matlawska et al. 1989). Sweet alyssum seed had been reported to contain high levels of 6-(methylthio)hexyl- and 6-(methylsulfinyl) hexyl glucosinolates, both of which yielded hydrolysis products of interest, 1-isothiocyanato-6-(methylthio) hexane (lesquerellin) and hesperin (Daxenbichler et al. 1991). Vaughn and Berhow (2005) found alyssum afforded high amounts of glucosinolate hydrolysis products: 3-butenyl isothiocyanate and lesquerellin.

Davis et al. (1998) found that six Brassicacean species including *L. maritima* produced nectar from both lateral nectaries (associated with the short stamens) and median nectaries (outside the long stamens); on average 95 % of the total nectar carbohydrate was collected from the lateral ones. Nectar from these glands possessed a higher glucose/fructose ratio (usually 1.0–1.2) than that from the median nectaries (0.2–0.9) within the same flower. Comparatively little sucrose was detected in any nectar samples. The volatile compound acetophenone was isolated from the flowers (Rohrig et al. 2008).

Four pigments were isolated from *Lobularia maritima* together with a known pigment, as well as three pigments from *Lunaria annua* L. and two known pigments from Cheiranthus cheiri (Tatsuzawa et al. 2006). These pigments were determined to be cyanidin 3-*O*-[2-*O*-((acyl-II)-(β-D-xylopyranosyl))-6-*O*-(acyl-I)-β-D-glucopyranoside]-5-*O*-[6-*O*-(acyl-III)-β-D-glucopyranoside], in which the acyl-I group is represented by glucosyl-*p*-coumaric acid, *p*-coumaric acid and ferulic acid; acyl-II by caffeic acid and ferulic acid; and acyl-III by malonic acid, respectively. Four acylated cyanidin 3-sambubioside-5-glucosides were isolated from the purple-violet flowers of *Lobularia maritima* cv. 'Easter Bonnet Violet' along with six known anthocyanins (Tatsuzawa et al. 2007). These new pigments were cyanidin 3-*O*-[2-*O* -(2-*O* -(*trans*-feruloyl)-β-D-xylopyranosyl)-6-*O*-(4-*O*-(β-D-glucopyranosyl)-*trans*-*p*-coumaroyl)-β-D-glucopyranoside]-5-*O*-β-D-glucopyranoside; cyanidin 3-*O*-[2-*O*-(β-D-xylopyranosyl)-6-*O*-(*trans*-feruloyl)-β-D-glucopyranoside]-5-*O*-β-D-glucopyranoside; cyanidin 3-*O* -[2-*O*-(2-*O*-(*trans*-caffeoyl)-β-D-xylopyranosyl)-6-*O*-(*trans*-feruloyl)-β-D-glucopyranoside]-5-*O*-β-D-glucopyranoside or cyanidin 3-*O*-[2 -*O* -(2-*O*-(*trans*-feruloyl)-β-D-xylopyranosyl)-6-*O*-(*trans*-caffeoyl)-β-D-glucopyranoside]-5-*O*-β-D-glucopyranoside; and cyanidin 3-*O*-[2-*O*-(2-*O*-(*trans*-feruloyl)-β -D-xylopyranosyl)-6-*O*-(*trans*-feruloyl)-β-D-glucopyranoside]-5-*O*-β-D-glucopyranoside.

Six acylated pelargonidin 3-*O*-sambubioside-5-*O*-glucosides were isolated from red-purple flowers *of Lobularia maritima* cv 'Easter Bonnet Deep Rose' (Tatsuzawa et al. 2010). These pigments were pelargonidin 3-*O*-[2-*O*-(2-*O*-(*trans*-caffeoyl)-xylosyl)-6-*O*-(4-glucosyl-*trans*-*p*-coumaroyl)-glucoside]-5-*O*-glucoside (1); pelargonidin 3-*O*-[2-*O*-(2-*O*-(*trans*-feruloyl)-xylosyl)-6-*O*-(4-glucosyl-*trans*-*p*-coumaroyl)-glucoside]-5-*O*-glucoside (2); pelargonidin 3-*O*-[2-*O*-(2-*O*-(*trans*-caffeoyl)-xylosyl)-6-*O*-(transp-coumaroyl)-glucoside]-5-*O*-glucoside (3); pelargonidin 3-*O*-[2-*O*-(caffeoyl)-xylosyl-6-*O*-(feruloyl)-glucoside]-5-*O*-glucoside (4);

pelargonidin 3-*O*-[2-*O*-(2-*O*-(*trans*-feruloyl)-xylosyl)-6-*O*-(*trans*-*p*-coumaroyl)-glucoside]-5-*O*-glucoside (5); and pelargonidin 3-*O*-[2-*O*-(2-*O*-(*trans*-feruloyl)-xylosyl)-6-*O*-(*trans*-feruloyl)-glucoside]-5-*O*-glucoside (6).

Six kaempferol glycosides, four of them characterized for the first time, were isolated from the leaf extract of *Lobularia maritima* (Fiorentino et al. 2009). The four new ones were kaempferol 3-*O*-β-glucopyranosyl-(1 → 2)–*O*-α-xylopyranoside; kaempferol 3-*O*-α-rhamnopyranosyl–(1 → 2)-*O*-α-arabinopyranoside; kaempferol 3-*O*-β-glucopyranosyl-(1 → 2) –*O*-β-glucopyranosyl-7-*O*-α-rhamnopyranoside; and kaempferol 3-*O*-β-glucopyranosyl-(1 → 2)–*O*-β-galactopyransoyl-7-*O*-α-rhamnopyranoside.

Traditional Medicinal Uses

In Spain, Alyssum is commonly used as a diuretic and antiscorbutic (Chopra et al. 1986). It is also highly regarded as an astringent in the treatment of gonorrhoea. In the Amalfi Coast, Campania (Southern Italy), *Lobularia maritima* subsp. *maritima* is used in folk phytotherapy to treat abdominal pains, cold and coughs (Savo et al. 2011).

Other Uses

Alyssum is primarily grown as an ornamental in pots, hanging baskets, mass planting in border fronts or rock gardens. Alyssum also provides a wonderful ground cover.

A hymenopteran parasitoid attractant, acetophenone, was isolated from *L. maritima* flowers (Rohrig et al. 2008). In flight tunnels test, the volatile chemical attracted females of the tephritid fruit fly parasitoid *Diachasmimorpha longicaudata*. The authors suggested that acetophenone could be a valuable monitoring tool in augmenting biological control using parasitoid species particularly species such as *D. longicaudata.*

Comments

Alyssum (*Lobularia maritima*) is deemed as an emerging environmental weed in Tasmania and as a potential environmental weed in other parts of southern Australia (Anonymous 2011). This widely cultivated garden ornamental has escaped cultivation and has become a weed of parks, footpaths, roadsides, waste areas, disturbed sites and coastal environs in southern and eastern Australia.

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Matthiola incana

Scientific Name

***Matthiola incana* (L.) R.Br.**

Synonyms

Cheiranthus albus Mill., *Cheiranthus annuus* L., *Cheiranthus coccineus* Mill., *Cheiranthus incanus* L., *Cheiranthus fenestralis* L., *Cheiranthus graecus* Pers., *Cheiranthus hortensis* Lam., *Cheiranthus viridis* Ehrh., *Hesperis fenestralis* (L.) Lam., *Hesperis incana* (L.) Kuntze, *Matthiola annua* (L.) Sweet, *Matthiola fenestralis* (L.) R.Br., *Mathiolaria annua* (L.) Chevall.

Family

Brassicaceae

Common/English Names

Brampton Stock, Common Stock, Gillyflower, Hoary Stock, Imperial Stock, Stock, 10-Week Stock

Vernacular Names

Czech: Fiala Šedivá
Eastonian: Aedlevkoi
Esperanto: Matiolo Nuda
Finnish: Tarhaleukoija
French: Giroflée, Mattiole Blanchâtre, Voilier Grisâtre
German: Garten-Levkoje, Weisslichgraue Levkoje
Hungarian: Kerti Viola, Nyári Viola, Szagos Viola
Peru: Alhelí (Spanish)
Polish: Lewkonia Letnia
Portuguese: Goiveiro-Encarnado, Goivo-Encarnado
Slovaščina: Fajgelj, Šeboj, Sorta'
Slovencina: Fiala Sivá
Swedish: Gillyflower, Lövkoja
Turkey: Yalancı Şebboy
Welsh: Murwyll Coesbren, Murwyll Lledlwyd

Origin/Distribution

It is native to the coastal areas of southern and western Europe and has naturalized elsewhere. It has been introduced into the New World and Australia.

Agroecology

Matthiola incana is a cool climate species, growing best in temperatures of 15–24 °C. It thrives in full sun to light shade and grows best in well-drained, moist, fertile, organic rich soil with a neutral or slightly alkaline pH range.

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Edible Plant Parts and Uses

Its flowers are eaten as a vegetable or used as a garnish, especially with sweet desserts (Tanaka 1976; Facciola 1990). Studies reported that *M. incana* seeds contained oil rich (55–65 %) in omega-3 linolenic acid and could replace marine oils and thereby contribute beneficially to the human diet (Yaniv et al. 1999).

Botany

A biennial or perennial tomentose herb, 15–75 cm high, unbranched or with sparingly basal branching. Basal leaves rosulate; cauline leaves shortly petiolate or sessile, oblanceolate, 3–16 cm long, (0.5-) 1–2 cm broad margin entire; base attenuate to cuneate, apex rounded (Plates 1 and 2). Racemes 10–30-flowered. Flower: sepals linear-lanceolate to narrowly oblong, 10–15 by 2–3 mm; petals purple, violet, pink, red or white (Plates 1, 2 and 3), obovate to ovate, 20–30 by 7–15 mm, long clawed, apex rounded or emarginate; stamens 7–9, filaments 5–8 mm, anthers 2–4 mm; style 1–5 mm, stigma bilobed, erect, sessile. Siliquae (7-) 10–15 cm long, 2.5–4 mm wide, pubescent-glandular. Seed sub-orbicular, 2 mm across, brown, winged.

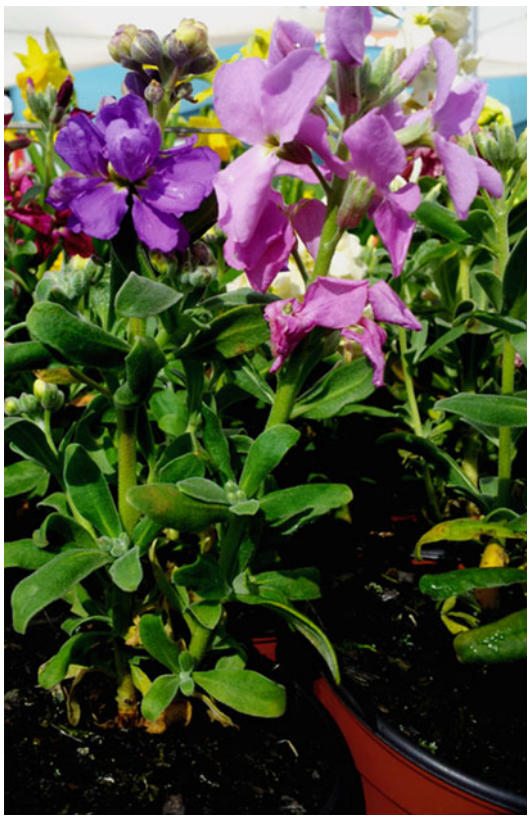

Plate 1 Purple flower stock and leaves

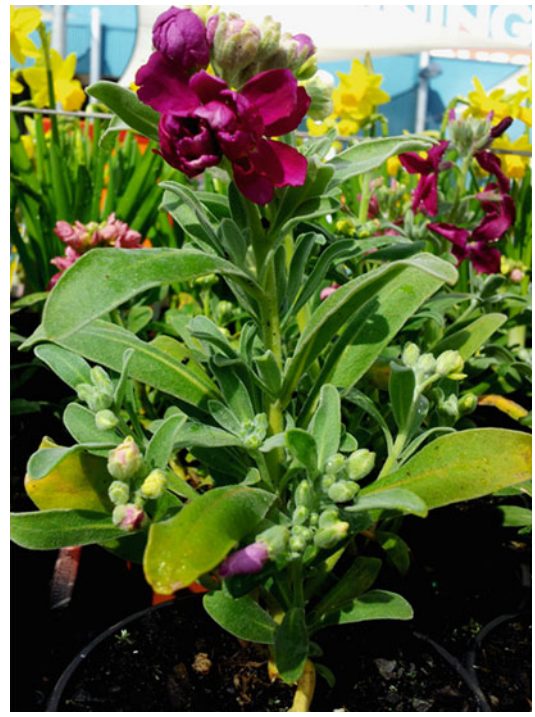

Plate 2 Maroon flower stock and leaves

Plate 3 Bunch of stock flowers

Nutritive/Medicinal Properties

Phytochemicals in Flowers

The flavonoid glycoside dactylin with the structure 5,7,3,4′- tetrahydroxy-3′-methoxyflavone-3-*O*-B-D-glucopyranoside was isolated from *M. incana* (Rahman and Khan 1962). The following phenolic compounds *p*-coumaric, caffeic, ferulic and sinapic acids and kaempferol and anthocyanin pigments were found in the flowers of healthy and virus-infected plants of *Matthiola incana* (Feenstra et al. 1963). In healthy red flowers larger amounts of cinnamic acids were present, bound to the acylated anthocyanins and other compounds and possibly also as free acids. When anthocyanin synthesis was blocked, the formation of cinnamic acids was also inhibited, except for small amounts of sinapic and ferulic acids. In anthocyanin-producing flowers of *Matthiola incana*, the presence of naringenin, naringenin 7-glucoside, dihydrokaempferol and dihydrokaempferol 7-glucoside was detected (Forkmann 1979). The four isolated compounds initiated anthocyanin synthesis after administration to acyanic flowers of genetically defined lines of *Matthiola incana* and *Antirrhinum majus*.

Nine anthocyanin pigments were reported to be present in the flowers of *M. incana*: 3-glucoside, 3,5-diglucoside and 3-feruloyl-pcoumaroylsambubioside-5-glucoside of pelargonidin and 3-glucoside, 3-sambubioside-5-glucoside, 3-caffeoylglucoside, 3-*p*-coumaroylglucoside, 3-*p*-coumaroylsambubioside and 3-caffeoylsambubioside of cyanidin (Harborne 1964, 1967; Seyffert 1960; Teusch et al. 1994). Anthocyanidin 3-glucosides and 3-sambubiosides acylated with 4-coumarate or caffeate were identified in flower extracts of lines of *Matthiola incana* with wild-type alleles of the gene u (Teusch et al. 1994). Accumulation of acylated 3-glycosides during bud development was correlated with acyltransferase activity. Four acylated cyanidin 3-sambubioside-5-glucosides were isolated from purple-violet flowers of *Matthiola incana* (Saito et al. 1995). Three acylated anthocyanins were cyanidin 3-*O*-(6-*O*-acyl-2-*O*-(2-*O*-sinapyl-β-D-xylopyranosyl)-β-D-glucopyranosides)-5-*O*-(6-*O*-malonyl-β-D-glucopyranosides), in which the acyl group was p-coumaryl, caffeyl or ferulyl, respectively. The remaining pigment was free from malonic acid and was identified as cyanidin 3-*O*-(6-*O*-*trans*-ferulyl-2-*O*-(2-*O*-*trans*-sinapyl-β-D-xylopyranosyl)-β-D-glucopyranoside)-5-*O*- (β-D-glucopyranoside). Analysis of the anthocyanin constituents in 16 purple-violet cultivars revealed that they contained the above triacylated anthocyanins in variable amounts as main pigments. An aromatic pair of pigments containing sinapic and ferulic acids was considered to produce an important intramolecular effect, making bluish colours in these flowers. Ten acylated pelargonidin 3-sambubioside-5-glucosides were isolated from the red-purple flowers of *Matthiola incana*, and pelargonidin 3-glucoside was isolated from the brownish-red flowers of *Matthiola incana* (Saito et al. 1996). Seven of the ten pigments were determined to be pelargonidin 3-*O*-[2-*O*-(2-*O*-(acyl-I)-β-D-xylopyranosyl)- 6-*O*-(acyl-II)-β-D-glucopyranoside]-5-*O*-[6-*O*-(malonyl)-β-D-glucopyranoside], in which acyl moieties varied between sinapic, ferulic, caffeic and *p*-coumaric acids. The acylated pelargonidin 3-sambubioside-5-glucosides were present as the dominant pigments in the red-purple, salmon-pink and apricot colour cultivars. In contrast, pelargonidin 3-glucoside was present as a dominant anthocyanin in the copper colour cultivars, and also pelargonidin 3-sambubioside-5-glucoside was found as a minor pigment in the copper colour flowers.

Tatsuzawa et al. (2012) classified *M. incana* flower colours into eight groups, A–H, based on the hue values of their flowers and the major anthocyanin pigment found as follows: in violet flowers (hue values b*/a* = –0.66 and –0.69, V 84A) of group A, cyanidin 3-dihydroxycinnamoyl-sambubioside-5-malonyl-glucosides; in purple flowers (–0.43 and –0.45, P 75A) and red-purple flowers (–0.14 and –0.16, RP 74A) of groups B and D, pelargonidin 3-dihydroxycinnamoyl-sambubioside-5-malonyl-glucosides; in red-purple flowers (–0.21 and –0.24, RP 72A) of group C, cyanidin 3-monohydroxycinnamoyl-sambubioside-5-malonyl-glucosides; in red flowers

(0.05 and 0.06, RP 66A) of group E, pelargonidin 3-monohydroxycinnamoyl-sambubioside-5-malonyl-glucosides; in copper (0.23 and 0.16, R 54A) and peach (2.37 and 2.09, R38C) flowers of groups F and G, pelargonidin 3-glucoside; and a small amount of pelargonidin 3-glucoside was present in yellow flowers of group H.

Phytochemicals in Seeds

The fatty acid composition of *M. incana* seed oil was found to be myristic (2.60 %), palmitic (4.73 %), stearic (4.37 %), arachidic (2.50 %), lignoceric (0.73 %), oleic (32.17 %), linoleic (21.70 %), linolenic (10.70 %), erucic (13.10 %) and resin acids (7.40 %) (Rahman and Khan 1961). Sitosterol was found in the unsaponifiable matter.

Studies reported that *M. incana* seeds contained oil rich (55–65 %) in omega-3 ($n-3$) linolenic acid and elicited a beneficial effect when fed to animals by reducing cholesterol levels and increasing ($n-3$) fatty acid levels in the plasma (Yaniv et al. 1999). Cholesterol levels were significantly lowest in rats fed with diets rich in *M. incana* oil (27 % reduction) for 6 weeks, and triglycerides were significantly lower in rats receiving either *M. incana* or sunflower oil (36 % reduction). The contents of arachidonic acid and other ($n-6$) fatty acids were significantly the lowest in the liver and plasma of rats that had received *M. incana* oil. The levels of ($n-3$) fatty acids were significantly greater in both the liver and plasma of rats fed with *M. incana* oil. The ratio of ($n-3$)/($n-6$) long-chain fatty acids in the plasma was seven times higher in rats fed with *M. incana* oil than in those fed with sunflower oil and 6 times higher than in those fed with coconut oil. *M. incana*, being a rich source of ($n-3$) fatty acids, could replace marine oils and thereby contribute beneficially to the human diet. Earlier, Ecker et al. (1991) found the breeding lines of *Matthiola incana* tested differed significantly with respect to the levels of palmitic, oleic, linoleic and linolenic acids in the seed oils. Embryonic-stage heterosis in linolenic acid concentration was demonstrated by F1 hybrid seeds, derived from mating horticulturally different lines. Linolenic acid content was negatively correlated with both oleic acid content ($R^2=-0.85$) and linoleic acid content ($R^2=-0.66$). A moderate negative correlation was found between the level of palmitic acid and that of oleic acid ($R^2=-0.40$). None of the breeding lines or the F1 hybrids significantly passed the limit of 67 % linolenic acid. Studies by Heuer et al. (2005) found that total yield, seed number and oil content of *M. incana* seeds were not affected by salinity, whereas the content of omega-3 was significantly increased.

Traditional Medicinal Uses

The seeds are reported to be aphrodisiac, bitter, diuretic, expectorant, stimulant, stomachic and tonic (Chopra et al. 1986). An infusion has been employed to treat cancer, and when mixed with wine it has been used as an antidote to poisonous bites.

Other Uses

Matthiola incana is a popular ornamental plant. The flowers are often harvested for use in floral arrangements and decorative displays.

Comments

The plant is readily propagated from seeds.

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Epiphyllum oxypetalum

Scientific Name

***Epiphyllum oxypetalum* (DC.) Hawthorn**

Synonyms

Cereus latifrons Zucc., *Cereus oxypetalus* DC., *Epiphyllum acuminatum* K.Schum., *Epiphyllum grande* (Lem.) Britton & Rose, *Epiphyllum latifrons* (Zucc.) Pfeiff., *Epiphyllum oxypetalum* var. *purpusii* (Weing.) Backeb., *Epiphyllum purpusii* (Weing.) F.M.Knuth, *Phyllocactus acuminatus* (K. Schum.) K. Schum., *Phyllocactus grandis* Lem., *Phyllocactus latifrons* (Zucc. ex Pfeiff.) Salm-Dyck, *Phyllocactus latifrons* (Zucc. ex Pfeiff.) Link ex Walp., *Phyllocactus oxypetalus* (DC.) Link, *Phyllocactus purpusii* Weing.

Family

Cactaceae

Common/English Names

Dutchman's Pipe, Jungle Cactus, Night Blooming Cereus, Night Queen, Orchid Cactus, Queen of the Night

Vernacular Names

Chinese: Jin Gou Lian, Qiong Hua, Tan-Hua, Yue Xia Mei Ren
French: Reine De La Nuit
German: Königer Der Nacht
India: Gul-E-Bakawali, Nishagandhi (Hindi), Brahma Kamal, Nishagandhi (Marathi), Bakavali (Urdu)
Indonesia: Wijaya Kusuma
Japanese: Gekka Bijin
Malaysia: Bunga Bakawali, Bunga Keng Wa, Bunga Raja
Spanish: Reina De La Noche
Sri Lanka: Kadapul (Sinhala)
Swedish: Stor Bladkaktus
Thai: Dtohn Boh Dtan
Vietnamese: Hoa Quỳnh, Quỳnh Hoa

Origin/Distribution

The species is native to Central America and Northern South America. It can be found from Mexico, Guatemala to Venezuela, as well as Brazil. It also can be found, cultivated in parts of America with warmer temperature such as Texas or California. It is widely cultivated elsewhere in tropical and subtropical areas and has escaped from cultivation and naturalized in many places.

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Agroecology

A warm climate species, widely cultivated in tropical and subtropical areas from 75 to 2,000 m altitude. The plant is epiphytic or lithophytic. It grows well in full sun or light afternoon shade. The plant requires compost containing humus and adequate moisture during the dry months.

Edible Plant Parts and Uses

The mucilaginous flower is often eaten in a vegetable soup (Hu 2005; Li and Taylor 2007).

Botany

An epiphytic cactus with aerial roots. Stems erect, ascending, scandent or sprawling, profusely branched, old primary stems woody at the base and basal shoots terete, flattened to 2–6 m long; secondary stems flattened, leaflike, lanceolate to oblong-lanceolate, to 30 × 10–12 cm, thin; margins shallowly to deeply crenate and undulate (Plate 1). Areoles small, spineless. Flowers produced from flattened portions, to 30 cm long, 12–17 cm wide, funnel form, nocturnal, very fragrant. Receptacle tube 13–18 cm, base green, 4–9 mm across, slightly angled, with triangular to lanceolate scales 3–10 mm. Sepaloids often recurved, pale green or pinkish red, linear to oblanceolate. Petaloids white, oblanceolate to obovate, 7–10 × 3–4.5 cm. Stamens numerous with white, slender filaments, 2.5–5 mm and pale cream anthers, 3–3.5 mm. Style usually white (or orangey, red), 20–22 cm long and curved, stigmas 15–20, usually white, cream (or yellow), narrowly linear, 1.6–1.8 mm (Plates 1 and 2). Fruits are rare, purplish red, oblong, 16 × 5.7 cm. Seed 2–2.5 × 1.5 mm.

Nutritive/Medicinal Properties

The main aroma ingredients of *E. oxypetalum* flowers were found to be benzyl salicylate and methyl linoleate (Matsuura 2002). The flavonoid, kaempferol-3-*O*-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside was isolated from *E. oxypetalum* (Hsu et al. 2008).

Plate 1 Flowers arising from the axils of the leaflike flattened stems (HF Chin)

Plate 2 Close-up of the flower (HF Chin)

Epiphyllum oxypetalum leaves were found to contain saponins, phenolic compounds, steroids, glycosides, tannins, terpenoids and resins, while reducing sugars, alkaloids, flavonoids, sterols, phlobatanins and acidic compounds were absent (Supendra and Khandelwal 2012). The leaves were found to have 14 mg/g protein, 4.6 mg/g lipids and 0.19 mg/g niacin dry basis. The acetone and petroleum ether leaf extracts showed inhibitory activity against *Escherichia coli* and *Staphylococcus aureus*, the acetone leaf extract against *Klebsiella pneumonia*, while the petroleum ether leaf extract against *Bacillus subtilis*. All the three leaf extracts were found to be ineffective against fungi (*Aspergillus niger,*

Aspergillus terreus, Aspergillus oryzae and *Rhizopus oryzae*) tested.

Epiphyllum oxypetalum extract was found to have moisturizing effect on the skin (Suzaki *2005*). The extract increased ATP content, cell propagating activity and the yield of natural moisturizing factor in the epidermal cells.

Traditional Medicinal Uses

Epiphyllum oxypetalum is used in homeopathy and recommended for urinary tract infections, for heart conditions such as the crushing pain of angina and for spasmodic pain and haemorrhage (Yến 2008). In folk medicine, the plant has also been used to treat the spitting up of blood sputum and heavy or painful menstrual periods (Yến 2008). The juice of the plant has been used for bladder infections, shortness of breath and water retention. Applied externally, it has been used for rheumatism. It is also assumed to be an aphrodisiac.

Other Uses

Epiphyllum oxypetalum is by far the most popular and widely cultivated ornamental species from this genus of cacti.

Comments

The plant is easily propagated from the leaflike stem cuttings.

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Mesua ferrea

Scientific Name

***Mesua ferrea* L.**

Synonyms

Calophyllum nagassarium Burm. f., *Mesua nagassarium* (Burm. f.) Kosterm

Family

Calophyllaceae

Common/English Names

Ceylon Ironwood, Cobra's Saffron, Indian Rose Chestnut, Ironwood, Ironwood Tree, Ironwood Of Assam, Mesua, Poached Egg Tree, Sembawang Tree

Vernacular Names

Arabic: Narae-Kaisar
Bangladesh: Nageshwar
Burmese: Gungen, Kenga
Chinese: Tie Li Mu
Dutch: Ijzerhout
French: Arbe De Fer, Bois D'anis, Bois De Fer
German: Eisenholzbaum, Nagasbaum, Nagassamen
India: Nahar, Nahor, Nageshwar, Negeshvar, Nokte (Assamese), Nagesvara, Nagkesar, Punnaga (Bengali), Nagachampa, Nagkesara, Nagchampa, Pilunagkesar, Sachunagkeshara, Tamranagkesar (Gujarati), Nagakeshara, Nagchampa, Nagesar, Naghesar, Nagkesara, Nahar, Narmishka, Pila Nagkesara (Hindi), Nagakesari, Nagasampige (Kannada), Nagkesarah (Kashmiri), Churuli, Nagppu, Nagappovu, Nangaa, Nauga, Peri, Vainav, Veluthapalau (Malayalam), Nageshor (Manipuri), Nagakesara Nagchampa, Thorlachampa (Marathi), Nahar, Herhse (Mizo), Nageswar (Oriya), Nageswar (Punjabi), Champeryah, Gajakesara, Hema, Kesara, Naga, Nagakesara, Nagakeshara, Nagkesar, Nagakesarah, Nagkeshara, Nagkeshwar, Nagpushpa, Nagapuspah (Sanskrit), Charu-Nagapu, Nagappu, Nakecuram, Naugu, Naugaliral, Nagachampakam, Sirunagappoo, Tadinangu, Veillutta Champakam (Tamil), Kesaramu, Nagachampakamu, Nagakesaramu, Nagashappu (Telugu), Nagkesar, Narmishka, Narmushk (Urdu)
Indonesia: Nagasari Gede, Nagasari
Italian: Croco Di Cobra
Japanese: Tagayasan
Khmer: Bosneak
Laotian: May Lek, Ka Thang
Malaysia: Langapus, Lagggapus, Matopus, Mentepus, Naga Sari, Penaga, Penaga Kunyit, Penaga Lilin, Penaga Putih, Penaga Sabut, Penaga Suga, Tapis

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Nepalese: Nagesvar Campa, Nagesvari, Nagkesar, Narisal, Potal, Ruk Keshar
Persian: Naz Mushik
Philippines: Kaliuas (Tagalog)
Russian: Indiiskoe Zheleznoe Derevo, Mezua Zheleznaia, Mezuia Zheleznaia, Haraкeшapa Nagakeshara, Zheleznoe Derevo
Sri Lanka: Na, Naa-Gaha, Naaga, Naaga-Dru, Naaga-Keasara, Naaga-Kignjalka (Sinhala)
Thai: Bhra Na Kaw, Bun Nak, Boon Naak, Ka Ko (Karen), Gaa Gaaw Gam Gaaw, Kam Ko (Shan), Saan Phee Daawy, Saraphi Doi (Chiang Mai)
Vietnamese: Vắp, Vếp

Origin/Distribution

Mesua ferrea is indigenous to the wet, tropical parts of Sri Lanka, India, southern Nepal, Burma, Thailand, Indochina, the Philippines, Malaysia and Sumatra.

Agroecology

In its native range, it occurs from near sea level to 2,300 m, as a canopy component in lowland evergreen forest, especially in river valleys, but also commonly features as an understory tree in montane evergreen or semievergreen forest. In Borneo, the species is associated with dipterocarps. It thrives best in a well-drained, moist, fairly fertile soil.

Edible Plant Parts and Uses

The ripe fruit (surli nuts) is edible, reddish and wrinkled when ripe and resembles chestnut in size, shape, rind, substance and taste. The oily seeds are edible when well cooked but unpleasant and not suitable as a cooking oil (Pongpangan and Poobrasert 1985). Young, tender leaves have a sour astringent taste and can be eaten raw. The flowers are edible and eaten in Thailand (Wessapan et al. 2007; Wetwitayaklung et al. 2008).

Botany

A medium to tall, evergreen, perennial tree growing 20 m to over 30 m high (Plate 1) with a buttressed base, smooth or weakly scaly, dark ash grey with a red-brown blaze bark and a trunk up to 2 m in diameter. Leaves are simple, opposite, narrow, oblong to lanceolate, blue-grey to dark green, 7–15 cm long and 1.5–3.5 cm wide, with a whitish underside (Plates 2 and 4). Juvenile leaves are reddish-yellowish pink. Flowers are terminal or axillary, fragrant, usually solitary, 4–7.5 cm across and borne on pedicels with small paired bracts. Flowers are bisexual with four white petals and a centre of numerous yellow stamens, free or connate only at the base (Plate 3). The ovary is superior with 1–2 axillary ovules, with a slender style and peltate to 4-lobed stigma. Fruit is an ovoid to subglobose, dehiscent capsule (Plate 4), often beaked, thinly woody containing 1–2 seeds.

Plate 1 Habit of tree

Plate 2 Flower buds and leaves

Plate 3 Flowers in bloom (HF Chin)

Nutritive/Medicinal Properties

Between 32 and 50 components were identified in the oils from the bark, leaves, buds and flowers (full bloom) of *Mesua ferrea*, accounting for 82–97 % of the total yields (Choudhury et al. 1998). The bark oil was rich in (*E*)-α-bisabolene (31.3 %) and α-selinene (12.2 %). The predominant components in the oils of tender and mature leaves were α-copaene (19.3 and 99 %) and β-caryophyllene (18.8 and 26.0 %). The bud and flower oils also contained α-copaene (28.7 and 20.2 %) and in addition germacrene D (190 and 16.1 %).

Plate 4 Fruits

Flower Phytochemicals

Mesuaferrone-b, a new biflavanone, was isolated from *Mesua ferrea* stamens (Raju et al. 1976). Petrol extracts of the stamens of *Mesua ferrea* afforded β-amyrin, β-sitosterol and a new cyclohexadione compound named mesuaferrol (Dennis et al. 1988).

A series of 4-alkyl and 4-phenyl 5,7-dihydroxycoumarins were extracted from *Mesua ferrea* blossoms (Verotta et al. 2004). The nine compounds were 5,7-dihydroxy-6-(isobutyryl)-8-(3-methylbut-2-enyl)-4-phenyl-2H-chromen-2-one (mesuol) (1); 5,7-dihydroxy-6-(2-methylbutanoyl)-8-(3-methylbut-2-enyl)-4-phenyl-2H-chromen-2-one (mammea A/AB) (1a); 5,7-dihydroxy-6-(3-methylbutanoyl)-8-(3-methylbut-2-enyl)-4-phenyl-2H-chromen-2-one (mammea A/AA) (mammeisin) (1b); 5,7-dihydroxy-6-(2-methylbutanoyl)-8-[(*E*)-3,7-dimethylocta-2,6-dienyl]-4-phenyl-2H-chromen-2-one (2); 5,7-dihydroxy-

6-(3-methylbutanoyl)-8-[(*E*)-3,7-dimethylocta-2,6-dienyl]-4-phenyl-2H-chromen-2-one (2a); 5,7-dihydroxy-8-(2-methylbutanoyl)-6-(3-methylbut-2-enyl)-4-phenyl-2H-chromen-2-one (mammea A/BB) (isomammeisin) (3); 5,7-dihydroxy-8-(3-methylbutanoyl)-6-(3-methylbut-2-enyl)-4-phenyl-2H-chromen-2-one (mammea A/BA) (3a); 5,7-dihydroxy-8-(2-methylbutanoyl)-6-[(*E*)-3,7-dimethylocta-2,6-dienyl]-4-phenyl-2H-chromen-2-one (4); 5,7-dihydroxy-8-(3-methylbutanoyl)-6-[(*E*)-3,7-dimethylocta-2,6-dienyl]-4-phenyl-2H-chromen-2-one (4a); 8,9-dihydro-5-hydroxy-8-(2-hydroxypropan-2-yl)-6-(2-methylbutanoyl)-4-phenylfuro[2,3-h]chromen-2-one (mammea A/AB cyclo F) (5a); 8,9-dihydro-5-hydroxy-8-(2-hydroxypropan-2-yl)-6-isobutyryl-4-phenylfuro[2,3-h]chromen-2-one (mammea a/AD ciclo F) (5); 8,9-dihydro-5-hydroxy-8-(2-hydroxypropan-2-yl)-6-(3-methylbutanoyl)-4-phenylfuro[2,3-h]chromen-2-one (mammea A/AA ciclo F) (5b); 5,7-dihydroxy-4-(1-hydroxypropyl)-8-(2-methylbutanoyl)-6-(3-methylbut-2-enyl)-2H-chromen-2-one (assamene) (6); 5,7-dihydroxy-4-(1-hydroxypropyl)-8-(2-methylbutanoyl)-6-[(*E*)-3,7-dimethylocta-2,6-dienyl]-2H-chromen-2-one (surangin C) (6a); 8,9-dihydro-5-hydroxy-6-(2-methylbutanoyl)-4-phenyl-8-(prop-1-en-2-yl)furo[2,3-h]chromen-2-one (7); 8,9-dihydro-5-hydroxy-6-(3-methylbutanoyl)-4-phenyl-8-(prop-1-en-2-yl) furo[2,3-h]chromen-2-one (7a); 5-hydroxy-6-isobutyryl-8,8-dimethyl-4-phenyl-2H-pyrano[2,3-h]chromen-2-one (mammea A/AD cyclo D) (mesuagin) (8); 5-hydroxy-8,8-dimethyl-6-(2-methylbutanoyl)-4-phenyl-2H-pyrano[2,3-h]chromen-2-one (mammea A/AB cyclo D) (mammeigin) (8a); 5-hydroxy-8,8-dimethyl-6-(3-methylbutanoyl)-4-phenyl-2H-pyrano[2,3-h]chromen-2-one (mammea A/AA cyclo D) (8b); 5-hydroxy-6-isobutyryl–8-methyl-8-(4-methylpent-3-enyl)-4-phenyl-2H-pyrano[2,3-h]chromen-2-one (9); and 5-hydroxy-8-methyl-6-(2-methylbutanoyl)-8-(4-methylpent-3-enyl)-4-phenyl-2H-pyrano[2,3-h] chromen-2-one (9a). Fourteen major volatile components of the methanol flower extract of *Mesua ferrea* (Nordin et al. 2004).

Seed Phytochemicals

Two different samples of *Mesua ferrea* seed oil yielded coumarins mammeigin and mesuol as the main phenolic components (Bala and Seshadri 1971). The synthesis of mammeisin and mammeigin and also the conversion of mesuol into mesuagin were carried out.

Mesua ferrea seeds were found to contain total lipid (66.91–70.23 g %), moisture (4.02–5.05 g %), ash (1.46–1.50 g %), total protein (6.99–7.19 g %), water-soluble protein (2.98–3.11 g %), starch (5.51–5.85 g %), crude fibre (1.22–1.98 g %), carbohydrate (15.88–18.68 g %) and energy value (700.55–724.15 kcal/100 g) (Abu Sayeed et al. 2004).

Mesua ferrea seed oils were found to have the following physicochemical characteristics: specific gravity (0.9287–09312), refractive index (1.4690–1.4739), solidification point [−4.0–(−4.3)], pour point [−1.0–(−1.3)], cloud point (5.5–6.0), flashpoint (90–98), fire point (110–116), smoke point (44–47), iodine value (89.17–93.01), saponification value (199.03–206.40), saponification equivalent (271.80–281.86), acid value (9.64–11.87), free fatty acid (4.85–5.96), ester value (188.95–1.95.44), unsaponifiable matter (1.44–1.50), acetyl value (2.70–2.84), peroxide value (3.58–3.64), Reichert–Meissl value (5.852–6.031) and Polenske number (0.7891–0.8401) (Abu Sayeed et al. 2004). Glyceride classes were estimated to be monoglycerides (1.05–1.35 %), diglycerides (2.12–2.32 %) and triglycerides (87.65–89.50 %), whereas total lipid extracts were fractionated into neutral lipid (89.83–92.18 %), glycolipid (3.65–4.15 %) and phospholipid (1.98–2.68 %). Saturated and unsaturated fatty acids present in the oils were separated and amounted to be (27.40–29.11 %) and (65.85–68.31 %), respectively. The oil contained the highest amount of oleic acid 55.93 %, while linoleic acid, stearic acid and palmitic acid contents were found to be 13.68, 14.19 and 10.87 %, respectively. The oil also contained small amount of myristic acid (2.13 %) and arachidic acid (2.92 %). Konwer et al. (1989) found *M. ferrea* seed oil consisted of triglycerides of linoleic, oleic, palmitic and stearic acids.

Leaf Phytochemicals

Mesua ferrea leaves were found to contain total lipid (2.32–2.44 g %), moisture (65.12–72.19 g %), ash (2.60–2.71 g %), total protein (4.23–4.85 g %), water-soluble protein (1.47–2.01 g %), starch (3.06–3.27 g %), crude fibre (3.12–3.29 g %), carbohydrate (14.82–22.30 g %) and energy value (100.24–128.40 kcal/100 g) (Abu Sayeed et al. 2004).

Furano-naphthyl-hydroxy cyclohexyl type of compound was isolated from the ethyl acetate leaf extract of *Mesua ferrea* and identified as 12, 13-furano-8-hydroxy napthyl-6-0-β-2′,3′,4′,6′ tetrahydroxy-5′,5′ dimethyl cyclohexyl ether (Rahman et al. 2008).

Thirty-five components constituting 81.4 % total volatile components were obtained from *M. ferrea* leaf essential oil (Keawsaard and Kongtaweelert 2012). The oil comprised 60–7 % sesquiterpene hydrocarbons (60.7 %), diterpenes and triterpenes (0.4 %), terpene-related compounds (0.4 %), carboxylic acids (0.5 %), saturated hydrocarbons (0.3 %) and others (0.2 %). Major components were *trans*-caryophyllene (30.9 %), β-caryophyllene oxide (19.9 %), α-humulene (6 %), δ-cadinene (4.1 %), γ-muurolene (3.5 %), γ-cadinene (2.3 %), β-selinene (1.9 %), germacrene D (1.8 %) and β-bisabolene (1.6 %). Other minor components included (*Z*)-3-hexanol (0.1 %), linalool (trace), edulan I (trace), α-cubebene (0.3 %), α-ylangene (0.3 %), α-copaene (1.1 %), β-bourbonene (0.8 %), β-elemene (0.5 %), (*cis*)-caryophyllene (0.4 %), (+)-aromadendrene (0.7 %), (−)-alloaromadendrene (1.1 %), valence (1 %), α-selinene (1.1 %), α-muurolene (0.7 %), (*cis*)-calamenene (0.5 %), α-calacorene (0.3 %), caryophyllenyl alcohol (0.5 %), τ-muurolol (0.5 %), hexahydrofarnesyl acetone (0.5 %), *n*-hexadecanoic acid (0.5 %), phytol (0.2 %), 4,8,12,16-tetramethyl heptadecan-4-olide (0.1 %), hexadecanoic acid bis(2ethylhexyl) ester (0.1 %), heptacosane (0.1 %), squalene (0.2 %) and nonacosane (0.2 %).

Wood/Trunk/Root Phytochemicals

Two new yellow pigments, mesuaxanthone-A and mesuaxanthone-B, and the known euxanthone were isolated from the heartwood extracts of *Mesua ferrea* (Govindachari et al. 1967a). Mesuaxanthone-A was elucidated as 1,5-dihydroxy-3-methoxy-xanthone and mesuaxanthone-B as 1,5,6-trihydroxyxanthone. Ferruol A, C23H30O5, a new 4-alkylcoumarin isolated from the trunk bark (Govindachari et al. 1967b). The heartwood of *Mesua ferrea* was found to contain 1,5-dihydroxyxanthone (II), euxanthone 7-methyl ether (IV) and β-sitosterol, in addition to the two xanthones previously isolated (Chow and Quon 1968). The following xanthones dehydrocycloguanandin, calophyllin-B, jacareubin, 6-desoxy jacareubin, mesuaxanthone-A, mesuaxanthone-B and euxanthone were found in *M. ferrea* (Gopalakrishnan et al. 1980). A new xanthone, ferrxanthone, was isolated from the heartwood of *Mesua ferrea* and its structure determined as 1,3-dimethoxy-5,6-dihydroxyxanthone (Walia and Mukerjee 1984). The root bark extracts of *Mesua ferrea* afforded two new pyranoxanthones, mesuaferrin A (1) and mesuaferrin B (2), and five other compounds—caloxanthone C (3), 1,8-dihydro-3-methoxy-6-methylanthraquinone (4), β-sitosterol (5), friedelin (6) and betulinic acid (7) (Teh et al. 2011).

Some of the pharmacological proprieties of the various plant parts are elaborated below.

Antioxidant Activity

Four edible flower extracts including *M. ferrea* elicited antioxidant activity in ABTS assay with the Trolox equivalent antioxidant capacity (TEAC) of 0.15–0.70 (Wessapan et al. 2007). Antioxidant activity in the flower extract was low, TEAC value = 0.15, IC_{50} = 61 μg/50μl (Wetwitayaklung et al. 2008). Total polyphenol yield was 33.78 %, and total polyphenol content in the dried flowers was 1.94 g/100 g and in the crude methanol flower extract was 5.74 g/g.

The water and hot water extracts of *M. ferrea* flowers exhibited strong DPPH radical scavenging activity with EC_{50} = 7.49, 6.95 μg/ml, respectively, which were stronger than BHT (Makchuchit et al. 2010). The ethanol flower extract exhibited potent inhibitory activity on LPS-induced NO production in RAW 264.7 cells with IC_{50} value 26.32 μg/ml.

The extracts of *M. ferrea* leaves showed good antioxidant activity with the ethanol (70 %) extract showing better activity than other extracts (methanol, ethyl acetate and hexane) in DPPH, superoxide and hydroxyl radical scavenging activities (Prasad et al. 2012). However, the antioxidant activities were lower than ascorbic acid. The leaf essential oil showed antioxidant in the DPPH assay with IC_{50} of 31.67 mg/ml (Keawsaard and Kongtaweelert 2012).

Analgesic Activity

The *n*-hexane extract of *M. ferrea* leaves administered orally to mice produced significant antinociceptive action against acetic acid-induced visceral pain models of nociception in mice (Hassan et al. 2006). In acetic acid-induced writhing model, the *n*-hexane, methanol and ethyl acetate partition fractions at a dose of 125 mg/kg body weight produced 36.08, 16.33 and 10.21 % reduction of writhing response. The extracts also produced 42.21, 19.63 and 17.06 % reduction of writhing response at a dose of 250 mg/kg body weight, respectively.

Immunomodulatory Activity

Mesuol isolated from *M. ferrea* seed oil exhibited immunomodulatory activity in experimental animals (Chahar et al. 2012). In humoral immune response model, mesuol evoked a significant dose-dependent increase in antibody titre values in cyclophosphamide-induced immunosuppression which was sensitized with sheep red blood cells (SRBC). In cellular immune response model, an increase in paw volume was recorded on the 23rd day in cyclophosphamide-induced immunosuppressed rats treated with SRBC on the 21st day. Mesuol restored the haematological profile in cyclophosphamide-induced myelosuppression model. Mesuol potentiated percentage neutrophil adhesion in neutrophil adhesion test in rats and phagocytosis in carbon clearance assay.

Anticancer Activity

The crude methanol flower extract exhibited a strong cytotoxic activity (i.e. IC_{50} of 12.5 μg/ml) towards T-lymphocyte leukaemia cell (Nordin et al. 2004). *M. ferrea* extract inhibited the growth of Ehrlich ascites carcinoma cells in Swiss albino mice (Masud Rana et al. 2004). The ethanol plant extract of *Mesua ferrea* exhibited promising in-vitro activity against human cholangiocarcinoma CL-6 cell line with survival of less than 50 % at the concentration of 50 μg/ml and an IC_{50} value of 48.23 μg/ml, for cytotoxicity activity (Mahavorasirikul et al. 2010). The extract also showed activity against human laryngeal (Hep-2) and human hepatocarcinoma (HepG2) cell lines. The leaf essential oil also exhibited anticancer activities against KB human oral carcinoma, MCF-7 breast cancer and small cell lung cancer NCI-H 187 cell lines with IC_{50} values of 24.02, 16.19 and 20.32 μg/ml, respectively, but was not toxic to primate Vero cell line (Keawsaard and Kongtaweelert 2012).

Antimicrobial Activity

Mesuol and mesuone from the seed oil were found to have antibacterial activity against *Staphylococcus aureus* (Chakraborty et al. 1959). Mesuol was more active than mesuone against *Mycobacterium phlei*. Both were inactive against fungi tested. The crude methanol flower extract exhibited weak antimicrobial activities against bacteria, namely, *Staphylococcus aureus, Bacillus subtilis* and *Pseudomonas aeruginosa* (Nordin et al. 2004).

A series of 4-alkyl and 4-phenyl 5,7-dihydroxycoumarins (9 compounds) extracted from *Mesua ferrea* blossoms were found to be

potent antibacterials on resistant Gram-positive bacterial strains but were weak antiprotozoal agents against *Plasmodium falciparum* (Verotta et al. 2004).

Methanol flower extracts of five edible flowers including *M. ferrea* exhibited antibacterial effect against *Staphylococcus aureus* with MIC at 50–800 μg/ml (Wessapan et al. 2007). The methanol leaf extract of *Mesua ferrea* exhibited significant antibacterial effects in vitro against *Staphylococcus aureus, Bacillus* spp., *Escherichia coli*, *Lactobacillus arabinosus*, *Shigella* and *Salmonella* bacteria (Mazumder et al. 2003). In in-vivo tests, methanol flower extract of *Mesua ferrea* at concentrations of 100 and 200 μg/g of body weight significantly protected Swiss strain of albino mice against a virulent strain *Salmonella typhimurium* (Mazumder et al. 2004). The extract at 200 μg/g dosage significantly reduced the viable count of the *Salmonella* strain in the liver, spleen and heart blood of the extract-treated challenged mice. The flower extract exhibited in vitro antimicrobial efficacy against five different strains of *Salmonella* spp. with MICs of 50 μg/ml (Mazumder et al. 2005). The extract at 2 and 4 mg/mouse significantly protected Swiss albino mice against *S. typhimurium*. The ethanol/methanol seed extract was more active in-vitro against *Proteus mirabilis* and *Klebsiella pneumoniae* than the aqueous extract (Parekh and Chanda 2007). The methanol seed extract was effective in vitro against *Candida albicans* and *Trichosporon beigelii* at 125 μg/disc (Parekh and Chanda 2008). The extract was also effective against *Aspergillus candidus* (500 μg/disc), *Aspergillus flavus* (125 and 250 μg/disc), *Aspergillus niger* (125 and 250 μg/disc) and *Mucor hiemalis* (250 and 500 μg/disc).

The chloroform bark extract exhibited strong activity against Gram-positive *Streptococcus aureus* and Gram-negative *Escherichia coli*, but the leaf extracts exhibited mild to moderate activity against the tested bacteria (Ali et al. 2004). Nahar seed kernel oil emulsion demonstrated appreciable bacterial disinfestations at high concentration using the pour plate method (Adewale et al. 2011). At concentrations of 2 mg/ml or higher, total disinfestations were obtained with little or no bacterial colonies seen after incubation. The ethanol leaf extract exhibited marked antibacterial property against selected microbes (*Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis* and *Staphylococcus aureus*) with the inhibition zones ranging from 16.0 to 18.05 mm for all the tested bacteria (Adewale et al. 2012). The MIC range of 2.5–0.625 mg/ml with MBC value of 5 mg/ml was obtained for the Gram-negative bacteria, while MIC range of 1.3–0.313 mg/ml with MBC value of 2.5 mg/ml was obtained for the Gram-positive bacteria. The leaves extract was found to be toxic to the Brine shrimps with LC_{50} of 500 ppm (μg/ml), suggesting that the extracts may contain bioactive compounds of potential therapeutic and prophylactic significance.

The leaf essential oil exhibited antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* with MIC values of 250 and 125 mg/ml, respectively (Keawsaard and Kongtaweelert 2012). Both leaf and fruit extracts of *M. ferrea* displayed good antibacterial activity against *Staphylococcus aureus* with a minimum inhibition concentration of 0.048 mg/ml (Aruldass et al. 2013). Both extracts are bacteriostatic at a minimum bacteriostatic concentration of 0.39 mg/ml. The treatment with the extracts caused extensive lysis of the cells, leakage of intracellular constituents and aggregation of cytoplasmic contents forming an open meshwork of the matrix.

Antiarthritic Activity

Studies demonstrated that *Mesua ferrea* seed extract protected rats against formaldehyde and complete Freund's adjuvant (CFA)-induced arthritis (Jalalpure et al. 2011). The body weight changes and haematological perturbations induced by CFA were maintained.

Antiinflammatory Activity

The xanthones of *Calophyllum inophyllum* and *Mesua Ferrea*, namely, mesuaxanthone-A and

mesuaxanthone-B, exerted 37 and 49 % reduction in carrageenan-induced hind paw oedema upon oral administration in normal and adrenalectomized rats (Gopalakrishnan et al. 1980). In the granuloma pouch test, mesuaxanthone-A and mesuaxanthone-B elicited 46 and 49 % reduction in inflammation, respectively, and 47 % reduction was observed in the cotton pellet granuloma test.

Antivenom Activity

M. ferrea extract was one of several plant species that was found to have antidote activity against *Heterometrus laoticus* scorpion venom activity on fibroblast cell lysis (Uawonggul et al. 2006).

Antiulcerogenic Activity

The xanthones of *Calophyllum inophyllum* and *Mesua Ferrea,* namely, jacareubin and -desoxy jacareubin exhibited antiulcer activity in rats (Gopalakrishnan et al. 1980). The untreated control animals had extensive ulceration, haemorrhage and perforation; in contrast, the xanthone-pretreated animals exhibited only scattered areas of hyperaemia and occasional haemorrhagic spots.

Anticonvulsant Activity

The ethanol extract of *Mesua ferrea* inhibited maximum electroshock seizure (MES)-induced convulsions in albino mice (Tiwari et al. 2012). The extract also reduced the duration of hind limb tonic extension in a dose-dependent manner against MES model.

Wound Healing Activity

The ethanol extract of *Mesua ferrea* aerial parts in the form of ointment (5 and 10 % w/w) exhibited wound healing activity in both excision and incision models in albino rats (Choudhary 2012). The results suggested that the wound healing activity of *Mesua ferrea* was due to its tannin content, which appeared to be responsible for wound contraction and increased rate of epithelialization.

CNS (Central Nervous System) Depressant Activity

The xanthones of *Calophyllum inophyllum* and *Mesua Ferrea,* namely, jacareubin (JR), dehydrocycloguanandin, calophyllin-B, 6-desoxy jacareubin, mesuaxanthone-A, mesuaxanthone-B and euxanthone, produced varying degrees of CNS depression characterized by ptosis, sedation, decreased spontaneous motor activity, loss of muscle tone, potentiation of pentobarbitone sleeping time and ether anaesthesia in mice and rats (Gopalakrishnan et al. 1980). None of the xanthones had any analgesic, antipyretic and anticonvulsant activities.

Antispasmodic Activity

The crude *M. ferrea* seed oil showed significant antispasmodic activity in the isolated rat ileum, but the purified oil was devoid of antispasmodic activity (Prasad et al. 1999).

Antihaemorrhoidal Activity

Paranjp et al. (2000) conducted a 4-week clinical assessment of a multiherbal indigenous formulation administered orally as capsule to 22 patients with bleeding piles. The Ayurvedic formulation was composed of *Berberis aristata, Holarrhena antidysenterica, Picrorhiza kurroa, Mesua ferrea, Terminalia chebula, T. belerica* and *Emblica officinalis.* After 4 weeks, only 6 out of 22 patients still complained of bleeding. The formulation was well accepted and no adverse effects were reported.

Estrogenic/Progestational Activities

M. ferrea flower extract was found to have compounds which exhibited estrogenic and

progestational activity in humans and mice (Meherji et al. 1978). The results suggested that these compounds in *M. ferrea* may help to correct hormonal imbalance in menstrual disorders.

Traditional Medicinal Uses

The root, leaves, flowers and seeds are used in traditional medicine (CSIR 1962; Burkill 1966; Chopra et al. 1986; Khare 2004). *M. ferrea* traditionally is being used for its antiseptic, antiinflammatory, blood purifier, anthelmintic, cardiotonic, diuretic, expectorant, antipyretic, purgative, antiasthmatic, antiallergic and several other effects (Chahar et al. 2013). It is an ingredient of Ayurvedic formulations like Brahma Rasayana and Chyawanprash which are being used to improve immunity. Nagakeshara (*M. ferrea*) is a hot, dry digestive and good for fever, foul breath, sweats, scabies, skin eruptions, itching, small tumours, headache, blood and heart problems, sore throat, cough, hiccough, vomiting, excessive thirst, dysentery and bleeding piles (Joseph et al. 2010). The dried flower bud is antidysenteric and used for dysentery with mucus; the dried flowers are astringent, haemostatic, antiinflammatory and stomachic and used in cough, bleeding haemorrhoids and metrorrhagia (CSIR 1962; Chopra et al. 1986; Khare 2004). Fresh flowers are prescribed for excessive thirst, excessive perspiration, cough and indigestion. The leaves are applied to the head in the form of a poultice for severe colds. Oil from the seeds is used for sores, scabies, wounds and rheumatism. The root of this herb is often used as an antidote for snake poison.

Nagakesara in Indian system of medicine is used as deodorant, diaphoretic and stimulant (Anandakumar et al. 1986). It is a brain tonic appetizer, antiemetic, anthelmintic, aphrodisiac, diuretic and antidote. Nagakesara is mostly attributed to the stamens or the flowers of *Mesua ferrea.* Dried fruits of *Dillenia pentagyna* and dried fruiting inflorescence of *Cinnamomum wightii* are also used as Nagakesara in different regions of India.

In Peninsular Malaysia, the pounded kernels or seed oil have been used for poulticing wounds; flowers were used in a draught taken after childbirth and so is a root decoction (Burkill 1966). In Singapore, ashes of leaves were used as a lotion for sore eyes.

In Thailand, the seed is used as a cardiotonic and expectorant, for wounds and for its aroma (Wetwitayaklung et al. 2008).

Other Uses

Mesua ferrea is an important forest tree for timber production. The deep dark red wood is hard, heavy and suitably strong for all forms of heavy construction, railway sleepers, transmission posts, heavy-duty furniture, parquet flooring, posts and tool handles. The tree is also popularly planted as landscape, avenue trees or hedgerows. The incense sticks made from the flowers of this plant are popular worldwide for their intense fragrance. Fragrant stamens are used for stuffing pillows and cushions in the bridal beds.

The fraction of *M. ferrua* seed oil distilling between 200 and 300 °C may be used as fuel for diesel engines (Konwer et al. 1989). Studies showed that blending of *M. ferrea* seed oil with diesel up to 15 % (by volume) can be used in a compression–ignition (CI) engine without any major engine modification (Kushwah et al. 2008). Due to higher viscosity and density and low volatility of straight *M. ferrea* oil, it was found suitable for direct use in Cl engine.

M. ferrea seed oil can be used in the manufacture of polyurethane paints, epoxy resins and nanocomposites. Three different polyester resins were synthesized from a purified seed oil (Dutta et al. 2004; Mahapatra and Karak 2004). The resins were formed by the reaction of monoglyceride obtained from the oil with phthalic and/or maleic anhydride and adipic acid separately. Poly(urethane amide) resins with varying ratio of NCO/OH (0.8:1–2:1) were synthesized from purified Nahar oil (*Mesua ferrea*) with toluene diisocyanate in the presence of dibutyl tin dilaurate as the catalyst (Dutta and Karak 2005). The results show better performance of the

poly(urethane amide) resins exhibited better performance compared to polyester or polyesteramide resins of the same oil. The study showed that these resins may hold promise for use as effective surface-coating materials. Thermogravimetric analysis demonstrated that the thermal stabilities of the cured resins prepared from *M. ferrea* seed oil increased with an increase in the NCO/OH ratios (Dutta and Karak 2006). The amounts of char residues at 550 °C were also found to be greater for higher NCO/OH ratios of the Nahar oil-modified polyurethane resins. A hyperbranched polyamine was utilized as an effective curing agent for a *Mesua ferrea* seed oil-based poly(ester-amide) resin (Mahapatra and Karak 2007). The hyperbranched polyamine not only enhance the rate of cross-linking reaction, but it also improved many desirable performance characteristics especially the thermostability, flame retardancy, hardness, impact strength, chemical resistance, etc. of the cured resin.

Two types of stoving paints had been prepared from *Mesua ferrea* seed oil-modified polyurethane ester (PUE) binder systems (Dutta et al. 2009a). Of the two test paints, the epoxy-modified PUE-based stoving paint was preferred. An epoxidized vegetable oil of *Mesua ferrea* seed was prepared and used as a reactive diluent for commercial BPA (bisphenol A)-based epoxy resin at different compositions and green nanocomposites (Das and Karak 2009). Epoxy-modified *Mesua ferrea* seed oil-based polyurethane nanocomposites also have the potential to be applicable as biomaterials (Dutta et al. 2009b). A bio-based sulphone epoxy resin (BPSE) was synthesized from the monoglyceride of *Mesua ferrea* seed oil, bis(4-hydroxyphenyl) sulphone, bisphenol A and epichlorohydrin (Das and Karak 2010). These bio-based epoxy/clay nanocomposites had improved flame retardancy and exhibited potential for multifaceted advanced applications. *Mesua ferrea* seed oil-based polyester was modified by methyl methacrylates to form a modified polyester for use as matrix for polyester resin/clay nanocomposite preparations with improved mechanical and thermal properties (Konwar et al. 2011).

Comments

The tree is sacred in India and is the national tree of Sri Lanka. The plant is propagated from seeds or cuttings.

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Lonicera confusa

Scientific Name

***Lonicera confusa* (Sweet) DC**.

Synonyms

Caprifolium confusum (Sweet) Spach, *Lonicera dasystyla* Rehder, *Lonicera multiflora* Champ. ex Benth., *Lonicera telfairii* Hook. & Arn., *Nintooa confusa* Sweet

Family

Caprifoliaceae

Common/English Names

Dasystyle honeysuckle, Tonkinese honeysuckle, Wild honeysuckle

Vernacular Names

Chinese: Mao Hua Zhu Ren Dong, Shui Ren Dong
French: Chevrefeuille Sauvage
Japanese: Kinginka
Korean: Keumeunhwa
Vietnamese: Kim ngân vòi nhám; Kim ngân dại

Origin/Distribution

The species is native to southern China (Guangdong, Guangxi, Yunnan, Hainan), Nepal and North Vietnam.

Agroecology

In its native range, it is found in scrub, margins of mixed forest, mountain slopes, river banks, roadsides, plains and terraced field banks from 300 to 800 m elevation. In North Vietnam, it is commonly found in limestone mountains of Ha Tay, Hoa Binh, Ha Nam and Ninh Binh (Le and Nguyen 1999). The species is hygrophilous and sun loving.

Edible Plant Parts and Uses

Flowers are used as food in China and Taiwan (Chau and Wu 2006).

Botany

A twining herb with greyish, pubescent or glabrous stems and branches, younger tender branches reddish and pubescent. Leaves are opposite, oval–lanceolate, 2–8 cm long by 1–4 cm wide with rounded bases and acuminate

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Plate 1 Twining herb with ovate leaves

Plate 2 White flowers

apices, glabrous adaxially and pubescent abaxially (Plate 1) on furrowed, slightly flattened petioles (4–10 mm) without large sessile orange glands. Older leaves (lower) are lobate while young leaves are entire. Inflorescence consists of 2-flowered axillary cymes with fragrant white flowers (Plate 2), 2.5–4 cm by 1–2.5 mm across, changing to yellow after anthesis; flowers have acuminate minute bracts, short calyx tube, 2–2.5 mm long with short triangular calyx lobes; corolla white, tinged with purple-red near base, later yellowish, 2–3.5 cm, bilabiate, corolla tube 1.4–1.7 cm, outside slightly adpressed pubescent or glabrous, inside densely pubescent on upper lip; lobes oblong–lanceolate, 2 lateral lobes deep to over 1/3, lower lip narrowly linear; stamens 5 subequaling corolla, filaments sparsely pubescent at base, anthers linear; ovary densely to sparsely hirsute; style exserted, densely pubescent in lower 1/3. Fruit is a globose berry turning black when ripe.

Nutritive/Medicinal Value

The plant contains saponins, tannin, luteolin, inositol, chlorogenic acid and a carotenoid—cryptoxanthin (Le and Nguyen 1999). Seven compounds were isolated from the dried flower buds of *L. confusa* and identified as rutin, quercetin, luteilin-7-*O*-β-D-galactoside, lonicerin, chlorogenic acid, β-sitosterol and tetratriacontane (Chai et al. 2004). Luteolin, chlorogenic acid, 3,5-dicaffeoylquinic acid and caffeic acid were detected in the dried flower buds, leaves and stems (three medicinal parts) of *Lonicera confusa* (Yao et al. 2006).

Ninety-three chemical components were separated from the volatile oil of fresh leaves in which 39 chemical components were identified (Xin et al. 2011). The main components were n-hexadecanoic acid (11.90 %), phytol (11.79) and 9,12,15-octadecatrienoic acid, methyl ester, (*Z*, *Z*, *Z*) (7.08 %). Eighty-eight chemical components were separated from the volatile oil from dry leaves in which 51 chemical components were identified. The main components were 1,6-octadien-3-ol, 3,7-dimethyl- (27.62 %), phytol (7.57 %) and 2, 6, 10, 14, 18, 22-tetracosahexaene, 2, 6, 10, 15, 19, 23-hexamethyl- (all-E) (4.70 %).

The flowers are used in traditional medicine for antiinflammation, antiallergy and detoxication to remove toxic heat and dispel wind-heat.

In Vietnam the flowers have been employed for the treatment of the following: carbuncles, boils, erysipelas, acute dysentery, pharyngitis, upper respiratory infection, epidemic febrile diseases, influenza, tonsillitis, acute conjunctivitis, enteritis, pyodermas, infected wounds and cervical erosion (Le and Nguyen 1999).

Other Uses

The flowers can be used to substitute *L. japonica* in herbal medicine.

Comments

The plant can be propagated from seeds and stem cuttings.

Selected References

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Lonicera japonica

Scientific Name

***Lonicera japonica* Thunb.**

Synonyms

Caprifolium chinense S. Watson ex Loudon, *Caprifolium hallianum* Hort., *Caprifolium japonicum* (Thunb.) Dum. Cours., *Caprifolium roseum* Lam., *Lonicera brachypoda* DC., *Lonicera flexuosa* Thun., *Lonicera japonica* var. *chinensis* (P.W. Wats.) Baker, *Nintooa japonica* (Thunb.) Sweet

Family

Caprifoliaceae

Common/English Names

Chinese Honeysuckle, Gold-And-Silver Flower, Hall's Honeysuckle, Honeysuckle, Japanese Honeysuckle, Woodbine

Vernacular Names

Brazil: Madressilva, Madressilva-Do-Japão (Portuguese)
Chinese: Er Hua, Jin Yin Hua, Rěn Dōng, Rěn Dōng Téng, Shaung Hua
Cook Islands: Mangamangā Rima, Pitate Papa'Ā, Pītete Papa'Ā (Maori)
Czech: Zimolez Japonský
Danish: Gedeblad, Japansk Kaprifolie
Dominican Republic: Madreselva
Dutch: Japanse Kamperfoelie
French: Chèvrefeuille Du Japon, Clématite Du Japon
French Reunion: Chèvrefeuille
German: Japanisches Geißblatt, Japanische Heckenkirsche
Hawaiian: Honekakala
Icelandic: Flekkutoppur
India: Madhumati (Manipuri)
Italian: Caprifoglio Giapponese
Japanese: Nindo, Suikazura
Korean: Geumeunhwa, In-Dong, In Dong Deong Gul
Polish: Wiciokrzew Japoński
Portuguese: Madressilva, Orlve Silva
Russian: Zhimolost' Iaponskaia, Žimolost Japonskaja
Spanish: Madreselva
Swedish: Slingertry
Thai: Dtôn-Gim-Ngîng-Huay, Dtôn-Jin-Yĭng-Hua, Dtôn Săai Náam Pêung, Dtôn-Yìm-dtang-dtîng
Vietnamese: Kim Ngân, Kim Ngân Nhật, Nhẫn Đông
Welsh: Gwyddfid Japan

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Origin/Distribution

The species is native to eastern Asia—northern and eastern China, Korea, Japan and Taiwan. It was introduced elsewhere and has become naturalized in Argentina, Australia, Brazil, Mexico, sub-Saharan Africa, New Zealand and much of the United States, including Hawaii, as well as a number of Pacific and Caribbean islands. Also it has become a major invasive species in North America.

Agroecology

Although a temperate species, it can grow in warm subtropical areas. It can climb over low-lying vegetation, shrubs and small trees and smother them. It occurs in mesic or wet areas, in both open and shaded areas, from sea level to 1,200 m elevation. It is adaptable to a diverse range of habitats and soil types from pH 4–8. It occurs in heathland, healthy woodland, damp sclerophyll forest, wet sclerophyll forest, riparian vegetation, edges of rivers and waterways, warm temperate rainforest, wasteland, scrub, thickets, parks and gardens. Soil types include sand, sandy clay, loamy clays, lateritic loams, granite, calcareous soils, silty alluvium, peat bogs and on soils derived from volcanic, sedimentary and metamorphic rock types. It has been reported to grow best on calcareous soils and moist forest soils, compared with excessively drained sandy soils or stony soils, where it is limited by moisture availability. It is tolerant of water-logged soils and is quite tolerant of seasonal droughts but is sensitive to frost which damages its shoots.

Edible Plant Parts and Uses

The flowers are used as a vegetable or made into syrup and puddings and also sucked for the sweet nectar (Facciola 1990). The flowers buds and leaves are also made into herbal teas (Kunkel 1984; Facciola 1990). The leaves are also eaten cooked or parboiled as vegetables (Facciola 1990).

Botany

Sprawling and twining, semi-deciduous to evergreen lianas with pithy stems, young stems pubescent climbing up to more than 10 m high on trees and shrubs. Leaves opposite on 5–13 mm long petioles, lamina ovate, elliptic, oblong or broadly lanceolate, 3–8 by 2–3 cm wide, apex acute or acuminate, base rounded or tapering, pubescent, becoming glabrate above, entire or young lower leaves sometimes lobed, glossy and deep green (Plate 1). Flowers, fragrant, pentamerous, two in axillary cymes, bracts 1–2 cm long, bracteoles suborbicular, 1 mm long; calyx of five joined deltoid sepals; corolla of five joined petals, bilabiate, lower lipped recurved, 3–5 cm, tube 1.5–3 cm long, white, turning yellowish (Plates 1 and 2) or tinged pink; stamens 5 free,

Plate 1 White and yellowish flowers and leaves

Plate 2 Close view of white flowers

exserted, adnate to perianth, alternating with petals, anthers versatile; ovary syncarpous, inferior 2-loculed each with 8–50 ovules, style one simple and glabrous. Fruit an indehiscent berry, fleshy, glossy, bluish-black, subglobose, 6–10 mm across. Seeds brown, ovoid or ellipsoid, 3 mm, shallowly pitted.

Nutritive/Medicinal Properties

Flower Phytochemicals

Phytochemical studies on *L. japonica* flowers revealed the presence of several saponins, triterpenoid saponins, monoterpenoids, sesquiterpenoids, cerebrosides, caffeoylquinic acids and esters, flavonoids, alkaloids, iridoid glycosides, secoiridoid glycosides, alcohols, aldehydes, ketones, oxygenated compounds, hydrocarbons, esters, phenolic acids and other phenolic compounds (Kawai et al. 1988a, b; Son et al. 1992, 1994a; Ikeda et al. 1994; Schlotzhauer et al. 1996; Kakuda et al. 2000; Peng et al. 2000; Teng et al. 2000; Kumar et al. 2005, 2006; Li and Li 2005; Song et al. 2006; El-Kashoury et al. 2007; Qian et al. 2007b; Lin et al. 2008; Qi et al. 2009; Tang et al. 2009; Li et al. 2009c; Lee et al. 2010a, b; Wang et al. 2009; Wang and Yang 2011; Zhou et al. 2012). Twenty-seven compounds were identified in *L. japonica* flowers among the three developmental stages (freshly opened, overnight and 24 hours) (Schlotzhauer et al. 1996). Germacrene D (28.33–53.17 %) was a major component at all stages; linalool and α-farnesene appeared in high concentrations in fresh and 24 hours flowers but were greatly reduced in overnight flowers. The latter, however, contained elevated levels of phenylpropanoid biosynthesized compounds, suggesting a marked diurnal influence on the biosynthesis of volatile flower constituents involving two modes of action: phenylpropanoid and lipoxygenase derivation. A total of 41 compounds including 13 iridoid glycosides, 11 phenolic acids, 7 saponins and 10 flavonoids were identified in a methanol extract of *L. japonica* flowers (Qi et al. 2009). A triterpenoid saponin, together with a known saponin, was isolated from the flowers, and their structures were deduced to be 3-β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1 → 3)-α-l-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl hederagenin28-*O*-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside and 3-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl hederagenin 28-*O*-α-L-rhamnopyranosyl-(1 → 2)-[β-D-xylcopyranosyl-(1 → 6)]-β-D-glucopyranoside, respectively (Teng et al. 2000).

Five caffeoylquinic acids and esters, 3-caffeoylquinic acid (57 mg), 3-caffeoylquinic acid methyl ester (132 mg), 3,5-dicaffeoylquinic acid (210 mg), 3,5-dicaffeoylquinic acid methyl ester (34 mg) and 3,5-dicaffeoylquinic acid butyl ester (20 mg), were isolated from 1.35 kg of dried flowers and buds of *L. japonica* (Peng et al. 2000). Two secoiridoid glycosides, loniceracetalides A and B, were isolated in very small amounts, together with ten known iridoid glycosides, from the flower buds of *Lonicera japonica* (Kakuda et al. 2000). The content of chlorogenic acid in flowers of *Lonicera macranthoides* (4.00–4.52 %) was higher than that in *Lonicera japonica* (2.20–2.46 %) (Zhou and Tong 2003). Nine compounds, namely, loganin, sweroside, 7-epi-vogeloside, 7-epi-loganin, secoxyloganin, caffeic acid, *p*-hydroxybenzoic acid, β-sitosterol and daucosterol, were isolated from the flower buds (Li and Li 2005). Caffeic acid, chlorogenic acid, methyl ester of chlorogenic acid, tricin, apigenin, 4′-*O*-methyl ether of apigenin (acacetin), quercetin and 3′-*O*-methyl ether of quercetin were isolated from *Lonicera japonica* flowers (Phan et al. 2005). Eight iridoid glycosides, namely, sweroside, 7-*O*-ethyl sweroside, 7-epi-vogeloside, secoxyloganin, secoxyloganin 7-butyl ester, dimethyl-secologanoside, centauroside and loganin, were found in the flower buds of five *Lonicera* species including *L. japonica* (Song et al. 2006).

Six novel cerebrosides, lonijaposides A_1–A_4, B_1 and B_2, were isolated from the flowers of *Lonicera japonica* (Kumar et al. 2006). Three pyridinium inner salt alkaloid-coupled secoiridoids, lonijaposides A–C together with seven known iridoids, were isolated from *Lonicera japonica* flower buds (Song et al. 2009). Thirteen bioactive compounds comprising iridoids (loganin, sweroside,

secoxyloganin and centauroside), phenolic acids (chlorogenic acid, caffeic acid, 4,5-di-*O*-caffeoylquinic acid and 3,4-di-*O*-caffeoylquinic acid) and flavonoids (rutin, hyperoside, quercetin-3-*O*-glucoside, luteolin-7-*O*-glucoside and lonicerin) were found in the flowers (Qian et al. 2007b). A new triterpenoid glycoside, oleanolic acid28-*O*-α-L-rhamnopyranosyl-(1 → 2)-[β-D-xylopyranosyl(1 → 6)]-β-D-glucopyranosyl ester, along with eleven known compounds, including chrysoeriol, luteolin, 5-hydroxymethyl-2-furfural, caffeic acid, protocatechuic acid, chrysoeriol 7-*O*-β-D-glucopyranoside, isorhamnetin 3-*O*-β-D-glucopyranoside, kaempferol 3-*O*-β-D-glucopyranoside, quercetin 3-*O*-β-D-glucopyranoside, hederagenin 3-*O*-α-L-arabinopyranoside and luteolin 7-*O*-β-D-glucopyranoside, were isolated from the ethyl acetate fraction of the methanol extract of *L. japonica* flowers (Choi et al. 2007). Two new triterpenoid saponins, loniceroside D and loniceroside E, along with seven known compounds, chlorogenic acid, sweroside, vogeloside, *epi*-vogeloside, loniceroside A, loniceroside B and loniceroside C, were isolated from the dry flowers and buds of *Lonicera japonica* (Lin et al. 2008).

A novel cyclic peroxide shuangkangsu was obtained from the water extract of *L. japonica* buds, and its structure was elucidated as 5,8-divinyl-1,4-dihydro-1,4-di-*O*-β-D-glucopyranosyl-2,3-dioxane (Yu et al. 2008). Li et al. (2009a) synthesized four novel cyclic peroxide glucosides 15a, 15b, 16a and 16b, optically pure analogues of shuangkangsu, an antiviral natural product with an unusual skeleton isolated from the buds of *Lonicera japonica.* They also synthesized four optically pure cycloperoxide glucosides 9a, 9b, 10a and 10b, analogues of shuangkangsu (Tang et al. 2009). A total of 41 compounds including 13 iridoid glycosides, 11 phenolic acids, 7 saponins and 10 flavonoids were identified in a methanol flower extract of *L. japonica* (Qi et al. 2009). Ten bioactive components were identified in the dried flowers: chlorogenic acid, luteolin-3-*O*-glucoside and 4,5-di-*O*-caffeoylquinic acid, 4-caffeoylquinic acid, quercetin-3-*O*-glucoside, lonicerin, 3,5-di-*O*-caffeoylquinic acid, 3,4-di-*O*-caffeoylquinic acid, caffeic acid and rutin (Qian et al. 2008). All the compounds had binding interaction with bovine serum albumin (BSA). The binding degrees of the compounds to BSA ranged from 4.8 to 61.2 (0.3 mM BSA) and from 11.1 to 76.2 % (0.6 mM BSA), respectively. Serum albumins are the most abundant proteins in the circulatory system of a wide variety of organisms and have the physiological function to maintain the osmotic pressure and to transport a wide variety of endogenous and exogenous compounds, such as fatty acids, steroids and drugs.

Thirty-three constituents were detected and characterized in the flower buds of *Lonicera* spp. (*L. japonica* Thunb., *L. hypoglauca* Miq., *L. hypoglauca* Miq. subsp. *nudiflora* Hsu et H. J. Wang, *L. fulvotomentosa* Hsu et S. C. Cheng, *L. nubium* Hand.-Mazz., *L. confusa* (Sweet) DC., *L. pampanini* Lévl.) comprising six caffeoylquinic acids (CQA), 3-*O*-caffeoylquinic acid (3-CQA), 4-*O*-caffeoylquinic acid (4-CQA), 5-*O*-caffeoylquinic acid (5-CQA), 3,5-di-*O*-caffeoylquinic acid (3,5-diCQA) and 4,5-di-*O*-caffeoylquinic acid (4,5-diCQA) (including caffeic acid); eight flavonoids, quercetin-3-*O*-rutinoside (rutin), quercetin-3-*O*-galactoside (hyperoside), luteolin-7-*O*-glucoside, kaempferol-3-*O*-glucoside, isorhamnetin-3-*O*-glucoside, luteolin-*O*-dihexoside, quercetin and luteolin; and eight iridoid glycosides, loganin, secologenic acid (swertiamarin), sweroside, secoxyloganin, *epi*-vogeloside, 7-*O*-ethyl sweroside or isomer and aldosecologanin and the rest unknown (Li et al. 2009c). From the polar fractions of a 70 % ethanol flower extract, ten constituents were isolated and identified as iridoid glycosides: 7-dehydrologanin (7-ketologanin), secologanin dimethyl acetal, (*E*)-aldosecologanin (centauroside), dimethyl secologanoside, secoxyloganin, epi-vogeloside, uracil, D-mannitol, sucrose and 1-*O*-β-D-glucopyranosyl-(2S,3S,4R,8*E*/*Z*)-2-[(2R)-2-hydroxy(docosanoyl, tricosanoyl, tetracosanoyl, pentacosanoyl)amino]-8-octadecene-1,3,4-triol (Lee and Kim 2010).

Thirteen phenolic constituents, luteolin; protocatechuic acid; caffeic acid; flavoyadorinin-B; 4,5-dicaffeoylquinic acid; luteolin 7-*O*-β-D-glucopyranoside; 3,5-dicaffeoylquinic acid methyl

ester; methyl chlorogenate; quercetin 3-*O*-β-D-glucopyranoside; 3,5-dicaffeoylquinic acid; rhoifolin; chlorogenic acid; and a novel phenolic glucoside benzoate, vanillic acid 4-*O*-β-D-(6-*O*-benzoylglucopyranoside), were isolated from the flower buds of *Lonicera japonica* (Lee et al. 2010a).

Twenty compounds were isolated from the dried buds of *L. japonica* and identified as sophoricoside, luteolin-7-*O*-β-D-glucopyranoside; rutin; quercetin; 3,5-*O*-dicaffeoylquinic acid methyl ester; 4,5-*O*-dicaffeoylquinic acid methyl ester; 3,4-*O*-dicaffeoylquinic acid methyl ester; 4,5-dicaffeoylquinic acid; 3,4-dicaffeoylquinic acid; chlorogenic acid; *epi*-vogeloside; sweroside; vogeloside; secoxyloganin; macranthoidin A; macranthoidin B; loniceroside A; loniceroside B; loniceroside C; and dipsacoside B (Wang and Yang 2011). Four new N-containing iridoid glycosides, lonijapospiroside A, L-phenylalaninosecologanin B, L-phenylalaninosecologanin C and dehydroprolinoylloganin A, were isolated from the flower buds (Zheng et al. 2012). Fifteen homosecoiridoids were isolated from the flower buds of *Lonicera japonica* (Yu et al. 2011). Compounds 1–4, designated as loniphenyruviridosides A–D, possessed unprecedented skeletons featuring phenylpyruvic acid-derived moieties coupled with an iridoid or a secoiridoid nucleus. Compounds 5–15 (lonijaposides D-N) represented additional examples of the unusual pyridinium alkaloid-coupled secoiridoids (lonijaposides A–C).

The following compounds were identified from the essential oil of *L. japonica* flowers: pinene; hexene-1; *cis*-3-hexanol-1; *cis*-2-methyl-2-vinyl-(α-hydroxy-isopropyl)-tetrahydrofuran;*trans*-2-methyl-2-vinyl-(α-hydroxy-isopropyl)-tetrahydrofuran; (−) *cis*-2,6,6-trimethyl-2-vinyl-5-hydroxytetrahydropyran; linalool; geraniol; α-terpineol; benzyl alcohol; β-phenylethyl alcohol; carvacrol; and eugenol (Wu and Fang 1980). Ji et al. (1990) identified 47 compounds in the essential oil of *L. japonica* flowers including ethyl palmitate and linalool. Twenty and thirty monoterpenoids and sesquiterpenoids were identified from the essential oil of the dry flower and fresh flower, respectively (Wang et al. 1992). The major constituents were linalool, geraniol, aromadendrene and eugenol. One hundred and fifty compounds, made up of 36 hydrocarbons, 28 alcohols, 21 aldehydes, 12 ketones, 38 esters and 15 miscellaneous, were identified, and the important components that characterized the volatiles of honeysuckle flowers were determined to be linalool, (*Z*)-jasmone, (*Z*)-jasmin lactone, methyl jasmonate and methyl epi-jasmonate (Ikeda et al. 1994). Sixty compounds were identified among the volatiles in the flowers prepared by the two methods, floral absolute volatiles (FAV) and hydrodistilled/hexane-extracted volatiles (HHV) (El-Kashoury et al. 2007). Linalool was the major constituent in both cases and was higher in the floral absolute volatiles (47.92 %). Nerolidol, 4-terpineol, *cis*-jasmone, *cis*-3-hexenyl tiglate, methyl palmitate and *trans*-linalool oxide were detected in lesser but appreciable quantities in both samples. The oxygenated compounds were dominant in both cases with alcohols as major (63.43 and 37.86 %), followed by esters (16.97 and 32.9 %) in FAV and HHV, respectively. Aldehydes were present in higher proportions in HHV (6.77 %) than in FAV (2.98 %), while ketones were higher in FAV (3.71 %) than HHV (1.76 %). *cis*-Jasmone, the principle component of the essential oil of jasmine flowers, was present in relatively high concentrations in FAV (3.27 %) and in lesser amounts in HHV (1.32 %). The profile of the volatiles in FAV were as follows: α-farnesene (1.195 %), *trans*-3-hexen-1-ol (0.21 %), *cis*-3-hexen-1-ol (0.41 %), *cis*-sabinene hydrate (2.58 %), linalool (47.92 %), 4-terpineol (3.67 %), *p*-menth-1-en-8-ol (0.78 %), nerol (0.30 %), geraniol (0.38 %), nerolidol (7.18 %), lilac aldehyde (1.86 %), methyl azealate semialdehyde (0.77 %), palmitic aldehyde (0.35 %), *cis*-jasmone (3.27 %), heptadecanone (0.44 %), *cis*-3-hexenyl tiglate (3.92 %), methyl jasmonate (1.18 %), methyl epi-jasmonate (0.26 %), methyl palmitoleate (0.91 %), ethyl palmitate (0.25 %), methyl linolenate (7.18 %), ethyl linolenate (0.19 %) and *trans*-linalool oxide (1.23 %) (El-Kashoury et al. 2007). The profile of the volatiles in HHV were as follows: *p*-cymene (0.56 %), α-copaene (0.10 %), β-bourbonene (0.67 %), germacrene D (0.47 %), pristane

(0.12 %), *n*-pentadecane (0.21 %), *n*-heptadecane (0.16 %), *n*-octadecane (0.21 %), *n*-docosane (0.23 %), *n*-tricosane (0.40 %), *n*-tetracosane (0.13 %), *n*-pentacosane (0.30 %), *cis*-3-hexen-1-ol (0.93 %), 2-methyl-5-hexanol (0.34 %),6-hepten-1-ol-5-methyl (0.13 %), linalool (22.08 %), 1-terpineol (0.34 %), 4-terpineol (3.34 %), *p*-menth-1-en-8-ol (2.81 %), *cis*-piperitol (0.11 %), geraniol (0.57 %), nerolidol (6.72 %), α-cadinol (0.16 %), alfol 14 (0.33 %), *n*-hexanal (0.81 %), neral (0.28 %), geranial (0.20 %), methyl azealate semialdehyde (2.25 %), myristaldehyde (0.46 %), palmitic aldehyde (2.77 %), *cis*-jasmone (1.32 %), *trans*-geranyl acetone (0.44 %), methyl octanoate (0.35 %), *cis-3-hexenyl* tiglate (3.15 %), methyl laurate (0.30 %), methyl jasmonate (0.33 %), methyl pentadecanoate (0.32 %), methyl palmitoleate (18.26 %), ethyl-9-hexadecanoate (0.10 %), ethyl palmitate (0.43 %), methyl heptadecanoate (0.20 %), methyl oleate (3.57 %), methyl stearate (0.98 %), arachidic acid methyl ester (0.17 %), hexadecanoic acid, cyclohexyl ester (0.09 %), *trans*-2,3-epoxyoctane (0.20 %), lavander lactone (0.09 %), *cis*-linalool oxide (3.39 %), *trans*-linalool oxide (2.51 %) and caryophyllene oxide (0.19 %) (El-Kashoury et al. 2007).

Wang et al. (2009) reported that the primary components of the volatile oil from flowers were linalool (0.15–15.35 %), linalool oxide (0.09–6.53 %), geraniol (0.24–8.17 %) and α-terpineol (0–10.57 %), and obvious variations in components of the volatile oil were observed at six different developmental stages. The chlorogenic (2.7–3.5 %) and total flavonoid contents (11.6–13.2 %) of *L. japonica* flowers varied with the different flowering stages (Li et al. 2009b). The volatile oil samples of the flowers were found to have three types of compounds, *n*-diolefins, fatty acids and steroids. These included nonacosane (40 %), hentriacontane (20 %), vitamin E (8.15–10.43 %), γ-5-sitostene-3-ol (4.90–6.9 %), stigmasta-5,2-diene-3-ol (1.06–4.10 %) and campesterol.

Thirty-nine compounds representing 92.34 % of the total oil were identified from the flower essential oil, of which *trans*-nerolidol (16.31 %), caryophyllene oxide (11.15 %), linalool (8.61 %), *p*-cymene (7.43 %), hexadecanoic acid (6.39 %), eugenol (6.13 %), geraniol (5.01 %), *trans*-linalool oxide (3.75 %), globulol (2.34 %), pentadecanoic acid (2.25 %), viridiflorol (1.83 %), benzyl alcohol (1.63 %) and phenylethyl alcohol (1.25 %) were the major compounds (Rahman and Kang 2009). Minor components included citronellyl acetate (0.97 %), geranylacetone (0.92 %), hexahydrofarnesyl acetone (0.87 %), α-cadinol (0.85 %), tetradecanoic acid (0.85 %), dodecanal (0.83 %), aromadendrene (0.82 %), 1,8-cineole (0.81 %), juniper camphor (0.76 %), octadecanoic acid (0.75 %), *p*-cymene (7.43 %), acetophenone (0.74 %), 1-octen-3-ol (0.70 %), β-ionone (0.70 %), *cis*-linalool oxide (furanoid) (0.69 %), spathulenol (0.69 %), *cis*-4-heptenal (0.66 %), α-terpineol (*p*-menth-1-en-8-ol) (0.65 %), β-caryophyllene (0.65 %), *cis, trans*-farnesol (0.68 %), *cis*-jasmone (0.58 %), dodecane (0.55 %), geranyl acetate (0.54 %), undecanal (0.52 %), elemol (0.52 %), epiglobulol (0.50 %) and decanal (0.46 %).

Constituents of the essential oil from the flower buds comprised 87.62 % monoterpenoids and 5.88 % sesquiterpenoids with a predominance of estragole (80.17 %) and were identified as follows: 1-octen-3-ol (0.04 %), β-pinene (0.03 %), (D)-limonene (0.175 %), 1, 8-cineole (0.31 %), benzyl alcohol (0.085 %), acetophenone (0.34 %), linalool (6.05 %), phenylethyl alcohol (0.25 %), α-terpineol (0.12 %), linalool acetate (0.28 %), (*Z*)-β-damascenone (0.16 %), α-cubebene (0.12 %), eugenol (0.23 %), β-geranyl acetate (0.12 %), β-caryophyllene (0.25 %), β-gurjunene (0.36 %), germacrene D (3.17 %), α-selinene (0.31 %), α-farnesene (1.01 %), β-cadinene (0.12 %), elemol (0.22 %), caryophyllene oxide (0.15 %), α-cadinol (0.11 %) and juniper camphor (0.18 %) (Zhou et al. 2012).

Han et al. (2012) reported that the volatile oil obtained from subcritical R134 extraction from *L. japonica* flowers comprised a complex mixture consisting of hydrocarbons, terpenes and esters. Twenty-seven compounds were identified. The oil contained 2.791 % of alkene and alkane which were probably derived from fatty acids. The major components in the volatile oil were fatty acids which represented 47.013 % of the

total oil composition. The major fatty acids were n-hexadecanoic acid (19.117 %), 9,12-octadecadienoic acid (9.062 %) and 9,12,15-octadecatrien-1-ol (18.432 %). In addition, the volatile oil also contained 29.340 % fatty acid ester, namely, hexadecanoic acid methyl ester (3.529 %), hexadecanoic acid ethyl ester (1.835 %), 9,12-octadecadienoic acid methyl ester (3.471 %), 9,12,15-octadecatrienoic acid methyl ester, (Z,Z,Z)- (4.662 %), octadecanoic acid methyl ester (0.793 %), linoleic acid ethyl ester (3.556 %), 7,10,13-hexadecatrienoic acid, methyl ester (4.622 %), octadecanoic acid, ethyl ester (0.923 %), eicosanoic acid, methyl ester (0.351 %), 11,14-eicosadienoic acid, methyl ester (0.314 %), docosanoic acid, methyl ester (0.664 %), nonadecanoic acid, ethyl ester (0.479 %), tetracosanoic acid, methyl ester (4.151 %) and octadecanoic acid (0.402 %). Other components included the following: tetradecanal (0.190 %), 2-heptadecanone (1.028 %), tricosane (0.886 %), eicosane (0.347 %), pentacosane (0.902 %), 7-methyl-Z-tetradecen-1-ol acetate (1.091 %), 17-pentatriacontene (0.393 %), triallylmethylsilane (0.656 %), *E*-15-heptadecenal (1.922 %) and squalene 1.235 %.

Secoiridoid sulfonates 1–3 were isolated from the 50 % ethanol/aqueous extract of the sulfiting-processed *Lonicera japonica* flower buds (Li et al. 2012). Analyses of the different samples of *Lonicera japonica* flowers obtained by various process techniques suggested that the sulphur fumigation led to the decrease of secologanic acid and the formation of secologanic acid-derived sulfonate 1 and its derivatives 2, 2a and 3 in the crude materials, which revealed that sulphur fumigation, the traditional process technique, could alter the phytochemical profiles of some Chinese herbal medicine.

Aerial Parts/Cell Suspension Culture Phytochemicals

From the aerial parts of *Lonicera japonica*, 12 triterpenoidal saponins having oleanolic acid and hederagenin as aglycones were isolated (Kawai et al. 1988b). Saponins 1,2,4,5,8 and 10 had the hederagenin as aglycones. Saponins 3, 1 and 7 had oleanolic acid as aglycone along with methyl sugars. Saponins 2, 3,7 and 8 contained the glucosyl-arabinosyl-type saponins, while saponins 4,9, 10 and 11 contained the rhamnosyl–arabinosyl-type saponins and 12 the acetyl derivative. The structures of four new saponins, 6,9,11 and 12,were established to be 3-*O*-α-L-arabinopyranosyl-28-*O*-[β-D-glucopyranozyl(1 → 6)-β-D-glucopyranosyl]oleanolic acid; 3-*O*-[α-L-rahmnopyranosyl(1 → 2)-α-L-arabinopyranosy]-28-*O*-β-D-glucopyranosyl hederagenin; 3-*O*-[α-L-rhamnopyranosyl(1 → 2)-α-L-arabinopyranosyl]-28-*O*-[β-D-glucopyranosyl(1 → 6)-β-D-glucopyranosyl]oleanolic acid; and 3-*O*-[α-L-rhamnopyranosyl(1 → 2)-α-L-arabinopyranoyl]-28-*O*-[6-acetyl-β-D-glucopyranosyl(1 → 6)-β-D-glucopyranosyl] hederagenin, respectively. A new iridoid glucoside, epi-vogeloside, was isolated along with secologanin dimethyl acetal, loganin and vogeloside from hot aqueous extract of aerial parts of *Lonicera japonica* (Kawai et al. 1988a). Fresh young shoots were found to be a rich source of secoxyloganin that could be converted into secologanin (Mehrotra et al. 1988).

Seven flavonoids hydnocarpin, quercetin, ochnaflavone, ochnaflavone 4′-*O*-methylether, astragalin, isoquercitrin and rhoifolin were isolated from the aerial parts of *Lonicera japonica* (Son et al. 1992). Two new triterpenoid saponins, loniceroside A and B, were isolated from the aerial parts of *Lonicera japonica,* and their structures were established as 3-*O*-α-L-arabinopyranosyl hederagenin 28-*O*-α-L-rhamnopyranosyl (1 → 2)-[β-D-xylopyranosyl(1 → 6)]-β-D-glucopyranosyl ester and 3-*O*-α-L-rhamnopyranosyl(1 → 2)-α-L-arabinopyranosyl hederagenin 28-*O*-α-L-rhamnopyranosyl(1 → 2)-[β-D-xylopyranosyl(1 → 6)]-β-D-glucopyranosyl ester, respectively (Son et al. 1994a). Two flavonoids, diosmetin 7-*O*-glucoside and lonicerin, and an iridoid vogeloside were isolated from the aerial parts (Son et al. 1994b). Four flavonoids, namely, luteolin-7-*O*-α-D-glucoside; luteolin-7-*O*-β-D-galactoside; quercetin-3-*O*-β-D-glucoside; and hyperoside, were isolated from the plant (Gao et al. 1995). Six compounds, namely, corymbosin,

5-hydroxy-3′,4′,7-trimethoxyflavone, myristic acid, palmitic acid, sucrose and β-sitosterol, were isolated from the plant (Huang et al. 1996). Six triterpenoid saponins A–F were isolated from *Lonicera japonica* (Chen et al. 2000). The structure of a new triterpenoid saponin F was determined as 3-*O*-β-D-glucopyranosyl(1 → 4)-β-D-glucopyranosyl(1 → 3)-α-L-rhamnopyranosyl(1 → 2)-α-L-arabinopyranosyl-hederagenin-28-*O*-β-D-glucopyranosyl(1 → 6)-β-D-glucopyranosyl ester. Other known saponins were identified as hederagenin-3-*O*-α-L-rhamnopyranosyl (1 → 2)-α-L-arabinopyranoside; 3-*O*-α-L-rhamnopyranosyl(1 → 2)-α-L-arabinopyranosyl-hederagenin-28-*O*-β-d-xylopyranosyl(1 → 6)-β-D-glucopyranosyl ester; 3-*O*-α-L-rhamnopyranosyl(1 → 2)-α-l-arabinopyranosyl-hederagenin-28-*O*-β-D-glucopyranosyl(1 → 6)-β-D-glucopyranosyl ester; 3-*O*-α-L-rhamnopyranosyl(1 → 2)-α-l-arabinopyranosyl-hederagenin-28-*O*-α-L-rhamnopyranosyl(1 → 2)[β-D-xylopyranosyl(1 → 6)]-β-D-glucopyranosyl ester; and 3-*O*-β-D-glucopyranosyl(1 → 3)-α-L-rhamnopyranosyl(1 → 2)-α-L-arabinopyranosyl-hederagenin-28-*O*-β-D-glucopyranosyl(1 → 6)-β-D-glucopyranosyl ester. Five iridoid glycosides, L-phenylalaninosecologanin, 7-*O*-(4-β-D-glucopyranosyloxy-3-methoxybenzoyl) secologanolic acid, 6′-*O*-(7α-hydroxyswerosyloxy)loganin, and (*Z*)-aldosecologanin and (E)-aldosecologanin, were isolated from the stems and leaves of *Lonicera japonica* (Machida et al. 2002). Thirty-six constituents were isolated from the volatile oil of flowers and stems, among which 18 were common to both, accounting for 85.23 and 83.42 %, respectively (Li et al. 2002). Palmitic acid and linoleic acid predominated. A triterpenoid saponin, loniceroside C, was isolated from the aerial parts of *Lonicera japonica,* and its structure established to be 3-*O*-β-D-glucopyranosyl hederagenin 28-*O*-α-L-rhamnopyranosyl (1 → 2)-[β-D-xylopyranosyl(1 → 6)]-β-D-glucopyranosyl ester (Kwak et al. 2003). Hyperoside, chlorogenic acid, luteolin and caffeic acid were found to be the major important active ingredients of *L. japonica* crude herb (Peng et al. 2005). Seven compounds were isolated from *L. japonica* extract and elucidated as luteolin, luteoloside, quercetin, quercetin-3-*O*-β-D-glucoside, quercetin-7-*O*-β-D-glucoside, rutin and chlorogenic acid (Chen et al. 2010b).

Secologanin synthase, an enzyme catalyzing the oxidative cleavage of the cyclopentane ring in loganin to form secologanin, was detected in microsomal preparations from cell suspension cultures of *Lonicera japonica* (Yamamoto et al. 2000). The activity of 7-deoxyloganin 7-hydroxylase, an enzyme catalyzing the conversion of 7-deoxyloganin into loganin, was detected in a microsomal preparation from the cell suspension cultures of *Lonicera japonica* (Katano et al. 2001). Two secoiridoid glucoside artefacts, 7-*O*-butylsecologanic acid and secologanin dibutylacetal, were isolated from a butanol extract of *Lonicera japonica*, along with loganin, sweroside and secologanin (Tomassini et al. 1995). The authors showed that acetalic iridoids could be easily formed by reaction of the aldehydic function with alcoholic solvents.

One hundred and thirteen compounds were separated from the volatile oil of *L. japonica* of which 89 representing 77.99 % of the oil were characterized (Yang et al. 2007). Constituents with relative content greater than 2 % were palmitic acid (6.05 %), menthol 5 %, L-linalool (3.95 %), caryophyllene oxide (3.49 %), 6,10,14-trimethyl-2-pentadecanone (3.47 %), 1-octanol (2.92 %), β-caryophyllene (2.70 %), camphor (2.59 %), borneol (2.40 %), β-selinene (2.37 %) and δ-cadinene (2.13 %). Remaining constituents included the following: 5-ter-butyl-1,3,cyclopentadiene (0.18 %), (*E*)-2-hexenal (0.117 %), *p*-xylene (0.042 %), 1-hexanol (0.104 %), heptanal (0.207 %), α-thujene (0.063 %), α-pinene (0.839 %), camphene (0.490 %), (*E*)-2-heptenal (0.089 %), benzaldehyde (0.696 %), β-pinene (0.618 %), 1-octan-3-ol (0.277 %), 2,3-octanedione (0.194 %), 6-methyl-5-hepten-2-one (0.368 %), 2-pentylfuran (1.015 %), 3-octanol (0.146 %), octanal (0.669 %), terpinolene (0.096 %), *p*-cymene (0.885 %), limonene (0.897 %), 1,8-cineole (1.229 %), *E*-3-octen-2-one (0.080 %), hyacinthine (0.187 %), γ-terpinene (0.484 %), artemisia

ketone (0.260 %), 1-menthone (0.530 %), isoborneol (0.522 %), *p*-menthone (0.204 %), 4-terpineol (1.612 %), α-terpineol (0.905 %), β-cyclocitral (0.255 %), bornyl formate (0.220 %), 3-methoxy-*p*-cymene (0.526 %), pulegone (0.526 %), carvacrol methyl ether (0.577 %), piperitone (0.733 %), cinnamal (0.248 %), durenol (0.349 %), bornyl acetate 0.330 %, *E*-anethole (0.803 %), thymol (1.301 %), carvacrol (1.106 %), junipene (0.167 %), α-cubebene (0.131 %), eugenol (0.532 %), α-copaene (0.483 %), β-elemene (0.501 %), tetradecane (0.509 %), isolongifolene (0.486 %), methyl eugenol (0.378 %), 3-ter-butyl-1,2-dimethoxybenzene (1.352 %), 1,3,-diisopropenyl-6-methylcyclohexene (1.695 %), 4-ter-butyl-catechol (0.625 %), geranyl acetone (1.878 %), β-bisabolene (0.789 %), aromadendrene (0.468 %), AR-curcumene (1.243 %), pentadecane (1.454 %), α-muurolene (0.547 %), α-bisabolene (0.924 %), γ-cadinene (0.495 %), coniferol (1.167 %), motrin methyl ester (0.4 %), spathulenol (0.78 %), hexadecane (0.94 %), α-cedrol (0.47 %), τ-muurolol (0.735 %), α-cadinol (1.388 %), heptadecane (0.729 %), hexadecanal (0.526 %), 3 N-butylphthalide (0.524 %), myristic acid (1.311 %), octadecan (0.293 %), neophytadiene (0.546 %), pentadecanoic acid (0.465 %), nonadecane (0.239 %), farnesyl acetone (0.917 %), methyl palmitate (0.270 %), sandaracopimaradiene (0.296 %), eicosane (0.463 %), heneicosane (0.403 %), phytol (1.771 %), oleic acid (0.830 %), stearic acid (0.377 %), docosane (0.356 %), tricosane (0.474 %), tetracosane (0.333 %), pentacosane (0.534 %), hexacosane (0.240 %), heptacosane (0.274 %), octacosane (0.170 %) and nonacosane (0.250 %).

A total of 89 compounds were identified in the essential oils from the flower, leaf and stems of *L. japonica* (Vukovic et al. 2012). The main constituents were (Z,Z)-farnesol (16.2 %) and linalool (11.0 %) for the flower fraction, hexadecanoic acid (16.0 %) and linalool (8.7 %) for the leaf fraction and hexadecanoic acid (31.4 %) for the stem. Monoterpene hydrocarbons were absent from all the oils, and oxygenated sesquiterpenes were not identified in the essential oil of the stem.

Fruit Phytochemicals

The following carotenes were identified in *L. japonica* berries: phytofluene, β-carotene, ζ-carotene, lycopene, γ-carotene, η-carotene and xanthophylls, cryptoxanthin, zeaxanthin and auroxanthin (Goodwin 1952). The xanthophylls existed almost exclusively as esters and cryptoxanthin were the major components.

An unusual carotenoid, η-carotene (7,8,7′,8′-tetrahydro-β,β-carotene), a natural C(40) carotenoid, first detected in the berries of *Lonicera japonica* was synthesized by olefin cross-metathesis/dimerization of a C(21) polyene derived from *trans*-7,8-dihydroretinal (Fontán et al. 2012).

Leaf Phytochemicals

Two biflavonoids 3′-*O*-methyl loniflavone [5,5″,7,7″-tetrahydroxy 3′-methoxy 4′,4‴-biflavonyl ether] and loniflavone [5,5″,7,7″,3′-pentahydroxy 4′,4‴-biflavonyl ether] along with luteolin and chrysin were isolated from the leaves of *Lonicera japonica* (Kumar et al. 2005). The leaves were found to be a source strictosidine, a key intermediate in the biosynthesis of the terpenoid indole alkaloid (T1A) pathway (Nam et al. 2007). Three monocaffeoylquinic acids (3-CQA, 4-CQA, 5-CQA) and 5-feruloylquinic acid (5-FQA) were detected in the leaves (Wang and Clifford 2008). Five caffeoylquinic acid derivatives were isolated from the leaves, and their structures were identified as 3,4-di-*O*-*caffeoylquinic* acid methyl ester; 5-*O*-caffeoylquinic acid methyl ester; 3,4-di-*O*-caffeoylquinic acid; 1,3-di-*O*-caffeoylquinic acid; and chlorogenic acid (Ma et al. 2009). The levels of rutin, luteoloside, isochlorogenic acid, chlorogenic acid and caffeic acid were determined in new leaves of *L. japonica* (Niu et al. 2012). The contents of chlorogenic acid and caffeic acid in *Lonicera* new leaves were 2.572 and 1.498 %, respectively, both higher than those cited in Chinese Pharmacopoeia.

Stem Phytochemicals

Seven major components, namely, chlorogenic acid, caffeic acid, loganin, sweroside, secoxyloganin, rutin and luteolin 7-*O*-glucoside, were found in the stem (Qian et al. 2007a). Thirteen compounds were isolated and identified from the stems: protocatechuic acid, caffeic acid, macranthoin G, esculetin, luteolin, quercetin, apigenin, luteolin-7-*O*-β-D-glucopyranoside, isorhamnetin-7-*O*-β-D-glucopyranoside, diosmetin-7-*O*-β-D-glucopyranoside, rhoifolin, lonicerin and hydnocarpin D (Zhang et al. 2009). The biflavones 7,7″-dimethyllanaraflavone, agathisflavone and 7″-methylagathisflavone were isolated from *L. japonica* stems (Pradhan et al. 2009).

Twelve compounds were isolated from the 70 % ethanol extract of the stem, and their structures were identified as six triterpenoids (24S)-cycloart-25-en-3β,24-diol, pomolic acid, ursolic acid, euscaphic acid, hederagenin and 23-hydroxytormentic acid and six sterols obtusifoliol, gramisterol, citrostadienol, β-sitosterol, ergosterol peroxide and β-sitosterol glucoside (Kim et al. 2009a). Six iridoids were isolated from the 70 % ethanol extract of the stem and their structures identified as epialyxialactone, secologanin dimethyl acetal, sweroside, loganin, loganic acid and demethylsecologanol (Kim et al. 2009b). Fourteen compounds were isolated from the 70 % ethanol extract of the stem, and their structures were elucidated as seven aliphatic compounds long-chain alcohols (1, 2), trilinolein (3), hexacosanol (4), fatty acids (6), 9,12,13-trihydroxyoctadeca-10(E),15(Z)-dienoic acid (10) and pinellic acid (11) and seven phenolics bis(2-ethylhexyl) phthalate (dioctylphthalate, DOP) (5), coniferaldehyde (7), caffeic acid docosanoyl ester (8), caffeic acid (9), coniferyl aldehyde 4-*O*-glucoside (12), linarin (13) and coniferin (14) (Kim et al. 2009c). A new 2,7′-cyclolignan named lonicerinol and eight known lignans, (−)-epipinoresinol, (−)-pinoresinol, 9α-hydroxypinoresinol, 7R,8S-dihydrodehydrodiconiferyl alcohol, (±)-neo-olivil, (+)-isolariciresinol, 3-methoxy-8,4′-oxyneoligna-3′,4,7,9,9′-pentol and (−)-pinoresinol 4-*O*-glucoside, were isolated from the stem (Yean et al. 2010).

Lonicera japonica was reported to contain more than 140 compounds comprising essential oils, organic acids and flavones (Shang et al. 2011), flavonoids, iridoid glucosides, saponins and phenolic acids (Chen et al. 2007a, b) and its active principles to possess wide pharmacological actions, such as antiinflammatory, antibacterial, antiviral, antioxidative and hepatoprotective activities (Shang et al. 2011). Some of the pharmacological properties of the various plant parts are discussed below.

Antioxidant Activity

Among the methanol extract and the dichloromethane, ethyl acetate, n-butanol and water fractions, the ethyl acetate fraction of *Lonicera japonica* flowers exhibited marked scavenging/inhibitory activities, as follows: IC50 values of 4.37, 27.58 and 12.13 μg/mL in the DPPH, total ROS, ONOO- and *OH assays, respectively (Choi et al. 2007). A new triterpenoid glycoside, oleanolic acid 28-*O*-α-L-rhamnopyranosyl-(1 → 2)-[β-D-xylopyranosyl(1 → 6)]-β-D-glucopyranosyl ester (12), and 11 known compounds, including chrysoeriol (1), luteolin (2), 5-hydroxymethyl-2-furfural (3), caffeic acid (4), protocatechuic acid (5), chrysoeriol 7-*O*-β-D-glucopyranoside (6), isorhamnetin 3-*O*-β-D-glucopyranoside (7), kaempferol 3-*O*-β-D-glucopyranoside (8), quercetin 3-*O*-β-D-glucopyranoside (9), hederagenin 3-*O*-α-L-arabinopyranoside (10) and luteolin 7-*O*-β-D-glucopyranoside (11), were isolated from the ethyl acetate fraction. Compounds 2, 4, 5, 7, 9 and 11 exhibited marked scavenging activities, with IC_{50} values of 2.08–11.76 μM for 1,1- diphenyl-2-picrylhydrazyl (DPPH) radicals and 1.47–6.98 μM for ONOO-.

Fourteen compounds, namely, chlorogenic acid, 1-*O*-caffeoylquinic acid (1-*O*-CQA), caffeic acid, 4-*O*-CQA, rutin, isoquercitrin, luteolin-7-*O*-glucoside, lonicerin, 4,5-*O*-dicaffeoylquinic acid (4,5-*O*-diCQA), 3,5-*O*-diCQA, 1,3-*O*-diCQA, 3,4-*O*-diCQA, 1,4-*O*-diCQA and luteolin, were isolated from *L. japonica* flower buds by HPLC-DAD-TOF/MS and found to have antioxidant activity as assayed by DPPH (Tang et al. 2008).

The ethanol extracts of various aerial parts were found to be highly enriched in the total phenolic contents as gallic acid equivalents and in the antioxidant capacity as ʏ-ascorbic acid equivalents (Dung et al. 2011). The extracts exhibited potent DPPH and superoxide radical scavenging activities, which were found to be stronger than butylated hydroxyanisole and slightly weaker than ascorbic and gallic acids. The IC_{50} values of DPPH and superoxide radical scavenging capacities of the extracts ranged between 19.45–57.97 and 16.60–38.63 μg/ml.

Antiinflammatory Activity

The *n*-butanol fraction of *Lonicera japonica* showed antiinflammatory activity in mice and rats (Lee et al. 1994). Several constituents such as loniceroside A and B, flavonoids and iridoids were isolated from this fraction. Loniceroside A, hederagenin, lonicerin and loganin, major constituents of *L. japonica* flower *n*-butanol fraction, showed antiinflammatory activity comparable to aspirin in the croton oil-induced ear oedema and adjuvant-induced arthritis models in mice (Lee et al. 1995a, b). Lonicerin was not tested in the adjuvant-induced arthritis model.

At oral doses of 100–400 mg/kg, the *n*-butanol fraction of *L. japonica* showed antiinflammatory activity against acute, granulomatic and chronic inflammation models in mice and rats (Lee et al. 1998). Although the activity was not potent compared with prednisolone, the results supported the traditional use and suggested that this fraction of *L. japonica* may yield a safe and mild antiinflammatory agent for treating various inflammatory disorders.

The aqueous extract from *Lonicera japonica* flower exhibited antiinflammatory effects in lipopolysaccharide (LPS)-induced rat liver sepsis (Lee et al. 2001). The extract inhibited the increase of nuclear factor (NF)-kappaBp65 and degradation of I-kappaBalpha in the liver of LPS-challenged rats. Immunohistochemical analysis of rat hepatocytes showed that LPS-induced inflammatory responses, involving degradation of I-kappaBalpha and induction of NF-kappaBp65, tumour necrosis factor (TNF)-alpha and inducible nitric oxide synthase (iNOS), were partially inhibited by pretreatment with the extract. The results suggested that the extract may act as a therapeutic agent for inflammatory disease through a selective regulation of NF-kappaB activation. Loniceroside C isolated from the aerial parts showed in-vivo antiinflammatory activity against mouse ear oedema provoked by croton oil (Kwak et al. 2003). At doses of 50, 100 and 200 mg/kg, *L. japonica* aqueous extract exhibited significant inhibition of both change in paw thickness and vascular permeability in proteinase-activated receptor 2 (PAR2)-mediated mouse paw oedema (Tae et al. 2003). The extract (100 mg/kg) also significantly inhibited PAR2 agonist-induced myeloperoxidase (MPO) activity and tumour necrosis factor (TNF)-alpha expression in paw tissue. An aqueous extract of *L. japonica* demonstrated potent inhibition of the production of the proinflammatory mediators, nitric oxide (NO) and tumour necrosis factor alpha (TNF-α) in a dose-dependent manner in an activated macrophage-like cell line, RAW 264.7 cells (Park et al. 2005). Aqueous fraction of *L. japonica* (10, 100 and 1,000 μg/ml) dose dependently inhibited TNF-alpha secretion (Kang et al. 2004). The extract at similar doses also inhibited TNF-alpha and tryptase mRNA expression in trypsin-stimulated human mast cell -1. Further, the extract inhibited trypsin-induced ERK phosphorylation. The results indicated that *L. japonica* may inhibit trypsin-induced mast cell activation through the inhibition of ERK phosphorylation than the inhibition of trypsin activity.

Ochnaflavone, isolated from *Lonicera japonica*, was found to dose dependently inhibit cyclooxygenase-2 (COX-2)-dependent phases of prostaglandin D2 (PGD2) generation in bone marrow-derived mast cells (BMMC) with IC_{50} values of 0.6 μM (Son et al. 2006). The decrease in quantity of the PGD2 product was accompanied by a decrease in the COX-2 protein level. Additionally, ochnaflavone consistently and dose dependently inhibited the production of leukotriene C4 (LTC4), with an IC_{50} value of 6.56 μM and degranulation reaction, with an IC_{50} value of

3.01 μM. The results demonstrated that ochnaflavone had a dual cyclooxygenase-2/5-lipoxygenase inhibitory activity and might provide a basis for novel antiinflammatory drugs. In another study, ochnaflavone (isolated from *Lonicera japonica*) treatment dose-dependently inhibited the production of nitric oxide and also blocked the lipopolysaccharide (LPS)-induced expression of iNOS lipopolysaccharide in RAW264.7 cells (Suh et al. 2006a). The inhibition of LPS-induced NO formation by ochnaflavone was mediated by ERK1/2 via NF-kappaB inhibition, which may be the mechanistic basis for the antiinflammatory effects of ochnaflavone. Boiled aqueous honeysuckle flower extracts directly inhibited both COX-1 and COX-2 activity, while non-boiled extracts stimulated COX-1 (Xu et al. 2007). Boiled extracts also inhibited expression of IL-1beta-induced COX-2 protein expression and suppressed its mRNA induction by IL-1beta in A549 cells. The findings suggested that direct inhibition of COX isoenzymes as well as downregulation of COX-2 mRNA and protein may represent the mechanism by which honeysuckle flower treatment decreased inflammation.

Luteolin, a major flavonoid of *Lonicera japonica*, was found to suppress TNF-alpha-induced IL-8 production in dose-dependent manner in human colonic epithelial cells HT29 cells (Kim et al. 2005). Further, luteolin inhibited TNF-alpha-induced phosphorylation of p38 MAPK and extracellular-regulated kinases (ERK), IkappaB degradation and NF-kappaB activation. The results suggested that luteolin elicited inhibitory effects on TNF-alpha-induced IL-8 production in the intestinal epithelial cells through blockade in the phosphorylation of MAPKs, following IkappaB degradation and NF-kappaB activation. Of 13 phenolic compounds isolated from the flower bud, only luteolin showed significant inhibitory activity against 5-lipoxygenase-catalyzed leukotriene production (Lee et al. 2010a). Luteolin, flavonoid from honeysuckle flowers, significantly inhibited the induction of inflammatory cytokines such as tumour necrosis factor (TNF)-alpha, interleukin (IL)-8, IL-6 and granulocyte-macrophage colony-stimulating factor (GM-CSF) induced by phorbol 12-myristate 13-acetate (PMA) plus A23187-induced mast cell activation (Kang et al. 2010b). Additionally, luteolin attenuated cyclooxygenase (COX)-2 expression and intracellular Ca2+ levels. In activated HMC-1 (human mast cell) cells, the phosphorylation of extracellular signal response kinase (ERK 1/2) and c-jun N-terminal kinase (JNK 1/2), but not p38 mitogen-activated protein kinase (p38 MAPK), were decreased by treatment of the cells with luteolin. Luteolin inhibited PMA plus A23187-induced nuclear factor (NF)-kappaB activation, IkappaB degradation and luciferase activity and suppressed the expression of TNF-alpha, IL-8, IL-6, GM-CSF and COX-2 through a decrease in the intracellular Ca2+ levels. Luteolin also suppressed ERK 1/2, JNK 1/2 and NF-kappaB activation. The results indicated that luteolin from honeysuckle flowers exerted a regulatory effect on mast cell-mediated inflammatory diseases, such as rheumatoid arthritis, allergy disease and inflammatory bowel disease.

The removal of tannin and saponin from *L. japonica* extract resulted in loganin- and sweroside-enriched *L. japonica* extract that showed reduced haemolysis and protein precipitation (Ryu et al. 2010). In efficacy tests, the enriched extract inhibited croton oil- and arachidonic acid-induced ear oedema, acetic acid-induced writhing and carrageenan-induced rat hind-paw hyperalgesia. Inhibition of cyclooxygenase-2, inducible nitric oxide synthase and 5-lipoxygenase activities by the enriched tannin- and saponin-free extract appeared to be the mechanism underlying antiinflammatory and analgesic efficacy. Loganin and sweroside also showed antiinflammatory and analgesic activities, suggesting that they might be active principles in the efficacy of the enriched extract.

Lonicera japonica fermented with *Lactobacillus casei* was found to exert a protective effect against lipopolysaccharide (LPS) induced lung inflammation into Balb/c mice (Lee et al. 2011b). In mice treated with the fermented extract, neutrophil influx, total neutrophil number, TNF-α and IL-6 levels in BAL fluid were significantly reduced compared to the LPS group.

The data suggested that fermented *L. japonica* may afford a novel therapeutic agent for lung inflammation and in particular for chronic obstructive pulmonary disease. Administration of water extract of *L. japonica* flowers to mice with dextran sulphate sodium-induced colitis elicited dose-dependent inhibitory effects against colon shortening, weight loss and histological damage (Park et al. 2012c). The extract downregulated interleukin IL-1β, tumour necrosis factor alpha (TNF-α), interferon-γ, IL-6, IL-12 and IL-17. However, the extract did not show any significant effects on IL-10, IL-23, transforming growth factor-β1 and regulatory T (Treg) cell populations. The authors concluded that *L. japonica* flower extract showed protective effects against dextran sulphate sodium-induced colitis via the helper T (Th1/Th17) pathway and not via Treg cell-related mechanisms. Studies showed that that polyphenol components isolated from Korea *L. japonica* exhibited antiinflammatory effect on lipopolysaccharide (LPS)-stimulated RAW 264.7 cells through the decrease of proinflammatory mediators tumour necrosis factor alpha, interleukin- (IL-) 1β and IL-6 expression by suppressing NF-κB and p38 MAPK activity (Park et al. 2012b).

WIN-34B, an herbal formula comprising *Lonicera japonica* dried flowers and *Anemarrhena asphodeloides* dried roots, exhibited better antiinflammatory activity than that of celecoxib in carrageenan-induced paw oedema at the dose of 200 mg/kg and croton oil-induced paw oedema and ear oedema at the doses of 200 and 400 mg/kg (Kang et al. 2010a). WIN-34B exhibited significant antiinflammatory effects on vascular permeability. WIN-34B also exhibited significant antinociceptive activities in the late phase of formalin-induced paw licking and writhing response model in mice. In radiant heat tail-flick and carrageenan-induced paw pressure tests, WIN-34B at the dose of 400 mg/kg and at the doses of 200 and 400 mg/kg presented similar activities to indomethacin and celecoxib. Compared to indomethacin, WIN-34B at 400 mg/kg showed similar or better antinociceptive activities after 1 and 2 hours of therapy in the hot-plate test and better antinociceptive activity than that of celecoxib in Hargreaves test. In the MIA-induced osteoarthritis animal models, WIN-34B at 400 mg/kg exhibited similar or better antinociceptive property than that of celecoxib throughout the pain measurement periods. In another study, WIN-34B, an herbal medicine of *L. japonica* dried flowers and *Anemarrhena asphodeloides* dried roots, significantly inhibited the IL-1β-induced cell viability in human osteoarthritis fibroblast-like synoviocytes without cytotoxicity (Huh et al. 2012). Compared to celecoxib, WIN-34B exhibited similar or better antiinflammatory effects through significant suppression of inflammatory mediators (IL-1β, TNF-α, PGE2 and NO), MMPs (MMP-1, MMP-3 and MMP-13) and aggrecanases (ADAMTS-4 and ADAMTS-5) and enhancement of TIMPs (TIMP-1 and TIMP-3). Moreover, WIN-34B reduced the phosphorylation of IκB-α, ERK1/2, p38 and JNK1/2 in IL-1β-stimulated human osteoarthritis fibroblast-like synoviocytes.

Pleuroprotective Activity

Pretreatment of Balb/c mice with *L. japonica* flower extract was found to have a protective effects against lipopolysaccharide (LPS)-induced lung inflammation which resembled a chronic obstructive pulmonary disease (Lee et al. 2011a). At 3 days after LPS stimulation, in-vivo study demonstrated that the influx of neutrophils and total cells were decreased significantly in *Lonicera* pretreated group compared to LPS only treated group. In addition, TNF-α and IL-6 levels in bronchoalveolar lavage (BAL) fluid were decreased in *Lonicera* pretreated group. The histological results demonstrated that *Lonicera* attenuated the LPS-induced lung inflammation and the expression of neutrophil elastase was decreased in *Lonicera* pretreated group.

Luteolin, the major polyphenolic component of *Lonicera japonica*, was found to have beneficial effects against lipopolysaccharide (LPS)-induced acute lung injury in mice (Lee et al. 2010b). The attenuation of neutrophil chemotaxis and respiratory burst by luteolin involved inhibition of MAPK/ERK kinase 1/2 (MEK),

extracellular signal-regulated kinase (ERK) and Akt phosphorylation signalling cascades. Another study showed luteolin, an active flavonoid compound isolated from *Lonicera japonica*, had potent antifibrotic activity; this effect was mediated, at least in part, by inhibition of lung inflammation as evidenced by suppression of neutrophil infiltration as well as TNF-α and interleukin IL-6 elevation in the bronchoalveolar lavage fluid in bleomycin-instilled C57BL/6J mice and suppression of TGF-β1-induced α-SMA, type I collagen and vimentin expression in primary cultured mouse lung fibroblasts as well as epithelial to mesenchymal transition (Chen et al. 2010a).

Gastroprotective Activity

The dried flowers of *Lonicera japonica* and the dried root of *Anemarrhena asphodeloides*, component herbs of WIN-34B, are traditionally used in eastern medicine to treat various inflammatory conditions including arthritis (Huh et al. 2011). Their studies showed that WIN-34B did not cause acute or chronic toxicity in male or female rats. In addition, WIN-34B did not cause significant gastric mucosal damage, instead appearing to protect the mucosa from diclofenac-induced gastric damage by reducing the production of prostaglandin E(2) and leukotriene B(4).

Antiangiogenic, Antinociceptive Activity

The ethanol flower extract of *L. japonica* dose-dependently inhibited chick chorioallantoic membrane angiogenesis (Yoo et al. 2008). The antinociceptive activity of the extract was determined using the acetic acid-induced constriction model in mice. The extract showed antiinflammatory activity in two in-vivo models: the vascular permeability and air pouch models. The extract suppressed the production of nitric oxide via downregulation of inducible nitric oxide synthase in lipopolysaccharide-stimulated RAW264.7 macrophage cells. The results showed that the flowers *of L. japonica* possessed potent antiangiogenic and antinociceptive activities, in addition to antiinflammatory activity.

Anticancer Activity

The floral absolute volatiles of the flowers showed appreciable cytotoxic activity on the brain cancer cell line U251 (IC_{50} value of 7.92 μg/ml) and were found to be more potent than cisplatin reference drug (IC_{50} = 8.66 μg/ml) (El-Kashoury et al. 2007). Meanwhile, the flower volatiles prepared by hydrodistillation/hexane extraction showed notable cytotoxic activity on the liver cancer cell line HepG2 with IC_{50} value of 7.58 μg/ml.

Protocatechuic acid, chlorogenic acid and luteolin from *Lonicera japonica* effectively killed the HepG2 hepatocellular carcinoma cells at 100 μmol/L (Yip et al. 2006). Among these three naturally occurring phenolic compounds, only protocatechuic acid was capable of stimulating the c-Jun N-terminal kinase (JNK) and p38 subgroups of the mitogen-activated protein kinase (MAPK) family. In addition, the aqueous extract of *Lonicera japonica* also triggered HepG2 cell death in a JNK-dependent manner, but the amount of protocatechuic acid alone in this herbal extract was insufficient to contribute to the subsequent cytotoxic effect.

Luteolin (3′,4′,5,7-tetrahydroxyflavone), active compound from *L. japonica*, was found to induce human lung carcinoma CH27 cell apoptosis by caspase-dependent and caspase-independent pathway, and the effect of luteolin on apoptosis of CH27 cells was associated with DNA damage and the expression of DNA repair enzyme (Leung et al. 2005). They found that luteolin-induced CH27 cell apoptosis was accompanied by activation of antioxidant enzymes, such as superoxide dismutase and catalase, but not through the production of reactive oxygen species and disruption of mitochondrial membrane potential (Leung et al. 2006). Therefore, the effects of luteolin on CH27 cell apoptosis were suspected to result from the antioxidant rather than the prooxidant action of luteolin. Leung et al. (2008) also showed

that photodynamic therapy with alcohol extract from *Lonicera japonica* as photosensitizer exhibited significant photocytotoxicity in lung CH27 carcinoma cells at a concentration range of 50–150 βg/ml, with 0.4–1.2 J/cm^2 light dose. This action was found to be mediated via P38-associated pathway. They found that photodynamic therapy with *L. japonica* extract-induced CH27 cells apoptosis was probably related to its ability to change the protein expression and distribution of heat shock protein 27.

The biflavones isolated from *L. japonica* stems exhibited in-vitro anticancer activity (Pradhan et al. 2009). The results show significant activities, particularly for 7,7″-dimethyllanaraflavone (IC_{50} values of 1.77, 3.42 and 3.59 mg/ml for NCl-H460, non-small cell lung carcinoma; MCF-7 breast; and OVCAR-3, ovarian adenocarcinoma cells, respectively), but low activity against HT-29 colon adenocarcinoma and RXF-393 renal cell carcinoma. In contrast, 7″-methylagathisflavone showed good inhibitory against all five cancer cell lines with IC_{50} values of 4 mg/ml. Polyphenolic extract from *L. japonica* dose-dependently inhibited hepatocarcinoma HepG2 cell proliferation at 48 hours (Park et al. 2012a). The polyphenolic extract affected HepG2 cell viability by inhibiting cell-cycle progression at the G2/M transition and inducing apoptosis. The extract also decreased the expression of CDK1, CDC25C, cyclin B1, pro-caspases-3 and pro-caspases-9 and poly (ADP-ribose) polymerase and affected the levels of mitochondrial apoptotic-related proteins. The results indicated that inhibition of PI3K/Akt and activation of MAPKs were pivotal in G2/M cell-cycle arrest and apoptosis of human hepatocarcinoma cells mediated by the polyphenolic extract.

Antiplatelet Aggregation Activity

Polyphenolic compounds isolated from *Lonicera japonica*, namely, methyl caffeate, 3,4-di-*O*-caffeoylquinic acid and methyl 3,4-di-*O*-caffeoylquinate, exhibited potent inhibitory effect on human platelet aggregation (Chang and Hsu 1992). They significantly inhibited the second wave of platelet aggregation induced by ADP. Regarding thromboxane biosynthesis triggered by calcium ionophore A23187 in platelets, methyl caffeate and methyl 3,4-di-*O-caffeoylquinate* elicited the most potent inhibitory effect. Methyl 3,4-di-*O*-caffeoylquinate directly inhibited the conversion of arachidonic acid to thromboxane by platelet microsomes, while methyl caffeate did not have any significant effect on thromboxane biosynthesis in platelet microsomes. In the prevention of hydrogen peroxide-induced endothelial cell injury in culture, protocatechuic acid, methyl caffeate, methyl chlorogenic acid and luteolin were significantly effective. The inhibitory effect on platelet activation and the cytoprotective effect on hydrogen peroxide-induced cell injury may explain the possible role of polyphenolic compounds isolated from *L. japonica* in maintaining vascular homeostasis. Ochnaflavone, isolated from *Lonicera japonica*, strongly and non-competitively inhibited rat platelet phospholipase A2 (IC_{50} about 3 μM) (Chang et al. 1994). Inactivation was concentration and pH dependent (maximum inactivation occurred between pH 9.0 and 10.0). The inhibitory activity of ochnaflavone was rather specific against group II phospholipase A2 than group I phospholipase A2 (IC_{50} about 20 μM).

Lonijaposide C, a pyridinium alkaloid-coupled secoiridoid from the flower bud, exhibited activity against the release of glucuronidase in rat polymorphonuclear leukocytes induced by the platelet-activating factor (Song et al. 2008). Loniphenyruviridosides A–D, homosecoiridoids from *L. japonica* flower buds, inhibited STAT-3 (signal transducer and activator of transcription-3) activity of HELF (human embryonic lung fibroblasts) cells, while lonijaposides F, H, I and K showed activity against the release of glucuronidase in rat polymorphonuclear leukocytes induced by platelet-activating factor (Yu et al. 2011).

Antipyretic Activity

Studies showed that intravenous injection of *Lonicera japonica* extract elicited antipyretic effects on interleukin-1β(IL-I β)-induced thermogenesis

in febrile rabbits and acted by inhibiting expression of E-type prostaglandin receptor-3 (EP3) mRNA in the preoptic anterior hypothalamus of rabbits (Dong et al. 2008).

Immunomodulatory Activity

L. japonica flower was one of 26 Chinese medicinal herbs that was found active in promoting blood neutrophil activity and increasing neutrophil phagocytosis by over 35 % (Hu et al. 1992).

Haemolytic Activity

Among the 12 saponins isolated from the aerial parts, monodesmosides 1–4 showed strong haemolytic activity, but bisdesmosides 5–12 showed weak haemolytic activity; saponin 5 and 6 with an arabinosyl moiety at C-3 and a gentiobiosyl moiety at C-28 showed no haemolytic activity (Kawai et al. 1988b).

Hepatoprotective Activity

Several iridoid glycosides, loganin, 7-epi-loganin and secoxyloganin, isolated from honeysuckle flower buds were found to possess hepatoprotective activity (Li and Li 2005). Sweroside, an active ingredient of iridoid glycoside isolated *Lonicera japonica* flower buds, was reported to have strong hepatoprotective effect (Luo et al. 2009). After intravenous administration of sweroside, the percentage of accumulation of free form sweroside in bile duct was 31.2 % of the total dosage. The oral bioavailabilities of sweroside and the active ingredients of purified herbal extracts (IGEs-1) was estimated to F(sweroside) 0.31 % and F(IGEs-1) 0.67 %. The majority of sweroside excreted to faeces revealed one reason of the low oral bioavailability. The much higher value of F(IGEs-1) much higher than that of F(sweroside) revealed that ingredients in IGEs-1 such as loganin, secoxyloganin and some phenolic acids may promote the absorption of sweroside. Metabonomics studies by Sun et al. (2010) showed that *L. japonica* extract had a protective effect in acute liver injury induced by dimethylnitrosamine in male Wistar rats.

Antiatherogenic Activity

Ochnaflavone, isolated from *L. japonica*, was found to inhibit dose-dependently tumour necrosis factor (TNF)-alpha-induced matrix metalloproteinase-9 (MMP-9) gene expression in human aortic smooth muscle cells (HASMC) (Suh et al. 2006b). These inhibitory effects were associated with reduced extracellular signal-regulated kinase 1/2 (ERK1/2) activity and G1 cell-cycle arrest. These findings indicated the efficacy of ochnaflavone in inhibiting cell proliferation, G1- to S-phase cell-cycle progress and MMP-9 expression through the transcription factors NF-kappaB and AP-1 on TNF-alpha-induced HASMC and thus elucidating the mechanism of the antiatherogenic activity of ochnaflavone.

Antiallergic Activity

The ethanol extract (35 %) of *L. japonica* buds was found to have allergy-preventive activity (Oku et al. 2011). Bioassay-guided fractionation of the 35 % EtOH extract led to isolation of chlorogenic acid (1) and three known iridoid derivatives, loganin (2), secoxyloganin (3) and sweroside (4), all of which inhibited the blood flow decrease in the tail vein of mice subjected to sensitization with hen egg-white lysozyme. The structure–activity relationship of iridoid derivatives, morroniside (5), geniposide (6), asperuloside (7), aucubin (8) and catalpol (9), was also tested using the same bioassay method. Compounds 2–5 and 9 having the sp(3) atom at C-8 showed an allergy-preventive effect, while compounds 6, 7 and 8 having a double bond at C-7 and C-8 did not.

Antibacterial Activity

The essential oil from the flowers and ethanol leaf extracts revealed a remarkable antibacterial effect against *Listeria monocytogenes, Bacillus*

subtilis, Bacillus cereus, Staphylococcus aureus, Salmonella enteritidis, Salmonella typhimurium, Enterobacter aerogenes and *Escherichia coli*. However, no effect was observed for *Pseudomonas aeruginosa* and *E. coli* O157:H7 (Rahman and Kang 2009). Ethanol leaf extract and its chloroform subfraction showed higher antibacterial activity by minimum inhibitory concentrations than did hexane and ethyl acetate subfractions. The butanol extract of *Lonicera japonica* was compared to other antimicrobial agents cefoxitin, imipenem, clindamycin and metronidazole for activity in-vitro against 104 clinical isolates of anaerobic bacteria (Rhee and Lee 2011). *L. japonica* extract and imipenem were the most active against *Bacteroides fragilis, Bacteroides ovatus, Clostridium difficile, Clostridium perfringens, Propionibacterium acnes* and Peptostreptococci. The ethanol extract of *L. japonica* flowering aerial parts exhibited significant antimicrobial activity in-vitro against *Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Candida albicans* and *Candida tropicalis* (Chen et al. 2012).

Antiviral Activity

Tannins such as caffeoylquinates (CQs) isolated from *Lonicera japonica* were shown to have selective inhibitory effect on HIV-1 reverse transcriptase (Chang et al. 1995). Kang Er Xin-I (KEX-I) a Chinese herbal recipe consisting of *Lonicera japonica, Ophiopogon japonicus* and *Astragalus membranaceus* had been proven useful to treat viral myocarditis (Yan 1991). In a random, paired and crossover design, after being treated with KEX-I for 2 weeks, the 26 patients' chief cardiac functional indexes assessed with systolic time intervals (STI) improved markedly. KEX-I was found to inactivate directly the virus of Coxsackie B3, protect the heart cells in mice, prevent attack by Coxsackie B3 virus, promote the growth of internal interferon and increase the NK cell's function to regulate immunity in the experimental mice. Thirteen caffeoylquinic acids, caffeic acid and caffeic acid methyl ester isolated from honeysuckle flowers showed antiviral activities against respiratory viruses (Ma et al. 2005). A novel cyclic peroxide, shuangkangsu, isolated from the buds showed significant antiviral activities against influenza virus in chicken embryo and respiratory syncytial virus in cells (Yu et al. 2008).

Lonicera japonica flower extracts were found to have anti-influenza virus activity (Shi and Guo 2010). The most active ingredients were from the petroleum and ethanol extract which were more effective with a lower EC_{50} value than ribavirin. Twelve functional protein components were determined in the anti-influenza virus serum marker of *L. japonica* using proteomics technology (Zhang et al. 2011).

Tyrosinase Inhibition Activity

The methanol and acetone extracts from *L. japonica* showed an inhibition effect against tyrosinase, xanthine oxidase and nitrite scavenging ability (Byun et al. 2004a, b). Tyrosinase inhibition effect of *L. japonica* was higher in the irradiated sample than the nonirradiated, and the effect was increased by irradiation doses. The high inhibitory effect against xanthine oxidase was not changed by irradiation. Nitrite scavenging activity was the highest in *L. japonica* extract at pH 1.2. The ethanol extracts of various aerial parts exerted significant tyrosinase inhibitory activity with IC_{50} values ranging from 11.16 to 17.18 μg/ml (Dung et al. 2011). The ethanol flower extract displayed the highest test activities as compared with the other extracts. The results indicated that *L. japonica* could be used as an active ingredient for antioxidant and natural skin-whitening agent in cosmetic products.

Neuroprotective Activity

Studies demonstrated that *Lonicera japonica* extract possessed potent neuroprotective activity in human SH-SY5Y neuroblastoma cells (Kwon et al. 2011). *L. japonica* extract elicited radical scavenging ability in 2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2-azinobis-(3-ethyl-benzthiazo-

line-6-sulfonic acid) (ABTS) assays and inhibited H(2)O(2)-induced up- and downregulation of cleaved PARP, cleaved caspase-3, Bcl-2 and Bcl-xL. Furthermore, the extract significantly attenuated the H(2)O(2)-induced phosphorylation of Akt, JNK, p38 MAPK and ERK1/2. They also found that *L. japonica* extract significantly increased cell viability decrease, lactate dehydrogenase release (LDH), morphological changes, nuclear condensation, fragmentation and reactive oxygen species (ROS) production induced by 6-hydroxydopamine (6-OHDA) in human SH-SY5Y neuroblastoma cells (Kwon et al. 2012). The cytoprotection afforded by pretreatment with the extract was associated with increases of the glutathione (GSH) level, superoxide dismutase (SOD) activity and catalase (CAT) activity in 6-OHDA-induced SH-SY5Y cells. In addition, the extract strongly inhibited 6-OHDA-induced mitochondrial dysfunctions including reduction of mitochondria membrane potential (MMP) and activation of cleaved poly (ADP-ribose) polymerase (PARP), cleaved caspase-3, cleaved caspase-9, increased Bax, as well as decreased Bcl-2 and Bcl-xL. These findings suggested that the extract had a potent anti-parkinsonism; this effect was mediated, at least in part, by inhibition of neurotoxicity, apoptotic cascade events and oxidative stress via activation of MAPKs, PI3K/Akt and NF-κB. The methanol extract of *L. japonica* flower significantly protected neuronal cells against glutamate-induced excitotoxicity via antioxidative activity by inhibiting the subsequent overproduction of nitric oxide, reactive oxygen species and peroxide to the level of control cells (Weon et al. 2011).

Cardioprotective Activity

Rutin, isolated from *L. japonica*, was found to reduce oxidative stress-mediated myocardial damage in-vitro model and in-vivo model, which might be useful in treatment of myocardial infarction (Jeong et al. 2009). Treatment with rutin decreased expression of both cleaved form of caspase-3 and increased Bcl-2/Bax ratio in H9c2 cells which were decreased by hydrogen peroxide. Further, rutin improved ischaemia/reperfusion (IR)-induced myocardial contractile function and reduced infarct size. Rutin administration also inhibited apoptosis in myocardial tissues in I/R rats by increasing Bcl-2/Bax ratio and decreasing active caspase-3 expression.

Wound Healing Activity

The ointment formulation prepared with 10 % (w/w) flowering *L. japonica* ethanol extract exhibited potent wound healing capacity as evidenced by the wound contraction in the excision wound model (Chen et al. 2012). The contents of hydroxyproline and hexosamine also correlated with the observed healing pattern. These findings were supported by the histopathological characteristics of healed wound sections, as greater tissue regeneration, more fibroblasts and angiogenesis were observed in the 10 % (w/w) *L. japonica* ointment-treated group. The results also indicated that the extract possessed potent antiinflammatory activity, as it enhanced the production of antiinflammatory cytokines that suppress proinflammatory cytokine production.

Hypoglycaemic Activity

The ethyl acetate fraction of the methanol extract of *Lonicera japonica* flower inhibited porcine pancreatic alpha-amylase activity in a dose-dependent manner, with an IC_{50} of 0.2 mg/ml. The ethyl acetate fraction also significantly inhibited both intestinal sucrase and isomaltase activities at a concentration of 0.5 mg/ml (Kwon et al. 2004).

Growth Hormone Induction Activity

Methanol extract of the flowers was found to increase induction of rat growth hormone to 732.65 % in the pituitary cell culture system (Jung et al. 2003). Ochnaflavone, a constituent from honeysuckle leaf, also increased growth hormone to 329.73 % in the pituitary cell culture system.

Toxicity/Safety Studies

Acute and subacute toxicity study of the ethanol leaf extract of *Lonicera japonica* at 5,000 mg/kg did not produce mortality or significant changes in the general behaviour and gross appearance of the internal organs of rats (Thanabhorn et al. 2006). There were no significant differences in the body and organ weights between the control and the treated group of both sexes. Haematological analysis and clinical blood chemistry revealed no toxicity effects of the extract. Pathologically, neither gross abnormalities nor histopathological changes were observed.

Challenge tests were performed according to the European Pharmacopoeia procedures and criteria for various cosmetic formulations containing antimicrobial extracts of *Lonicera caprifolium* and *Lonicera japonica* alone or in combination with glyceryl caprylate and/or levulinic acid, *p*-anisic acid and ethanol (Papageorgiou et al. 2010). Formulations such as shampoo, shower gel and conditioning cream fulfilled criterion A, while tonic lotion, anticellulite cream, cleansing milk and peeling cream fulfilled criterion B, in regard to contamination from *A. niger*. The addition of antimicrobial fragrance ingredients such (< or = 0.3 % w/w) levulinic acid or (0.1 % w/w) *p*-anisic acid and/or (5 % w/w) ethanol afforded products that met criterion A in challenge tests and were also microbiologically safe during use. The small quantity (5 % w/w) of ethanol afforded an important assistance in order to boost the self-preserving system and to produce stable and safe products.

Allergy Problem

A case of linear itchy raised blisters on the wrist of a patient that pulled Japanese honeysuckle (*Lonicera japonica)* was reported by Webster (1993).

Traditional Medicinal Uses

Lonicera japonica, a widely used traditional Chinese medicine, is taken to treat the exopathogenic wind-heat, epidemic febrile diseases, sores, carbuncles and some infectious diseases (Shang et al. 2011). Honeysuckle is used in Chinese medicine to address what are called excess heat conditions such as fevers, skin rashes and sore throat associated with inflammatory processes involving heat, redness, pain and swelling often due to external pathogenic factors such as bacteria and viruses (Yeung 1985). Also, according to traditional Chinese medicine, honeysuckle is contraindicated for patients with medical conditions that are diagnosed as deficient and cold in nature unless combined with other herbs to balance the cold temperature property of honeysuckle. The plant is also used to reduce blood pressure (Yeung 1985; Bown 1995). Honeysuckle dispels heat and detoxicates and is good for treating carbuncles, skin swelling, rheumatoid arthritis, hepatitis, scrofula, dysentery and haemorrhoids (Peng et al. 2000; Lu 2005). Dried flower buds of *Lonicera japonica* is one of the most widely used traditional Chinese medicines (TCMs) and recorded in China Pharmacopoeia with the Chinese name Jin Yin Hua for the treatment of acute fever, headache, pharyngodynia, respiratory infection, pyocutaneous disease and epidemic disease (Qian et al. 2008). In Malaysia, the Chinese import the flowers for use medicinally for their antifebrile and astringent properties (Burkill 1966). An infusion of the flower buds is used in the treatment of a wide range of ailments including syphilitic skin diseases, tumours, bacterial dysentery, colds, enteritis, pain and swellings (Yeung 1985; Duke and Ayensu 1985; Foster and Duke 1998; Bown 1995). Honeysuckle flower buds and stems are alterative, antibacterial, antiinflammatory, antispasmodic, depurative, diuretic and febrifuge (Yeung 1985; Bown 1995). Externally, the flowers are applied as a wash to skin inflammations, infectious rashes and sores, and the stems are used internally in the treatment of acute rheumatoid arthritis, mumps and hepatitis (Bown 1995). *Lonicera japonica* and *Anemarrhena asphodeloides* components of an herbal formula WIN-34B have been used for the treatment of a variety of inflammatory diseases, arthritis, cold

and infective diseases in many countries, including Korea and China (Kang et al. 2010a; Huh et al. 2011).

Other Uses

A very vigorous climbing plant, it makes a good dense ornamental ground cover plant. In both its native and introduced range, Japanese honeysuckle can be a significant source of food for deer, rabbits, hummingbirds and other wildlife. The bark is tough and can be used for plaiting.

The essential oil from the flower buds has insecticidal property and was found to be toxic to storage insects. The essential oil exhibited strong contact toxicity against maize weevil *Sitophilus zeamais* and book louse *Liposcelis bostrychophila* with LD_{50} values of 21.54 μg/adult and 64.04 μg/cm^2, respectively (Zhou et al. 2012). The constituent compounds, estragole (LD_{50} = 49.95 μg/cm^2) and linalool (LC_{50} = 172.54 μg/cm^2), also possessed contact toxicity against *L. bostrychophila*. *L. japonica* essential oil and its constituent compounds (estragole and linalool) exhibited fumigant toxicity against *S. zeamais* with LC_{50} values of 13.36, 14.10 and 10.46 mg/L, respectively. The essential oil of *L. japonica* (LC_{50} = 0.20 mg/L) and its constituent compounds, estragole (LC_{50} = 0.16 mg/L) and linalool (LC_{50} = 0.41 mg/L), also elicited fumigant toxicity against *L. bostrychophila*.

Comments

In the United States, Japanese honeysuckle is classified as a noxious weed in Texas, Illinois and Virginia and is banned in New Hampshire (Miller 2003). It is listed on the New Zealand National Pest Plant Accord as an unwanted organism (NBII and ISSG 2005). It is regarded as an environmental weed in Queensland, New South Wales, the ACT, Victoria, Tasmania, South Australia and Western Australia (Anonymous 2006; Blood 2001).

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Dianthus barbatus

Scientific Name

***Dianthus barbatus* L.**

Synonyms

Caryophyllus barbatus Moench, *Cylichnanthus barbatus* Dulac, *Dianthus aggregatus* Poir, *Dianthus corymbosus* F. Dietr., *Dianthus girardini* Lamotte, *Dianthus hispanicus* Dum Cours. nom. illeg., *Dianthus latifolius* Willd., *Dianthus pulcherrimus* Loisel., *Dianthus splendidissimus* Hoffmanns.

Family

Caryophyllaceae

Common/English Names

Carnation, Pink, Sweet William

Vernacular Names

Burmese: Mani Soythu Pan
Chinese: Tou Shi Zhu
Czech: Hvozdík Bradatý, Hvozdík Vousatý
Danish: Busk Nellike, Studenter-Nellike
Dutch: Duizendschoon
Estonian: Habenelk
Esperanto: Dianto Barba
Finnish: Harjaneilikka
French: Oeillet Barbu, Oeillet Des Poètes
German: Bart-Nelke, Busch-Nelke
Icelandic: Busknellik
Italian: Garofano Montano
Japanese: Amerika-Nadeshiko, Hosoba-Hige-Nadeshiko
Norwegian: Busknellik
Polish: Goździk Brodaty
Slovaščina: Brkati Nageljček, Klinček Brkati, Nageljček, Sorta
Slovencina: Klinček Bradatý
Spanish: Clavel Imperial
Swedish: Borstnejlika
Turkey: Hüsnüyusuf
Welsh: Penigan Barfog

Origin/Distribution

The species is found in the mountains of southern Europe from the Pyrenees East to the Carpathians and the Balkans, with a variety disjunct in northeastern China, Korea and southeastern-most Russia (Lu and Turland 2001; Flora Europaea 2013).

Agroecology

Sweet William is a cool climate species. It prefers a rich, well-drained loamy, mildly alkaline soil in a sunny position but succeeds in most soils

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including moderately dry soil and partial shade. It is propagated from seeds, cuttings or division, but seeds of cultivars will not breed true.

Edible Plant Parts and Uses

The flowers are edible, have a mild flavour and are used as a garnish for vegetable and fruit salads, cakes, desserts, cold drinks, tea and sorbet (Facciola 1990; Barash 1993; Brown 2011). The petals of Sweet William will add zest to ice cream, sorbets, salads, fruit salad, dessert sauces, seafood and stir-fries.

Botany

An herbaceous short-lived perennial, 30–60 cm tall with erect angular stems. Leaves green to glaucous, lanceolate 4–10 cm by 1–2 cm wide, apex acute, base tapering (Plates 1 and 2). Flowers (2–3.5 cm across) numerous produced in clusters at the top of the stem; bracts 4 almost as long as calyx tube, with membranous, ciliate margins; calyx tubular with acute teeth; petals 5 pink to red or purplish with a white base or variegated (Plates 1 and 2), limb ovate, bearded and apex dentate; stamens slightly exserted, ovary suboblong to ovoid, style linear. Capsule suboblong to ovoid, 4 valved, 1 cm across with smooth, compressed, brown ovoid seeds.

Plate 1 Purple-white variegated flowers and lanceolate leaves

Plate 2 Red-white, variegated and pink flowers and lanceolate leaves

Nutritive/Medicinal Properties

Plant Phytochemicals

Two saponins (barbatosides A and B) were isolated from the aerial parts of *Dianthus barbatus* cv. 'China Doll'; the aglycone of each saponin was identified as quillaic acid (Cordell et al. 1977). The glycone of barbatoside A consisted of rhamnose, arabinose, fucose, xylose, galactose, glucose and one unidentified sugar, whereas the glycone of barbatoside B contained arabinose, fucose, xylose, mannose, galactose, glucose and three unidentified sugars. Astragalin, kaempferol-3-*O*-β-D-sophoroside, D-pinitol and L-leucine were also isolated.

The floral scent volatiles of *D. barbatus* were characterized by the predominance of two compounds n-nonanal (14.7 %) and the sesquiterpene β-caryophyllene (10.3 %) (Jürgens et al. 2003). Other compounds included decanal, 1,2,3-trimethylbenzene, 1-methoxy-4-methylbenzene, hexanal, heptanal, octanal, α-phellandrene, α-pinene, benzaldehyde, β-pinene, *cis*-β-ocimene, linalool, methyl benzoate, *O*-xylene, *p*-cymene, *R*-limonene, sulcatone and (*Z*)-3-hexenyl acetate.

A single-chain ribosome-inactivating protein with RNA *N*-glycosidase activity, designated dianthin 29, was isolated from *Dianthus barbatus* leaves (Prestle et al. 1992). Dianthin 29 was found to inactivate *Escherichia coli* ribosomes.

Two saponins (barbatosides A and B) isolated from the aerial parts of *Dianthus barbatus* cv. 'China Doll' exhibited analgesic and antiinflammatory activities (Cordell et al. 1977).

Other Uses

Sweet William is a popular ornamental plant in gardens, planted in pots, flats or in beds. The plant produces nectar that attracts birds, bees, moths and butterflies.

Comments

Two varieties have been recognized:

- *Dianthus barbatus* var. *barbatus*. Southern Europe. Leaves broader, up to 2 cm broad
- *Dianthus barbatus* var. *asiaticus* Nakai. Northeastern Asia. Leaves slenderer, not over 1 cm broad

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The Plant List (2013) http://www.theplantlist.org/

Dianthus caryophyllus

Scientific Name

***Dianthus caryophyllus* L.**

Synonyms

Caryophyllus tunica Garsault [Invalid], *Dianthus acinifolius* Schur, *Dianthus arbuscula* Lindl., *Dianthus arrectus* Dumort., *Dianthus binatus* Schur, *Dianthus caryophyllus* var. *coronarius* L., *Dianthus coronarius* (L.) Burm.f., *Dianthus corsicus* Link ex Spreng., *Dianthus kayserianus* Schur, *Dianthus longicaulis* Costa, *Dianthus miniatus* A. Huet ex Nyman, *Dianthus morrsii* Hance, *Dianthus moschatus* J.F. Gmel., *Dianthus multinervis* Vis., *Silene caryophylla* E.H.L. Krause, *Tunica caryophyllus* Scop., *Tunica morrisii* (Hance) Walp.

Family

Caryophyllaceae

Common/English Names

Border Carnation, Carnation, Common Carnation, Clove Pink, Dianthus, Divine Flower, Gillyflower, Pinks, Wild Carnation

Vernacular Names

Bohemian: Hvozdik, Vrsta Karanfila
Brazil: Craveiro, Cravo
Burmese: Zaw-Hmwa-Gyi
Catalan: Clavell, Claveller, Clavellina, Clavells, Clavillinera, Clevellina
Chinese: Kang Nai Xin
Corsican: Caròfanu, Gaiofinu, Uchjellu
Czech: Hvozdík Karafiát, Hvozdík Zahradní
Danish: Havenellike
Dutch: Tuinanjelier
Estonian: Šaboonelk
Esperanto: Dianto Ĝardena
Finnish: Tarhaneilikka
French: Oeillet Des Fleuristes, Oeillet Girofle
German: Garten-Nelke, Land-Nelke, Nelke
Hungarian: Kerti Szegfű
Icelandic: Goðadrottning
Indonesia: Bunga Anyelir
Italian: Dianto, Garofano, Garofano Coltivato
Japanese: Oranda-Nadeshiko
Malaysia: Bunga Teluki
Norwegian: Hagenellik
Polish: Goździk Ogrodowy
Portuguese: Craveiro, Cravelinha, Cravina, Cravo, Cravina-Dos-Jardins
Russian: Gvozdika Gollandskaja, Gvozdika Sadovaja
Slovaščina: Vrtni Nageljček
Slovencina: Klinček Záhradný

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Spanish: Clavel, Clavel Canario, Clavel Común, Claveles, Clavelina
Swedish: Trädgårdsnejlika
Turkish: Bahçe Karanfili, Karanfil Familyasından Çiçek
Vietnamese: Cẩm Chướng Thơm, Cẩm Nhung, Hương Nhung Hoa
Welsh: Ceinan Gwyllt, Clows, Penigan Pêr, Penigan Rhuddgoch

Origin/Distribution

Carnation is probably indigenous to the Mediterranean region, but its exact range is unknown due to extensive cultivation for the last 2,000 years.

Agroecology

Carnation is a cool climate crop. Carnation is a heliophilous and a facultative long-day plant. Temperature, light intensity and day length affect carnation growth. Optimum growth has been reported in location of high light intensity during winter and cool temperatures during summers. During summer, the optimum temperature for achieving good plant growth and flowers is between 13 and 15 °C, while during winter a relatively lower temperature 10–11.1 °C is preferred; carnation is not frost tender. Hot dry wind during summer months is very detrimental for the growth and development of plants.

A well-drained, rich sandy-loam or loamy sand soil is considered to be the most ideal for successful production of carnation. Soils with higher amount of clays or silt should be amended by incorporating organic matter or compost. The optimum soil pH is between 6.0 and 7.0.

Edible Plant Parts and Uses

Petals are edible (Facciola 1990; Barash 1993; Creasey 1999; Roberts 2000; Brown 2011; Rop et al. 2012). The flower petals have a strong smell of cloves and are candied and used as a garnish in salads, for flavouring fruit, fruit salads, soups, punch bowl, etc. They can also be used as a substitute for rose petals in making a syrup. The petals should be removed from the calyx, and their bitter white base should be removed.

Botany

An herbaceous perennial plant growing to 50–80 cm tall with erect, branching herbaceous stem that is woody at the base. Leaves are opposite, glaucous, lanceolate to linear lanceolate 10–15 cm long (Plate 1). Flowers solitary or in few-flowered cymes, sweetly scented, bisexual, 3.5–6 cm diameter, single flowers with 5 petals, double flowers with 10–40 petals, peduncle with swollen nodes. Calyx with four leafy ovate bracteoles at the base, gamosepalous, cylindric and five dentate. Petals obovate or broadly cuneate, clawed or serrated, red, purple, orange, pink, white, yellow and green, spotted or variegated (Plates 1, 2, 3 and 4). Stamens 10 in two whorls, ovary one celled, styles two. Capsule with many seeds.

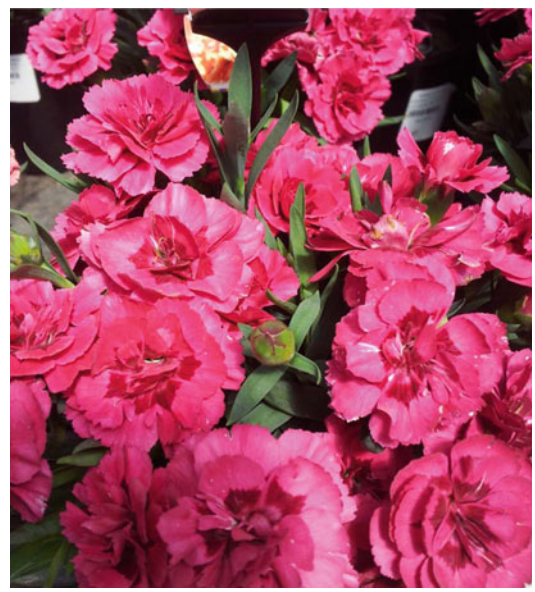

Plate 1 Red carnations and leaves

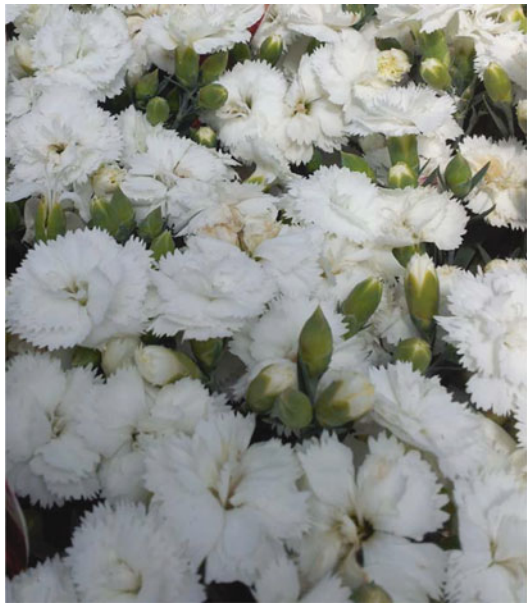

Plate 2 White carnations

Plate 3 Purple carnations cv. Moondust

Plate 4 Variegated carnations

Nutritive/Medicinal Properties

Flower Nutrients and Phytochemicals

Rop et al. (2012) reported that edible flowers of *Dianthus caryophyllus* had a dry matter content (%w/w) of 11.55 %, crude protein of 6.89 g/kg and the following elements (mg/kg fresh mass (FM)): P 531.35 mg, K 3544.81 mg, Ca 491.89 mg, Mg 186.55 mg, Na 114.29 mg, Fe 9.85 mg, Mn 7.49 mg, Cu 2.88 mg, Zn 7.17 mg and Mo 0.55 mg. The flowers had total antioxidant capacity of 6.96 g ascorbic acid equivalents/kg FM, total phenolic content of 5.28 g gallic acid/kg FM and total flavonoid content of 2.27 g rutin/kg FM.

Cytosolic lipid-protein particles containing phospholipid as well as the same fatty acids were found in microsomal membranes of carnation petals (Hudak and Thompson 1997). The lipid-protein particles were also enriched in hexanal, *trans*-2-hexenal, 1-hexanol, 3-hexen-1-ol and 2-hexanol, volatiles of carnation flower fragrance that were derived from membrane fatty acids through the lipoxygenase pathway.

The flower scent volatiles of flowering carnations were differentiated by the proportion of eugenol (trace-84.1 %) and methyl salicylate (0.1–1.4 %) (Clery et al. 1999). Some modern varieties produce low levels of eugenol but higher levels of benzoic acid derivatives (methyl benzoate and benzyl benzoate) and the sesquiterpene β-caryophyllene (Clery et al. 1999; Lavy et al. 2002). At the petal emerging from the bud stage (6 days before anthesis), only five scent volatiles (μg/g) were detected in carnation cv. Eilat-detached petal extract, dominated by *p*-vinylphenol (65.5 μg) and 4-vinyl guaiacol (10 μg); the remaining volatiles included maltol (5.4 μg), guaiacol (1.1 μg) and *cis*-3-hexenylbenzoate (0.1 μg) (Lavy et al. 2002). At the mature flower opened stage (anthesis), benzoic acid (40 μg) and its derivatives, benzyl benzoate (19.7 μg) and phenylethyl benzoate (13.4 μg), predominated 4-vinyl guaiacol (16.8 μg) and *p*-vinylphenol (21.6 μg) and were

still high but the latter less than in the young flower stage. Other scent volatiles (μg/g) detected included *cis*-3-hexenyl benzoate (6.5 μg), benzyl salicylate (2.8 μg), hexyl benzoate (0.6 μg), vanillic acid (4.3 μg), methyl homovanillate (3.1 μg), coumaric acid (3.9 μg), guaiacol (1.1 μg), nonanal (1.7 μg) maltol (0.8 μg), nonanoic acid (0.6 μg) and the sesquiterpene β-caryophyllene oxide (0.8 μg). No monoterpenes were detected. The profile of the major scent volatiles in carnation flower headspace was different. The young flower contained *cis*-3-hexenyl acetate (82.3 %), 3-hexen-1-ol (9.9 %), *cis*-3-hexenyl tiglate (2.2 %),1-hexyl acetate (0.5 %), methyl benzoate (0.2 %), nonanal (1.6 %), decanal (0.4 %), *cis-3*-hexenyl isovalerate (0.3 %), β-caryophyllene (1 %) and *cis*-3-hexenyl benzoate (0.8 %). The mature opened flower contained β-caryophyllene (23.4 %), *cis*-3-hexenyl acetate (19.6 %), methyl benzoate (17.9 %), *cis*-3-hexenyl benzoate (16.8 %), 3-hexen-1-ol (1.3 %), *cis*-3-hexenyl tiglate (1.0 %),1-hexyl acetate (0.6 %), nonanal (0.4 %), decanal (0.5 %), *cis*-3-hexenyl isovalerate (0.3 %), phenylacetaldehyde (1.3 %), 2-hydroxy methyl benzoate (0.6 %), pentyl benzoate (0.4 %), hexyl benzoate (3.5 %), caryophyllene oxide (5.6 %), benzyl benzoate (1.7 %) and isoamyl salicylate (2.6 %). Transgenic plants expressing the linalool synthase gene from *Clarkia breweri* were generated, and from their leaves and flowers, linalool and its derivatives, *cis*- and *trans*-linalool oxide, were detected.

In an another study, 12 volatiles were identified as the main components of carnation flower fragrance signature (El-Ghorab et al. 2006). The major components of the volatiles found were phenyl ethyl alcohol, eugenol, hexyl benzoate, hexenyl benzoate (z), benzyl benzoate, benzoin, nootkatone, benzyl salicylate, m-cresyl phenyl acetate, hexadecanoic acid and eicosane.

Anthocyanin flower pigments of carnations had been reported for some pink, red, red-purple and mauve cultivars. Pelargonidin 3-*O*-glycoside was found in salmon and red cultivars, pelargonidin 3,5-di-*O*-glycoside in pink, cyanidin 3-*O*-glycoside in lavender and crimson and cyanidin 3,5-di-*O*-glycoside in lavender and magenta ones (Geissman and mehlquist 1947; Geissman et al. 1955). Cyanic carnation flowers (reds and pinks) that contained the factor *R* in homozygous or heterozygous conditioned were found to contain cyanidin glycosides; the homozygous recessive *rr* contained pelargonidin derivatives (Geissman et al. 1962). Kaempferol was clearly visible in all the red and pink genotypes and quercetin absent from these but visible in the Woburn sample. All the acyanic white genotypes contained kaempferol, but only one contained quercetin as well. Apigenin was not observed in these whites. Isosalipurposide was identified as the yellow pigment in carnation petals (Harborne 1966). Carnation genotypes with recessive (ii) alleles were found to produce yellow flowers, which contained the chalcone isosalipurposide (naringenin-chalcone-2′-glucoside) as the major petal pigment in the vacuole (Forkmann and Dangelmayr 1980). This naringenin-chalcone was the first product of the synthesis of the flavonoid skeleton and that only the conversion of naringenin-chalcone to naringenin furnishing the substrate for the further reactions to flavonol and anthocyanin. Based on the analysis of pigment composition, Onozaki et al. (1999) classified 13 white cultivars into three types: nearly pure white cultivar, ‘White Mind’ lacking flavonoid compounds in the petals, ‘Kaly’ and ‘White Barbara’ accumulating a large amount of naringenin derivatives and the normal white cultivars containing kaempferol derivatives as the major flavonoid. Ogata et al. (2004) reported that chalcone, which was synthesized from the condensation of *p*-coumaroyl-CoA and malonyl-CoAs by chalcone synthase, was converted to chalcone 2′-*O*-glucoside by UDP-Glc: chalcone glucosyltransferase (chalcone 2 -GT). Chalcone 2′-*O*-glucoside could then be transported and accumulated into vacuoles.

Incubation of crude extracts prepared from pink, magenta or white carnation flowering genotype with [2-^{14}C]malonyl-CoA and 4-coumaroyl-CoA and co-chromatography on cellulose TLC plates with different solvent systems and enzymatic conversion yielded naringenin, naringenin chalcone, eriodictyol, eriodictyol chalcone, dihydrokaempferol and

dihydroquercetin (Spribille and Forkmann 1982). In carnation genotypes with wild-type alleles (R), 4′- and 3′,4′-hydroxylated flavonoids were formed. Independent of the genetic state at the locus r, however, naringenin chalcone T-glucoside (isosalipurposide) was the only chalcone present in the flowers of genotypes which lack chalcone isomerase activity. Eriodictyol chalcone 2′-glucoside was not detected in either the flowers of genotypes with the dominant allele R or in the flowers of recessive (rr) genotypes. 3′-Hydroxylase activity could be readily detected in the flower extracts of all genotypes with the wild-type allele R but was completely deficient in the flower extracts of recessive (rr) genotypes. The gene r is known to control the hydroxylation pattern of the B-ring of anthocyanins. Recessive genotypes (rr) produced pelargonidin derivatives in the flowers, whereas cyanidin was formed under the influence of wild-type alleles R. The gene i is known to control the activity of chalcone isomerase Recessive genotypes (ii) lacked chalcone isomerase activity, and therefore, naringenin chalcone 2′-glucoside (isosalipurposide) was accumulated. In contrast chalcone isomerase activity being present in genotypes with the wild-type allele, higher oxidized flavonoids, including anthocyanins, were synthesized. The gene a interferes with the anthocyanin pathway after dihydroflavonol formation but before anthocyanin synthesis. Recessive genotypes (aa) produced white flowers containing flavonols. Thus, six carnation genotypes were established based on chemogenetic and enzymatic characteristics (Spribille and Forkmann 1982):

(a) IIAARR with magenta flower, producing cyanidin, isomerase and 3′-hydroxylase activities present
(b) IIAArr pink flower, producing pelargonidin derivatives, isomerase activity present, 3′-hydroxylase activity absent
(c) IIaarr with white flower producing kaempferol, isomerase activity present, 3′-hydroxylase activity absent
(d) iiAARR yellow-magenta flower producing isosalipurposide (naringenin chalcone 2′-glucoside) some cyanidin, isomerase activity absent, 3′-hydroxylase activity present
(e) iiAArr yellow-pink flower producing isosalipurposide some pelargonidin, isomerase and 3′-hydroxylase absent
(f) iiaarr pure yellow flower producing isosalipurposide some kaempferol, isomerase and 3′-hydroxylase absent

Malylated anthocyanins from carnation *Dianthus caryophyllus* flowers were confirmed as pelargonidin3-*O*-(6-*O*-malyl-β-D-glucopyranoside) from red cv. 'Scania' and cyanidin 3-*O*-(6-*O*-malyl-β-D-glucopyranoside) from the purplish-red 'Nina' (Terahara and Yamaguchi 1986; Yamaguchi et al. 1988). The major anthocyanin in pink and red forms of *Dianthus caryophyllus* was identified as pelargonidin 3-malylglucoside (Terahara et al. 1986). Flowers of the red\mauve carnation cultivars 'Kortina Chanel' and 'Purple Torres' contained a macrocyclic anthocyanin pigment, a malylated cyanidin 3,5-diglucoside that readily converted by ring opening to yield cyanidin 3-*O*-(6-*O*-malyl glucoside)-5-*O*-glucoside (Bloor 1998). Cyclic-malyl anthocyanins 3, 5-di-*O*-(β-glucopyranosyl) pelargonidin 6″-*O*-4, 6‴-*O*-L-cyclic malate and a 3, 5-di-*O*-(β-glucopyranosyl) cyanidin 6″-*O*-4, 6‴-*O*-L-cyclic malate were identified from petals of deep pink and red-purple flower cultivars of *Dianthus caryophyllus*, respectively (Nakayama et al. 2000). White-flowered Sim carnations were found to contain mainly flavonol glycosides: kaempferol glycosides and naringenin glycosides and the genes dihydroflavonol 4-reductase and anthocyanidin synthase involved in flavonoid biosynthesis (Mato et al. 2000). A new macrocyclic anthocyanin, pelargonidin 3,5-di-*O*-β-glucoside(6″, 6‴-malyl diester), and 3-*O*-(6″-*O*-malylglucoside)-5-*O*-glucoside were found in 'cyclamen' red (or pink) colours in carnation flowers–cultivars Red Rox and eight others (Gonnet and Fenet 2000). Characterization of anthocyanins in the flowers of the modern carnation cv Eilat revealed that only the orange pelargonidin accumulated, due to a lack of both flavonoid 3′,5′-hydroxylase and flavonoid3′-hydroxylase activities (Zuker et al. 2002).

Wild-type carnations with a flavonoid 3′,5′-hydroxylase gene were found to contain pelargonidin- or cyanidin-type anthocyanins, such as pelargonidin or cyanidin 3,5-diglucoside-6″-*O*-4, 6‴-*O*-L-cyclic-malyl diester (Fukui et al.

2003). In contrast, the anthocyanins in the transgenic flowers of cv Moondust and Moonshadow were delphinidin 3,5-diglucoside-6″-*O*-4, 6‴-*O*-L-cyclic-malyl diester (main pigment), delphinidin 3,5-diglucoside-6″-malyl ester and delphinidin 3,5-diglucoside-6″,6‴-dimalyl ester. Additionally, the petals contained flavonol and flavone glycosides. Three of them were identified to be kaempferol 3-*O*-(6‴-rhamnosyl-2‴-glucosyl-glucoside), kaempferol 3-*O*-(6‴-rhamnosyl-2‴-(6-malyl-glucosyl)-glucoside) and apigenin 6-C-glucosyl-7-*O*-glucoside-6‴-malyl ester. This flavonoid exhibited the strongest copigment effect. Chalcononaringenin 2′-*O*-glucoside (Ch2′G) was found to be the major pigment molecule in the petals of carnations bearing yellow flowers (Yoshida et al. 2004). The concentration of this pigment varied from 5.5 to 100.0 %.

Transcription of the following genes was found in the yellow flowers: anthocyanidin synthase, anthocyanin acyltransferase, chalcone 2′-glucosyltransferase, chalcone–flavanone isomerase, chalcone synthase, dihydroflavonol 4-reductase, flavanone 3-hydroxylase, UDP-glucose:flavonoid glucosyltransferase and phenylalanine ammonia-lyase. The activity of flavanone 3β-hydroxylase gene (FHT) was demonstrated in carnation flowers (Dedio et al. 1995). A phenylalanine ammonia-lyase (PAL) cDNA clone was isolated from carnation petals (Yoshimoto et al. 2001). The yellow colour of the carnation petals was attributed to the synthesis and accumulation of chalcone 2′-glucoside (Itoh et al. 2002). In several of the carnation cultivars that bear yellow flowers variegated with white flecks and sectors, both the chalcone isomerase (*CHI*) and dihydroflavonol 4-reductase (*DFR*) genes were disrupted by a transposable element *dTdic1*. Glucosylation of anthocyanin in carnations was found to involve novel sugar donors, aromatic acyl-glucoses, in a reaction catalyzed by the enzymes acyl-glucose-dependent anthocyanin 5(7)-*O*-glucosyltransferase (AA5GT and AA7GT) (Matsuba et al. 2010).

An acyl donor substance of anthocyanin malyltransferase, 1-*O*-β-D-malylglucose, was extracted and partially purified from carnation petals (Abe et al. 2008). This was synthesized chemically to analyse AMalT activity in a crude extract from carnation. Changes in the AMalT activity showed close correlation to the accumulation of pelargonidin 3-malylglucoside (Pel 3-malGlc) during the development of red petals of carnation, but neither AMalT activity nor Pel 3-malGlc accumulation was detectable in roots, stems and leaves.

Three flavonol glycosides were isolated from the flowers of carnation cultivars ‘White Wink’ and ‘Honey Moon’ and their structures established as kaempferol 3-*O*-neohesperidoside, kaempferol 3-*O*-sophoroside and kaempferol 3-*O*-glucosyl-(1 → 2)-[rhamnosyl-(1 → 6)-glucoside] (Iwashina et al. 2010).

Leaf/Plant Phytochemicals

Dianthin 30 and dianthin 32, two proteins with molecular weights 29,500 and 31,700, respectively, were isolated from the leaves of *Dianthus caryophyllus* (carnation) (Stirpe et al. 1981). Both dianthins were glycoproteins containing mannose. Three gypsogenic acid glycosides including 3-*O*-β-D-glucopyranoside of gypsogenic acid with the trivial name diantoside A, 3,28-*O*-diglucopyranoside of gypsogenic acid with the trivial name dianoside A and 3-*O*-glucopyranosy1,28-*O*-[glucopyranosyl(1 → 6)] glucopyranoside with the trivial name azukisaponin IV were isolated from aerial parts of carnation (*Dianthus caryophyllus* var. remontant) (Gumnicka and Oleszek 1998). *Lepidium sativum* seedling root growth was affected severely at the presence of gypsogenic acid 3-*O*-glucopyranoside. Bidesmosidic form showed marginal stimulatory activity.

Two benzoic acid derivatives, protocatechuic acid (3,4-dihydroxybenzoic acid) and vanillic acid (4-hydroxy-3-methoxybenzoic acid), and together with the flavonol glycoside peltatoside (3-[6-*O*-(α-L-arabinopyranosyl)-β-D-glucopyranosyl] quercetin) were found within healthy and fungal-inoculated tissues of carnation cultivars (Curir et al. 2003a). 2,6-Dimethoxybenzoic acid was detected in small amounts only in the inoculated cultivar ‘Gloriana’, while the highly resistant cultivar ‘Roland’ showed the presence of the flavone datiscetin (3,5,7,2′-tetrahydroxyflavone).

A new enzyme, *S*-adenosyl-L-methionine:flavonoid 4′-*O*-methyltransferase (F 4′-OMT), has been purified 1,399-fold from carnation tissues (Curir et al. 2003b). Arginine decarboxylase (ADC), a key enzyme in the biosynthesis of polyamines, comprising 725 amino acids with a molecular mass of 78 kDa was found in carnation (Ha et al. 2004).

Flavonoids, kaempferol 3-*O*-β-D-glucopyranosyl (1→2)-*O*-β-D-glucopyranosyl (1→2)-*O*-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside; apigenin 6,8-di-C-β-D-glucopyranoside; kaempferol 3-*O*-β-D-glucopyranosyl (1→2) –*O*-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside; kaempferol *O*-diglycosides; and rutin, were isolated from carnation (*Dianthus caryophyllus*) (Galeotti et al. 2008a). One flavone-C-glycoside apigenin 6,8-di-C-β-D-glucopyranoside (vicenin-2) and two flavonol-*O*-glycosides kaempferol 3-*O*-β-D-glucopyranosyl-(1 → 2)-*O*-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside and kaempferol 3-*O*-[α-l-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside (nicotiflorin) isolated as the main flavonoidal components in nine different carnation cultivars (Galeotti et al. 2008b).

Yang et al. (1997) reported that benzoyl-CoA:anthranilate *N*-benzoyltransferase catalyzed the first committed reaction of phytoalexin biosynthesis in carnation, and the product *N*-benzoylanthranilate was found to be the precursor of several sets of dianthramides. Cell suspension cultures of *Dianthus caryophyllus* was found to accumulate, upon challenge with crude fungal elicitor, various dianthramide phytoalexins, all of which were derived from *N*-benzoylanthranilate (Reinhard and Matern 1991). In-vitro, microsomes from the elicited carnation cells hydroxylated *N*-benzoylanthranilate to yield the hydroxyanthranilate and/or salicyloyl derivatives, and both these activities depended strictly on NADPH and molecular oxygen. 2′-Hydroxylation was shown to precede 4-hydroxylation in the formation of *N*-salicyloyl-4-hydroxyanthranilate. 4-Hydroxylation was shown to be catalyzed by cytochrome P-450-dependent monooxygenase(s), whereas the 2′-hydroxylating activity appeared to be due to a novel class of enzymes, also responding synergistically to NADH in combination with NADPH and showing apparent inhibition by cytochrome c but not by carbon monoxide. The results demonstrated the requirement of two different classes of hydroxylase activities that appeared to introduce the antimycotic quality to the dianthramides for phytoalexin defence. Further, they proposed that methoxydianthramide B was derived from *N*-benzoylanthranilic acid via *N*-benzoyl-4-hydroxyanthranilic acid catalyzed by increases in *N*-benzoyltransferase and phenylalanine ammonia-lyase activities (Reinhard and Matern 1989). The rapid induction of both enzyme activities suggested that the shikimate pathway was of crucial importance in the disease-resistance response of carnation cells.

Antioxidant Activity

Treating carnation plants with 400 ppm stigmasterol gave the highest DPPH scavenging of the oil compared to other treatments (El-Ghorab et al. 2006).

Antimicrobial Activity

Two known compounds were isolated from the essential oils of aerial parts of *Thymus kotschyanus*, and flower buds of *Dianthus caryophyllus* exhibited antibacterial activity (Mohammed and Al-Bayati 2009). Thymol MIC values ranged from 15.6 to 250 μg/ml, and *Bacillus cereus* was found to be the most sensitive pathogen with an MIC value of 15.6 μg/ml. Eugenol achieved stronger MIC values against most tested pathogens, and the best MIC value (15.6 μg/ml) was observed against *Bacillus cereus*, *Listeria monocytogenes* and *Klebsiella pneumoniae*, whereas *Staphylococcus aureus*, *Proteus mirabilis* and *Escherichia coli* were inhibited with an MIC value of 31.2 μg/ml.

Antiviral Activity

The virus inhibitor from carnation was found to compose of probably ϵ-groups of lysine that were

responsible for the biological activity of the molecule (Ragetli and Weintraub 1962). Acid hydrolysis yielded 14 amino acids, none of which contained sulphur. The inhibitor, which had already been found to protect *Nicotiana glutinosa* from infection by either intact tobacco mosaic virus (TMV) or the infectious nucleic acid (RNA) derived from it, was shown to possess no ribonuclease (RNase) activity and to be unable to prevent enzymatic breakdown of RNA by pancreatic RNase.

Dianthin 30 and dianthin 32, two antiviral proteins isolated from the leaves, inhibited protein synthesis in a lysate of rabbit reticulocytes, with an ID_{50} (concentration giving 50 % inhibition) of 9.15 ng/ml (dianthin 30) and 3.6 ng/ml (dianthin 32) (Stirpe et al. 1981). They acted by damaging ribosomes in a less-than-equimolar ratio. Protein synthesis by intact cells was partially inhibited by dianthins at a concentration of 100 μg/ml. Dianthins mixed with tobacco mosaic virus strongly decreased the number of local lesions on leaves of *Nicotiana glutinosa*.

Nontoxic concentration (20 μg/ml) of *Dianthus caryophyllus* seed extracts applied to both Vero and HepG2 cells showed potent antiviral activity against herpes simplex virus (HSV-1) and hepatitis A virus (HAV-27) using plaque infectivity count assay (Barakat et al. 2010). *D. caryophyllus* exhibited strong virucidal activity against HSV-1 and HAV-27, 92.3 and 92.6 %, respectively.

Anticancer Activity

In in-vitro studies, kaempferide triglycoside, a glycosylated flavonol from carnation, inhibited proliferation of native and oestrogen receptor beta overexpressing HTC8 colon cancer cells through a mechanism not mediated by ligand binding dependent oestrogen receptor activation (Martineti et al. 2010). It arrested G0/G1 phase of HCT8 cell-cycle progression. The biological effects of this kaempferide triglycoside were strengthened by the presence of high levels of oestrogen receptor beta.

Parasitic Activity

The essential oil of *D. caryophyllus* exhibited moderate larvicidal activity, displaying an $LC_{50} > 50$ mg/l against the West Nile vector *Culex pipiens* (Kimbaris et al. 2012). Its component eugenol had an LC_{50} of 18.28 mg/l.

Traditional Medicinal Uses

Carnation has been prescribed in European traditional herbal medicine to treat coronary and nervous disorders (Chevallier 1996). It is an aromatic, stimulant herb that has been used in tonic cordials in the past to treat fevers, though this use is now obsolete (Bown 1995). The flowers are reared to be alexiteric, antispasmodic, cardiotonic, diaphoretic and nervine and used as a vermifuge (Chopra et al. 1986).

Other Uses

Carnation is a very popular ornamental and cut-flower crop. Carnations are be cultivated the world over for cut flowers. It has excellent postharvest quality, a wide array of forms and colours, capacity to withstand long-distance transportation and a remarkable ability to rehydrate; the carnations are preferred for commercial purpose than other flowers by growers.

An essential oil obtained from the flowers is used in perfumery (Hill 1952; Uphof 1968). The flower heads are dried and used in potpourri, scented sachets and cosmetic products (Bown 1995). The leaves can be simmered in water, and this water can then be used as a soap for cleaning the skin, clothes, etc. (Allardice 1993).

The plant also has antifungal activity. Flavonoid glycosides isolated from carnation exhibited antifungal activity against different *Fusarium oxysporum* f.sp. *dianthi* pathotypes (Galeotti et al. 2008a). Two benzoic acid derivatives, protocatechuic acid and vanillic acid; the flavonol glycoside peltatoside; and 2,6-dimethoxybenzoic acid, from carnation plant tissues, exhibited weak inhibitory activity

towards the phytopathogen, *Fusarium oxysporum* f. sp. *dianthi*, while the flavone datiscetin exhibited an appreciable fungitoxic activity towards the pathogen (Curir et al. 2003a).

Comments

Colombia is the largest carnation producer in the world; other leading producers include Israel, Kenya and Spain where carnation is the national flower (Perry 2001).

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Dianthus chinensis

Scientific Name

***Dianthus chinensis* L.**

Synonyms

Dianthus amurensis Jacques, *Dianthus chinensis* var. *amurensis* (Jacques) Kitagawa, *Dianthus chinensis* var. *dentosus* (Fischer ex Reichenbach) Debeaux, *Dianthus chinensis* f. *ignescens* (Nakai) Kitagawa, *D. chinensis* var. *ignescens* Nakai, *Dianthus chinensis* var. *jingpoensis* G. Y. Zhang & X. Y. Yuan, *Dianthus chinensis* var. *liaotungensis* Y. C. Chu, *Dianthus chinensis* var. *longisquama* Nakai & Kitagawa, *Dianthus chinensis* var. *macrosepalus* Franchet ex L. H. Bailey, *Dianthus chinensis* var. *morii* (Nakai) Y. C. Chu, *Dianthus chinensis* var. *subulifolius* (Kitagawa) Y. C. Ma, *Dianthus chinensis* var. *sylvaticus* W. D. J. Koch, *Dianthus chinensis* var. *trinervis* D. Q. Lu, *Dianthus chinensis* subsp. *versicolor* (Fisher ex Link) Voroschilov, *Dianthus chinensis* var. *versicolor* (Fisher ex Link) Y. C. Ma, *Dianthus dentosus* Fischer ex Reichenbach, *Dianthus fischeri* Sprengel, *Dianthus morii* Nakai, *Dianthus sequieri* Chaix, *Dianthus sequieri* var. *dentosus* (Fischer ex Reichenbach) Franchet, *Dianthus subulifolius* Kitagawa, *Dianthus subulifolius* f. *leucopetalus* Kitagawa, *Dianthus versicolor* Fisher ex Link, *Dianthus versicolor* f. *leucopetalus* (Kitagawa) Y. C. Chu, *Dianthus versicolor* var. *subulifolius* (Kitagawa) Y. C. Chu.

Family

Caryophyllaceae

Common/English Names

Annual Pink, China Pink, Chinese Pink, Dianthus, French Mignonette, Indian Pink, Japanese Pink, Pinks, Rainbow Pink

Vernacular Names

Burmese: Zaw-Hmwa-Gale
Chinese: Qú Mài, Shi Zhu
Euskera: Krabelin txinar
French: L'oeillet De La Chine
German: Chinenser-Nelke, Kaiser-Nelke
Japanese: Kara-Nadeshiko, Sekichiku
Korean: Kara-Nadeshiko
Philippines: Clavel (Tagalog)
Polish: Goździk Chiński
Portuguese: cravina-da-Arrábida, cravina-da-China, cravinhos-da-China
Spanish: Clavel Chino, Clavellina
Swedish: Sommarnejlika
Turkish: Çin Karanfili

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Origin/Distribution

The species is indigenous to northern China (Gansu, Hebei, Heilongjiang, Henan, Jilin, Liaoning, Nei Mongol, Ningxia, Qinghai, Shaanxi, Shandong, Shanxi and Xinjiang), Korea, Mongolia, Kazakhstan and southeastern Russia and has naturalized in southern China. It is widely cultivated elsewhere in temperate and subtropical areas.

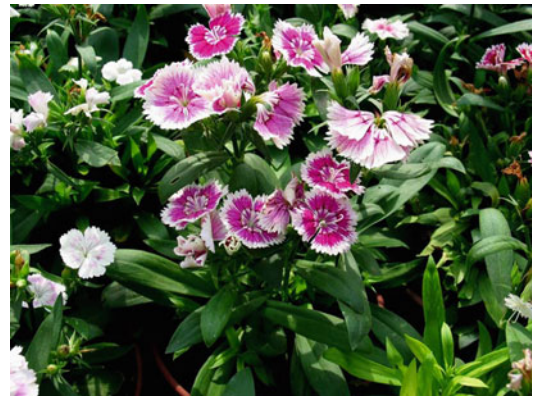

Plate 1 Pink-white flowers and leaves

Agroecology

In its native range, the species occurs in forest edges, forest grasslands, scrub on mountain slopes, hillside grasslands, dry hillsides, sandy hill summits, valleys, rocky ravines, meadows, streamsides, mountain stream wetlands, rocks, steppes, steppe sands, fixed dunes and seashores.

The species requires well-drained, neutral to slightly alkaline soil and full sun to partial shade.

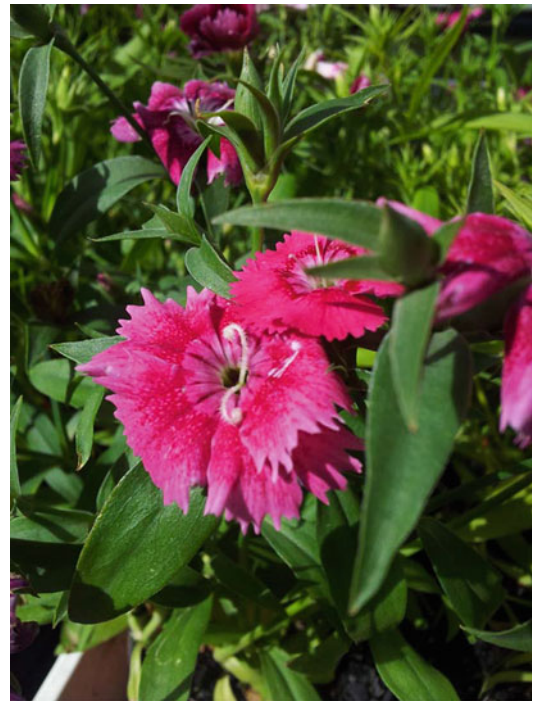

Plate 2 Red flowers and leaves

Edible Plant Parts and Uses

Like most Dianthus, it has a pleasant spicy, floral, clove-like taste and is ideal for decorating or adding to cakes (Barash 1993; Creasey 1999; Brown 2011; Thompson and Morgan 2013). They also make a colourful garnish to soups, salads and the punch bowl. It is advisable to remove the bitter white base of the petal.

Botany

A small, glabrous, herbaceous, perennial growing in dense tufts to 30–50 cm high with erect and distally branched stem. The leaves are green to greyish linear-lanceolate, 3–5 cm long by 2–4 mm wide, with acuminate apex, tapering base and entire margin (Plates 1, 2 and 3). Flowers, 2.5–4 cm across, solitary or in a few-flowered cymes with four ovate bracts and on 1–3 cm pedicels; calyx cylindric with lanceolate 5 mm, pointed teeth; petals 1.6–2 cm; limb bright red, purple-red, pink or white, obovate-triangular, throat spotted and laxly bearded, apex irregularly dentate; stamens exserted; ovary suboblong, style linear (Plates 1, 2 and 3). Capsule suboblong with 4-toothed apex. Seeds black, oblate.

Plate 3 White flowers and leaves

Nutritive/Medicinal Properties

Plant (Aerial Parts) Phytochemicals

Two malylated anthocyanins were found in fresh petals of *D. chinensis* (Nadanasabapathy and Sayeed 1991).

Two triterpene saponins, named dianchinenosides A and B, were isolated from *Dianthus chinensis* and their structures determined as 3β-*O*-α-L-arabinopyranosyl-16α-hydroxyolean-12-ene-23 alpha, 28β-dioic acid 28-*O*-β-D-glucopyranoside [1] and 3β-*O*-β-D-xylopyranosyl-16α-hydroxyolean-12-ene-23α, 28β-dioic acid 28-*O*-D-glucopyranoside, respectively (Li et al. 1993). Four triterpenoid saponins, dianchinenosides E, F, G and H, were from the aerial parts of *Dianthus chinensis* (Koike et al. 1994). Two triterpenoid saponins, dianchinenoside C [23-*O*-β-D-glucopyranosyl 3β, 16α-dihydroxyolean-12-ene 23α, 28β-dioic acid 28-*O*-β-D-glucopyranoside] and dianchinenoside D [3β, 16α-dihydroxyolean-12-ene 23α, 28β-dioic acid 28-*O*-β-D-glucopyranosyl [(1→6)-β-D-glucopyranoside] were isolated from the aerial parts of *Dianthus chinensis* (Li et al. 1994a). In addition, known compounds, 3-*O*-α-L-arabinopyranosyl hederagenin 28-*O*-β-D-glucopyranosyl (1→6)-β-D-glucopyranoside, sitosterol 3β-*O*-β-D-glucopyranoside, isoorientin-2″-*O*-glucoside, isovitexin-2″-*O*-glucoside and chrysoeriol-7-*O*-glucoside, were also identified. L-dianose, a new monosaccharide, was isolated from *D. chinensis* (Li et al. 1994b). The plant also contained melosides A and L which were first reported in melon (Monties et al. 1976; NPRI and SNU 1998; Nho et al. 2012). *Qu Mai* (dried aerial parts of *Dianthus chinensis)* was reported to contain Dianthus saponins A, B, C and D; volatile oil components—eugenol, phenylethyl alcohol, benzyl benzoate and methyl salicylate; phosphoric acid; vitamin A; alkaloids; and flavones (Xu 2002).

Antioxidant Activity

The methanol extract of *D. chinensis* exhibited strong antioxidant activity on the oxidation of linoleic acid (Kim et al. 1994).

Anticancer Activity

D. chinensis extract was found to have antitumour activity against Ehrlich ascites carcinoma in-vitro (Kosuge et al. 1985). Treatment of human HepG2 hepatocellular carcinoma cells with the ethanol extract of *Dianthus chinensis* significantly inhibited cell growth in vitro in a concentration- and time-dependent manner by inducing apoptosis through the mitochondrial pathway and caspase activation (Nho et al. 2012). This induction was associated with chromatin condensation and cleavage of poly (ADP-ribose) polymerase protein. Further, the extract selectively downregulates the expression of bcl-2 and bcl-xl in HepG2 cells.

Traditional Medicinal Uses

The species has been used for over 3,000 years in Chinese herbal medicine (Bown 1995). The

whole plant is a bitter tonic herb that stimulates the digestive and urinary systems and also the bowels. It is also anthelmintic, antibacterial, antiphlogistic, diaphoretic, diuretic, emmenagogue, febrifuge and haemostatic (Duke and Ayensu 1985; Bown 1995). It is used internally in the treatment of acute urinary tract infections (especially cystitis), urinary stones, constipation and failure to menstruate and externally to treat skin inflammations and swellings (Bown 1995). The old leaves are crushed and used for clearing eyesight (Duke and Ayensu 1985). *Qu Mai* (dried aerial parts of *Dianthus chinensis)* is used in Chinese herbal medicine to promote urination and menstruation, to break up blood stasis and to treat red, sore and swollen eyes (Xu 2002).

In Korea, this herb is used as a folk remedy for the treatment of menostasis, gonorrhoea and cough and as a diuretic and emmenagogue (NPRI and SNU 1998).

Other Uses

The species is popularly cultivated as an ornamental garden plant. It is excellent for beds, borders, edgings, rock gardens and pots.

Comments

Dianthus chinensis is a very variable species represented in China by both cultivated and wild plants and the most important source of herba dianthi in Shandong. Several varieties were identified in Shandong: *D. chinensis* L. var. *versicolor* (Fich. ex Link) Y. C. Ma, *D. chinensis* L. var. *versicolor* and *D. chinensis* L. var. *liaotungensis* Y. C. Chu (Zhou et al. 1997).

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Combretum indicum

Scientific Name

***Combretum indicum* (L.) DeFilipps**

Synonyms

Combretum indicum (Linnaeus) Jongkind nom illeg., *Kleinia quadricolor* Crantz, *Mekistus sinensis* Loureiro ex B. A. Gomes, *Quisqualis bracteata* P. Beauv., *Quisqualis glabra* N. L. Burman, *Quisqualis grandiflora* Miquel, *Quisqualis indica* L., *Quisqualis indica* var. *oxypetala* Kurz, *Quisqualis. indica* var. *villosa* (Roxburgh) C. B. Clarke, *Quisqualis longiflora* C. Presl, *Quisqualis loureiroi* G. Don, *Quisqualis madagascariensis* Bojer inval., *Quisqualis obovata* Schumacher & Thonning, *Quisqualis pubescens* N. L. Burman, *Quisqualis sinensis* Lindley, *Quisqualis spinosa* Blanco, *Quisqualis villosa* Roxburgh

Family

Combretaceae

Common/English Names

Burma Creeper, Chinese Honeysuckle, Drunken Sailor, Liane Vermifuge, Love and Innocence, Rangoon Creeper

Vernacular Names

Bangladesh: Basantilata, Begunlata, Madhabilata, Modhumalati, Modhumanjuri, Ranganbel

Burmese: Hta:Wèý-Mheing

Chinese: Bing Gan Zi, Dong Jun Zi, Liu Qiu Zi, Se Gan Zi, Shan Yang Shi, Shih Chun Tze, Shi Jun Zi, Wu Leng Zi

Czech: Hranoplod Indický

German: Quisqualis

India: Madhumalti, Madhumanjari (Bengali), Madhu Malti, Madhumalti (Hindi), Akar Dani, Udani (Malayalam), Parijat (Manipuri), Vilayati Chambeli (Marathi), Irangan Malli (Tamil), Radha Manoharam (Telugu), Ishq Pechaan (Urdu)

Indonesia: Ceguk, Cekluk Kacekluk, Kecukluk, Wedani (Javanese), Kunji Rhabet, Rabet Dani, Rhabet Besi, Saradengan (Madurese), Udani (Malay), Udani (Sumatra), Bidani (Sundanese)

Japanese: Shikunshi

Khmer: Dong Preah Phnom, Khua Hung Sa Mang Vor Romiet Nhi

Korean: Saguncha

Laotian: Dok Ung, Kheua hung, Sa Mang

Malaysia: Akar Dani, Akar Cucur Atap, Akar Setanduk, Ara Dani, Akar Pontianak, Bunga akar dani, Redani, Selimpas, Setanduk

Nigeria: Ọ̀gàn Fúnfún, Ọ̀gàn-Igbó (Yoruba)

Philippines: Kasunbal, Tanglon, Tañgolon, Tañgulo (Bikol), Balitadham, Pinion, Piñones (Bisaya), Talulong, Talulng (Ibanag),

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Talolong, Tartarau, Tartaraok (Iloko), Tauñgon (Manabo), Bonor (Panay Bisaya), Niog-Noigan, Tagarau, Tagulo, Talolong, Tañgolon, Totoraok (Tagalog)
Polish: Cudacznik Indyjski
Portuguese: Arbusto-Milagroso
Spanish: Quiscual
Thai: Cha Mang (Northern), Thai-Mong (Karen-Mae Hong Son), Lep Mue Naang (Central, Peninsular)
Tongan: Kaloni Kakala
Togo: Gargu (Anyi-Anufo)
Vietnamese: Cha ro, Chúa sá nằng, Dây Giun, Dây quân tử Hoa Giun, Quả nấc, Sứ Quân Tử

Origin/Distribution

The plant is indigenous to India, Southeast Asia (Kampuchea, Laos, Myanmar, Thailand, Vietnam, Malaysia, Papua New Guinea and the Philippines) and tropical Africa (Benin, Ivory Coast, Ghana, Mali, Nigeria, Sierra Leone, Togo, Tanzania, Zaire and Angola). It is now widely cultivated as ornamental and naturalized in the tropics. The plant is cultivated in China and Taiwan and has naturalized in northern Queensland and the northern parts of the Northern Territory, in New Caledonia, Southeastern United States (i.e. Florida) and the Caribbean (e.g. Puerto Rico and the Virgin Islands).

Agroecology

In its native range, it is found along edges of primary forests; in secondary forests, woodlands and hillsides; and alongside riverbanks from sea level up to 1,500 m. Elsewhere it is also found in disturbed habitats, thickets and rice fields and along roadsides and railway tracks. The plant is also cultivated in gardens as fences/hedges and in parks. The plant grows and flowers best in full sun. Although fairly drought tolerant, it requires moderate watering during the hot dry seasons. It grows on a wide range of soils, including poor soils, and does best in well-drained, moist soil rich in humus.

Edible Plant Parts and Uses

The plant has edible fruit that tastes like almond, and the flowers are eaten in Thailand (Wessapan et al. 2007; Wetwitayaklung et al. 2008). In tropical Africa and parts of Southeast Asia, it is cultivated for production of the drug (fruits and seeds) and as a leafy vegetable. In Indonesia, very young reddish-brown leafy shoots are eaten raw or steamed as 'lalab'.

Botany

A deciduous, sub-woody climber or scrambling shrub with pubescent terete branches and reaching lengths of 3–8 m. Leaves simple, oblong-elliptic to elliptic, 5–18 cm by 3–7 cm, with acuminate tips, obtuse to rounded base sand entire margin, abaxially brown pilose and adaxially glabrous, rarely tomentose of both surfaces (Plate 1). Inflorescences in lax terminal racemes, 10–15 cm long, with linear-filiform to ovate, brown pilose deciduous bracts (Plates 1 and 2). Flowers fragrant, bisexual, pentamerous and tubular; calyx tube yellow pilose with five deltoid lobes 1.5–2.5 mm long with acuminate apices; petals 5 obovate to oblanceolate, 8–16 mm long, with obtuse apices, white turning to pink or red; stamens 10 in two rows, adherent, scarcely exserted, ovary inferior, style filiform and stigma knob shaped. Fruits dry capsule, 3–4 cm long,

Plate 1 Inflorescences and leaves

Plate 2 Close view of flowers

red turning to dark chestnut brown when ripe, narrowly ellipsoid to fusiform and sharply 5 ridged and usually one seeded.

Nutritive/Medicinal Properties

Flower Phytochemicals

Rutin and pelargonidin-3-glucoside have also been isolated from flowers (Nair et al. 1979). The major components detected in the flower extracts included *E*- and *Z*-linalool oxides (furanoid form); 2,2,6-trimethyl-6-vinyl-3-keto-tetrahydropyran; 2,2,6-trimethyl-6-vinyl-3-hydroxy-tetrahydropyran (linalool oxide pyranoid form); (*E,E*)-α-farnesene, *Z*-3-hexenyl benzoate and benzyl benzoate; and a tentatively identified compound quinoline carbonitrile along with some waxy components (Rout et al. 2008). Tannin (gallic acid), flavonoid (quercetin and rutin) and terpenoids (β-sitosterol and lupeol) were isolated from leaves and flowers of *Quisqualis indica* (Bairagi et al. 2012b).

Fruit Phytochemicals

The fruit was found to contain the following amino acids: arginine, aspartic acid, glutamic acid, serine, glycine, proline, leucine, valine, alanine, threonine, asparagine, histidine, lysine, an acidic amino acid named quisqualic acid along with γ-amino butyric acid and trigollenine (Takemoto et al. 1975c). The structure of quisqualic acid was proposed as β-(3,5-dioxo-1,2,4-oxadiazolidin-2-yl)-L-alanine (Takemoto et al. 1975b). A new hydroxyureido derivative, 2-amino-3-(1-hydroxyureido) propionic acid, was obtained by an alkaline treatment of quisqualic acid, and isoquisqualic acid [β-(3,5-dioxo-1,2,4-oxadiazolidin-4-yl)alanine] was also synthesized. Quisqualic acid was synthesized from 3,5-dioxo-1,2,4-oxadiazolidine and from methyl 3-chloro-2-benzoxycarbonylaminopropionate (Takemoto et al. 1975a). Related compounds are the following: D-L-2-amino-3-(1-hydroxyureido)propionic acid and L-2-amino-4-(3-hydroxyureido)-butyric acid were also synthesized. Quisqualic acid was also found in the seeds (Flippen and Gilardi 1976). A new acylglycosyl sterol, 3-*O*-[6′-*O*-(8Z-octade-cenoyl)-β-D-glucopyranosyl]-clerosterol, plus 4 known compounds clerosterol, betulinic acid, methylursolate and α-xylofuranosyluracil were isolated from the methanol extract of *Quisqualis* fruit (Kwon et al. 2003). The peel of *Quisqualis* fruit was found to contain trigonelline (Iang and Tian 2004). Twelve compounds were isolated from the ethanol extracts of *Quisqualis indica* fruit (Huang et al. 2006). The compounds were glyceryl monosterate, glyceryl monopalmitate, clerosterol, 1-linoloyl-3-palmitoylglycerol, stigmasterol, methylursolate, betulinic acid, ethyl gallate, gallic acid, butanedioic acid, benzoic acid and sucrose.

Fixed oil extracted from the fruits could be stored for a year in bottles with charcoal as desiccants and covered with polythene sheets without appreciable loss of quality (Quitana et al. 1983). However, there were significant changes in some parameters such as acid value, saponification ester values which represented degradation indices that began at 6 months but were not expressed in terms of off-flavour/odour. After a year storage, crude oil content changed from 38.347 to 30.25 %, pure fixed oil from 28.30 to 26.78 %, moisture content 7.25 to 7.83 %, weight 628 to 4.88 g, oxygen 20.64 to19.82 %, specific gravity (25 °C)s 0.924 to 0.904, refractive index (28 °C) 1.48 to 1.514, acid value 1.047 to 5.552, saponification value 201.11 to 153.89 and ester value 208.07 to 148.34.

The oil yield from *Quisqualis* fruit was 27.70 % (Wang and Chen 2004). Among the fatty acids, oleic acid, linoleic acid and palmitic acid were dominant. The unsaturated fatty acids accounted for 63.93 % of the total fatty acids, and the major saturated fatty acid was palmitic acid.

Leaf Phytochemicals

Four crystalline constituents were isolated from the leaves of shih-chun-tze, *Quisqualis indica* and identified to be nicotinic acid methylbetaine (trigonelline), L-proline, L-asparagine and potassium quisqualate (Fang and Chu 1964). Two cysteine synthase isoenzymes A and B were purified from the leaves (Murakoshi et al. 1986). Both isoenzymes catalyze the formation of cysteine from *O*-acetyl-L-serine and hydrogen sulphide, but only isoenzyme B catalyzes the formation of L-quisqualic acid. Two ellagitannins, quisqualin A and quisqualin B, were isolated from the fruits (Lin et al. 1997). Twenty-one additional tannins were isolated from either the fruits or leaves including 11 ellagitannins (2,3,-(*S*)-HHDP-D-glucose; 2,3-(*S*)-HHDP-4-galloyl-D-glucose; 2,3-(*S*)-HHDP-6-galloyl-D-glucose; 2,3-(*S*)-HHDP-4,6-di-*O*-galloyl-D-glucose, pedunculagin; punicalagin; eugeniin; 1-desgalloyleugeniin; casuariin;5-desgalloylstachyurin; and castalagin), five gallotannins (6-*O*-galloyl-D-glucose; 1,6-di-*O*-galloyl-β-D-glucose; 2,3 di-*O*-galloyl-D-glucose; 3,4-di-*O*-galloyl-D-glucose; and 4,6-di-*O*-galloyl-D-glucose), four phenol-carboxylic acids (gallic acid, ellagic acid, falvogallonic acid and brevifolin carboxylic acid) and one hydrolyzable tannin (punicalin). *Q. indica* leaves were reported to have 8 % moisture content, 9 % total ash, 12.5 % acid-insoluble ash, 6.55 % water-soluble ash values and 5.45 % sulphated ash (Singh et al 2011). Alcohol-soluble extractive value and petroleum ether-soluble extractive value of the leaves were observed to be 10, 3 and 1% w/w, respectively. The phytochemical test revealed the presence of alkaloids, slight amount of glycosides, tannins, flavonoids and protein in both extracts.

Antioxidant Activity

Four edible flower extracts including *Q. indica* elicited antioxidant activity in ABTS assay with the trolox equivalent antioxidant capacity (TEAC) of 0.15–0.70 (Wessapan et al. 2007). Of 24 edible Thai flowers, both dried flowers and crude extract of *Quisqualis indica* gave the highest total phenol contents and showed the highest antioxidant activities (Wetwitayaklung et al. 2008). The antioxidant activity of *Q. indica* was (TEAC = 0.70, IC_{50} = 13.26 µg). Total polyphenol in terms of g/100 g dried flower was 7.71 g, and 31.49 g/100 g crude extract and percent polyphenol yield was 24.47 %.

The amount of total phenolic content varied for different partitionates ranging from 22.95 to 39.45 g of GAE/100 g of dried *Q. indica* bark extract (Kaisar et al. 2009). The highest total phenolics were found in chloroform-soluble partitionate (CSP) (39.45 g of GAE/100 g of dried extract) and the lowest in the n-hexane-soluble partitionate (HSP) (22.95 g of GAE/100 g of dried extract). Total phenolic content of carbon tetrachloride (CTP) and aqueous soluble partitionates (ASP) were found to be 30.81 and 29.87 g of GAE/100 g of dried extract, respectively. Among the partitionates tested, the most potent fraction was found to be CSP. Free radical scavenging activity of the CSP was highest having IC_{50} value of 30.65 µg/ml. CTP, ASP and HSP demonstrated moderate free radical scavenging activity with the IC_{50} value of 68.46, 72.20 and 84.23 µg/ml, respectively, as compared to the standards, i.e. *tert*-butyl-1-hydroxytoluene (BHT) (IC_{50} = 24.35 µg/ml) and ascorbic acid, ASA (IC_{50} = 5.80 µg/ml).

Antidiabetic Activity

The methanolic flower extract of *Quisqualis indica* at doses of 200 and 400 mg/kg, p.o. elicited significant decrease in the biochemical parameters, glucose, triglyceride, total cholesterol, HDL-cholesterol and LDL-cholesterol levels in alloxan-induced diabetic rats as compared to

untreated diabetic control group (Bairagi et al. 2012a). The extract at both doses was also effective in normalizing the levels of triglyceride and cholesterol levels in heart homogenates as compared with diabetic control.

Antihyperlipidemic Activity

Co-administration of the methanolic or aqueous extract of aerial parts (100, 200 mg/kg) to high-cholesterol diet-induced hyperlipidemic rats reduced total cholesterol, triglycerides, low-density lipoproteins (LDL) and VLDL and increased high-density lipoproteins (HDL) (Sahu et al. 2012a). The methanol extract was more effective than the aqueous extract and was comparable to atorvastin. The extracts were found to contain glycosides, alkaloids, saponins, flavonoids, carbohydrates and fixed oil.

Acetylcholinesterase Inhibition Activity

Wetwitayaklung et al. (2007) demonstrated that the methanolic flower extract of *Q. indica* exhibited acetylcholinesterase inhibition activity (Wetwitayaklung et al. 2007). The extract inhibited electric eel acetylcholinesterase in a dose-dependent manner with an IC_{50} value of 0.77 µg/ml.

Antimicrobial Activity

Methanol flower extracts of five edible flowers including *Quisqualis indica* exhibited antibacterial effect in-vitro against *Staphylococcus aureus* with MIC at 50–800 µg/ml (Wessapan et al. 2007). *Candida albicans* was inhibited by flower extracts from *Sonneratia caseolaris* and *Quisqualis indica*, with MIC at 50 and 800 µg/ml, respectively (Wessapan et al. 2007). Four diphenylpropanoids: 1-(4-hydroxy-3-methoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy) propan-1-ol (1); 1-(3,4-dimethoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propan-1-ol (2); 1-(3,4- dime thoxyphenyl)-2- (4-al lyl-2,6-dime thoxyphenoxy)propan-1-ylac e tat e (3); and 1-(4-hydroxy-3,5-dimethoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy) propan-1-ol (4) were isolated from the chloroform-soluble fraction of a methanol stem bark extract of *Quisqualis indica* (Jahan et al. 2009). All compounds were tested for their anti-staphylococcal activity against a total of five multidrug-resistant (MDR) and methicillin-resistant *Staphylococcus aureus* strains, and the minimum inhibitory concentrations (MICs) were in the range of 128–256 µg/ml. Studies showed that the methanol dry flower extract of *Quisqualis indica* showed highest antimicrobial property than other flowers (*Calotropis gigantea* and *Polianthes tuberosa*) studied (Kiruthika et al. 2011). *Q. indica* methanol flower extract showed significant in-vitro antibacterial activity against the microbes *Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Escherichia coli,* methicillin-resistant *Staphylococcus aureus* and *Bacillus subtilis*. Sanguri et al. (2011) found that *Q. indica* leaf extracts were more effective on fungal species *Alternaria porri, Aspergillus flavus, Aspergillus niger, Aspergillus oryzae* and *Penicillium chrysogenum* than bacterial species. The methanol extract was more effective than aqueous extract.

Antiinflammatory Activity

Oral administration of the hydroalcoholic flower extract at the doses 100 and 150 mg/kg body weight to rats elicited dose-dependent and significant antiinflammatory activity in acute (acetic acid-induced vascular permeability) and chronic (cotton pellet granuloma) inflammatory models (Yadav et al. 2011a).

Immunomodulatory Activity

Oral administration of the hydroalcoholic flower extract at the doses 100 and 150 mg/kg body weight elicited an immunomodulatory response in rats (Yadav et al. 2011b). Administration of the flower extract was found to increase phagocytic

activity by stimulation of macrophages, total WBC and differential leukocytes count. Delayed-type hypersensitivity reaction was also stimulated by *Quisqualis indica* at the higher dose significantly indicating that the extract could stimulate the haematopoietic system.

Antitumour Activity

Efferth et al. (2008) identified 25-*O*-acetyl-23,24-dihydro-cucurbitacin F as a cytotoxic constituent of *Quisqualis indica* that possessed activity against tumour cells.

Anthelminthic Activity

Quisqualic acid (from *Q. indica* fruits) at 0.1 and 0.2 % w/v and kainic and α-allokainic acid at 0.025 and 0.05 % w/v were effective in causing cessation of movement but did not kill the worms (Ishizaki et al. 1973). Pyrantel pamoate at 10–6 and 10–4 w/v had a similar effect but was also proteolytic and fatal. Quintana et al. (1983) reported that clinical tests found that adults eating 8–10 dried seeds as a single dose significant reduced ova counts of *Ascaris* and *Trichiuris;* for 9–12-years-old 6–7 seeds; for 6–8 years old 5–6 seeds; for 4–5 years old 4–5 seeds; and that children below 3 years old should not be treated with the seeds.

Forty subjects with intestinal ascariasis., aged 2–12 years old, comprising 82 % with purely *Ascaris lumbricoides* ova and 17.5 % with mixed *Ascaris lumbricoides* ova and *Trichuris trichiura* ova, were assigned to *Quisqualis indica* (niyog-niyogan) treatment and pyrantel pamoate (combantrin) treatment group at random (Carpio 1997). Follow-up fecalyses after 7 days posttreatment revealed complete cure of 85 % for *Quisqualis indica* and 90 % for pyrantel pamoate. A second dose of the corresponding antihelmintic was given which resulted in complete eradication of ova. Ten percent of the *Quisqualis indica* group developed side effects as compared to 55 % of those given pyrantel pamoate. In a randomized double-blind controlled trial involving 135 children 3–7 years old, treatment of ascariasis using ipil-ipil (*Leucaena glauca*) and niyog-niyogan (*Mesua ferrea*) plant medicines significantly produced a change in the number of ova count before and after treatment (Bonagua 1998). Both ipil-ipil and niyog-niyogan were almost similar in their effectiveness with pyrantel pamoate. The treatment was safe without any untoward effects noted.

Larvicidal Activity

Quisqualis indica was reported to have larvicidal activity against *Aedes aegypti* mosquitoes but at comparatively high doses (LC_{50}>263 ppm and LC_{90}>562.3) (Kaushik and Saini 2009).

Central Nervous System CNS Activity

Quisqualic acid, an excitatory amino acid, had been reported to be an agonist for both AMPA ((S)-2-amino-3-(3-hydroxy-5-methyl-4-isoxazole) propionic acid)-subtype glutamate receptors and metabotropic glutamate receptors such as mGluR1, mGluR3 and mGluR4 (Jin et al. 2002; Kuang and Hampson 2006; Zhang et al. 2006). These receptors are tetrameric ion channels that mediate most of the fast excitatory synaptic transmission in the mammalian central nervous system. Quisqualic acid causes excitotoxicity and is employed in neuroscience to selectively damage cholinergic neurons in the brain or spinal cord (Unger and Schmidt 1992; Muir et al. 1993; Giovannelli et al. 1998). Quisqualic acid had been reported to cause neuronal damage and seizures in animals (Zaczek and Coyle 1982). Quisqualic acid induced neuronal necrosis and glial infiltration in the stratum and hippocampus of 7-day-old rat (pups) when intracerebrally injected (Silverstein et al. 1986). An intrahippocampal injection of quisqualic acid induced hippocampal seizure in unanesthetized cats (Funda et al. 1985). The authors suggested that a mild but constant epileptogenic potency of quisqualic acid had an advantage for an experimental model of temporal lobe epilepsy in man.

Kaijima et al. (1987) found that microinjection of quisqualic acid into unilateral amygdala in chronically implanted cats resulted in various types of limbic seizures. They asserted the strict dose dependency of quisqualic acid in the production of limbic seizures to be a valid advantage for an experimental model of a complex partial epilepsy in man. Numerous wet-dog shakes were associated with limbic seizures in the course of focal epilepsy induced by kindling stimulations or local injections of kainic or quisqualic acid and progressively disappeared during generalization (Rondouin et al. 1987). Addae and Stone (1988) found that pentobarbital and diphenylhydantoin blocked the effect of quisqualic acid in the rat cerebral cortex but only at concentrations higher than the therapeutically relevant levels. Studies showed that the chloroform fraction of a hot aqueous water extract of *Quisqualis indica* inhibited cyclic AMP phosphodiesterase by about 80 % (Thein et al. 1995).

Hippocampal CA1 pyramidal cell neurons were found to be sensitized over 30-fold to depolarization by L-2-amino-4-phosphonobutanoic acid (L-AP4) following exposure to L-quisqualic acid; the phenomenon was termed the QUIS effect (Subasinghe et al. 1992). Replacement of the oxadiazolidinedione ring of L-quisqualic acid with several other types of heterocyclic rings yielded the following quisqualic acid analogues: maleimide 2, *N*-methylmaleimide 3, *N*-(carboxymethyl)maleimide 4, succinimides 5A and 5B and imidazolidinedione 6, but none of these analogues were able to mimic the effects of L-quisqualic acid and sensitize hippocampal CA1 neurons to depolarization by L-AP4. Also none of the analogues were able to preblock or reverse the QUIS effect.

Antipyretic Activity

The methanolic leaf extract of *Quisqualis indica* was found to possess significant dose-dependent, antipyretic activity against brewer's yeast induced pyrexia in Wistar rats (Singh et al 2011). The animal group that received methanolic extracts 100 and 200 mg/kg showed significant decrease in rectal temperature from 38.40 to 37.44 and 38.99 to 37.49, respectively, as compared with the group that received aspirin, the standard drug.

Antitremor Activity

Studies in mice showed that systemic administration of excitatory amino acids, kainic acid and quisqualic acid could modify drug-induced tremor (Shinozaki et al. 1987). Kainic acid enhanced the tremor induced by tremorine but depressed the tremor induced by harmaline. Quisqualic acid depressed the tremor induced by both tremorine and harmaline in a dose-dependent manner. Kainic acid shifted the frequency of each component of the tremor induced by tremorine to the high-frequency side, but quisqualic acid did not affect the frequency of tremor of the tremor induced by tremorine. The frequency of tremor of the tremor induced by harmaline was shifted by both excitatory amino acids to the low-frequency side.

Toxicity Studies

Quisqualis indica seed has long been used in folk medicine as an ascaricide. Studies by Chivapat et al. (1998) found that mice receiving water extract equivalent to *Quisqualis indica* seed at the dose of 20.0 g/kg/day orally showed no acute toxicity and therefore LD_{50} was more than 20.0 g/kg/day. The subacute toxicity study in Wistar rats by administration of water extract equivalent to the seed at the doses of 0.2, 2.0, 6.0, 10.0 and 20.0 g/kg/day for 60 consecutive days showed that after receiving the extract equivalent to the seed of 6.0, 10.0 and 20.0 g/kg/day for 2 days, the animals showed abnormal clinical signs; the notable ones were clonic with tonic seizures followed by respiratory arrest and death. The percentages of rats presenting toxic symptoms and death at the doses of 6.0, 10.0 and 20.0 g/kg/day in male were 26, 53 and 80, respectively, and in female were 0, 6 and 80, respectively. All rats died after receiving the highest dose only for 3 consecutive days. The growth rate and feed

consumption of the survived rats receiving the extract for 60 days were not different from control group.

Traditional Medicinal Uses

In Vietnam, the fruits are used for treatment of ascariasis and oxyuriasis in children and for treating infantile malnutrition due to intestinal parasitosis; a decoction of the fruit is used as gargle for toothache (NIMM 1999). In Thailand the seeds are used as anthelminthic and leaf for healing of abscesses (Wetwitayaklung et al. 2008). In the Philippines, the fruit is used as vermifuge and the plant as cure for cough (PBI). According to BPI, seeds macerated in oil are applied to parasitic skin diseases in China, and seeds are also used as vermifuge. In the Moluccas and India, the seeds are given with honey as an electuary for the expulsion of entozoa in children; ripe seeds are roasted and administered for diarrhoea and fever (Chopra et al. 1986; Kirtikar and Basu 1989). In Malaysia, the fruits and leaves are used as vermifuge and the roots as so in Java (Burkill 1966). A plant decoction is used for diarrhoea in children. The Malays used the leaf juice as a lotion for boils and ulcers and the leaves are applied directly for headaches. Ripe seeds are sweet and if the ovary wall and seed coat are removed are pleasant to eat but there are cases of people becoming ill on eating only two or three. Excess causes drowsiness as the seeds are soporific. The fruits and the seeds are used in Nigeria, Ivory Coast and Gabon for their anthelmintic properties and to cure diarrhoea (Burkill 1985).

Other Uses

The plant is widely grown as a medicinal plant; as an ornamental over fences, pergolas and trellises; and as hedges in gardens and parks. In West Africa, the long, flexible stems are used for basketry, fish weir and fish traps (Dalziel 1955). The plant extract exhibited mild repellency against the female oriental fruit fly *Dacus dorsalis* (Areekul and Sinchaisri 1988) *Q. indica* extract exhibited anticoccidial effect against *Eimeria tenella* in chicken (Youn and Noh 2001).

Comments

Quisqualis indica can be propagated by leafless stem cuttings with at least three nodes: air layering and root division. Propagation from seed is easy, but fruits and seeds are seldom formed.

The plant is regarded as an emerging environmental weed in Northern Queensland and the northern parts of the Northern Territory and is a potential environmental weed or 'sleeper weed' in other warmer and wetter parts of Australia.

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Ipomoea alba

Scientific Name

***Ipomoea alba* L.**

Synonyms

Calonyction aculeatum (L.) House, *Calonyction aculeatum* var. *lobatum* (Hallier f.) C.Y. Wu, *Calonyction album* (L.) House, *Calonyction bona-nox* (L.) Bojer, *Calonyction bona-nox* var. *lobatum* Hallier f., *Calonyction pulcherrimum* Parodi, *Calonyction speciosum* Choisy, *Convolvulus aculeatus* L., *Convolvulus aculeatus* var. *bona-nox* (L.) Kuntze, *Convolvulus bona-nox* (L.) Spreng., *Convolvulus pulcherrimus* Vell., *Ipomoea aculeata* (L.) Kuntze, *Ipomoea aculeata* var. *bona-nox* (L.) Kuntze, *Ipomoea bona-nox* L.

Family

Convolvulaceae

Common/English Names

Evening Glory, Giant Moonflower, Good-Night Flower, Moon Flower, Moon-Flower, Moonflower, Moonflower Vine, Moon Vine, Moonvine, Prickly Ipomoea, Tropical White Morning Glory, Tropical White Morning-Glory, White Morning Glory, White-Flowered Morning Glory

Vernacular Names

Afrikaans: Maanblom
Brazil: Boa-Noite, Flor-Da-Lua, Jetirana-Branca (Portuguese)
Burmese: Kran-Hing
Chamorro: Alaihai-Tasi
Chinese: Yue Guang Hua, Yuek Kuang Hua
Czech: Povíjnice Bílá
El Salvador: Bejuco De Tabaco, Campanilla Blanca, Flor De Luna, Galán De Noche, Garza, Pitoreta (Spanish)
Fijian: Wa Ia
French: Liane Bla
German: Mondblüte Weiße Prunkwinde
Guatemala: Haapolin, Luna Blanca, Zutub (Spanish)
Hawaiian: Koali Pehu
Honduras: Panal De Niño (Spanish)
Japanese: Yakai-Sō, Yoru-Gao
Mexico: Camotillo, Haapolin, Nicua, Oración (Spanish)
Swedish: Månvinda
Thai: Ban Duek, Dok Phra Chan
Vietnamese: Bìm Trắng

Origin/Distribution

The species is indigenous to tropical and subtropical regions of the New World, from South America (French Guiana, Guyana, Surinam, Venezuela, Brazil, Bolivia, Colombia and Argentina) to Central America (Belize, Costa

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Rica, Guatemala, Honduras, Nicaragua, El Salvador, Panama, Mexico) and the Caribbean (Bahamas, Cuba, the Dominican Republic and Haiti) to Florida in the Southeastern United States.

The species has become widely naturalized in the tropical regions of the world, including Asia (Indonesia, Japan (Ryukyu Islands), Brunei, Malaysia, Myanmar, Nepal, New Guinea, Philippines, Sri Lanka, Thailand) and many Pacific islands (American Samoa, French Polynesia, Hawaii, Tonga, New Caledonia, Fiji and the Galapagos Islands) and in Australia—southeastern and central Queensland and the coastal districts of northern New South Wales. It has also naturalized in Lord Howe Island and Norfolk Island.

Agroecology

The species thrives in a warm and humid climate. This species has escaped cultivation and invaded watercourses, riparian areas, moist forests, urban bushland and disturbed areas (e.g. in parks and along roadsides and railway lines) in the subtropical and tropical regions of the world.

Edible Plant Parts and Uses

Bundles of unopened flowers are sold in the markets in Brunei where the people consumed it as vegetable (Ng 2011). Young leaves and fleshy calyces are cooked or steamed and eaten as a vegetable or used in curries, soups, stews, etc. (Facciola 1990). The immature seeds are also consumed. In China, leafy shoots and fleshy sepals are eaten as potherbs; dried flowers are used for soup and also in pastries in Yunnan (Hu 2005).

Botany

A scrambling or climbing perennial or annual herbaceous liana with twining, glabrous up to 10 m long stem with soft prickles and milky sap. Leaves are alternate, large, 10–20 by 5–16 cm, ovate to

Plate 1 Moon flower (Marlene Deller)

circular in outline, entire or slightly trilobed with acuminate to mucronulate tips and cordate bases, glabrous and borne on 5–20 cm long petioles. Inflorescences in axillary helicoids cymes, 1-several flowered, peduncle stout and bracts small and deciduous. Flowers are nocturnal, fragrant, slightly zygomorphic and borne on 7–15 cm long pedicels. Sepals 5, elliptic to ovate, leathery, glabrous and strongly mucronate. Corolla salverform (trumpet shaped), tube greenish white, 7–12 cm long and 5 mm in diameter, lobes white, spreading, shallowly 5-undulate (Plate 1). Stamens 5, white and exerted. Style exserted with bilobed stigma. Ovary narrowly conical and glabrous. Fruit an ovoid capsule, 2.5–3 cm, apiculate. Seeds white, brown or black and glabrous.

Nutritive/Medicinal Properties

Nutritive information on the edible flower has not been analysed. Of six *Ipomoea* species, *Ipomoea alba* had the highest nectar volume secreted per flower (50.12 µl), while in the other taxa, it ranged from 2.42 to 12.00 µl (Galetto and

Bernardello 2004). All nectar samples contained amino acids and sugars. Most species had sucrose-dominant nectars. Mean nectar sugar concentration throughout the lifetime of the flower ranged from 34.28 to 39.42 % for four species including *I. alba*, except for *I. cairica* (49.25 %) and *I. rubriflora* (25.18 %).

Ipalbine, a new hexahydroindolizine alkaloid, ipalbidine and an unidentified minor alkaloid were isolated from *I. alba* seeds (Gourley et al. 1969). Three new resin glycosides, albinosides I–III, were isolated and purified from a chloroform-soluble extract of *Ipomoea alba* seeds (Cruz-Morales et al. 2012). Compounds 1–3 were found to be partially acylated branched pentasaccharides derived from three new glycosidic acids (albinosinic acids A–C).

A plant growth regulator calonyctin A was isolated from the dried leaves (Fang et al. 1993). Each molecule comprises two hydroxy fatty acid residues 3-hydroxy-2-methylbutanoic acid and 11-hydroxytetradecanoic acid or 11-hydroxyhexadecanoic acid and four 6-deoxyhexose units (three of quinovose and one of rhamnose) containing a tetrasaccharide. The long-chain hydroxy acid is linked glycosidically through its O-11 to Qui D and esterified to O-2 of Qui C, forming a macrocyclic lactone. The 3-hydroxy-2-methylbutanoic acid is ester-linked to O-3 of Qui C.

Studies showed that an organic extract obtained from *Ipomoea alba* did not show any positive influence on the progression of ligature-induced periodontitis in Wistar rats when administered according to the regimen used in the study (Barrella et al. 2012). Morphometrical analysis demonstrated that topically administered extract showed no effect on reducing bone loss when compared with the control group. In addition, the extract did not present toxicity in the single- and multidose acute toxicity assays.

The whole plant is used in treating snakebite in folkloric medicine.

Other Uses

The ancient Mesoamerican civilizations used the sap of *Ipomoea alba* morning glory vine containing organic compounds to coagulate the latex from the *Castilla elastica* tree and the guayule plant to produce bouncing rubber balls (Wildman et al. 1943; Hosler et al. 1999). These ancient peoples' control over the properties of latex and processed rubber gave rise to the Mesoamerican ball game, a central ritual element in all ancient Mesoamerican societies.

The species is widely cultivated as an ornamental plant for its flowers. In areas too cold for winter survival, it can be grown as an annual plant. Since it is of tropical origin, it flowers best under a summer short day photoperiod.

Comments

In some countries, moonflower is deemed as an invasive species as it can cause problems in agricultural production areas. Moonflower (*Ipomoea alba*) is regarded as an environmental weed in New South Wales and Queensland. It has the potential to become a serious weed of rainforest gaps and margins and wet sclerophyll forests and riparian areas throughout the coastal districts of Queensland and northern New South Wales.

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Cheilocostus speciosus

Scientific Name

***Cheilocostus speciosus* (J. Koenig) C.D. Specht**

Synonyms

Banksia speciosa J. Konig, *Banksia speciosa* Koenig nom. illeg., *Costus sericeus* Blume, *Costus speciosus* (J. Koenig) Sm., *Banksia speciosus* J. König, *Costus formosanus* Nakai, *Costus speciosus* var. *hirsutus* Blume, *Costus speciosus* var. *leocalyx* Nakai, *Costus spicatus* var. *pubescens* Griseb., *Hellenia grandiflora* Retz. nom. illeg., *Planera speciosa* Giseke, *Tsiana speciosa* J.F. Gmel

Family

Costaceae, also placed in Zingiberaceae

Common/English Names

Cane reed, Crape Ginger, Crepe Ginger, Elegant Costus, Malay Ginger, Spiral Flag, Spiral Ginger, White Costus, Wild Ginger

Vernacular Names

Arabic: Quste Talkh
Chinese: Zhang Liu Tou
French: Costus Elegant
German: Kostus, Kostwurz, Kreppingwer, Malayischer Ingwer, Prachtige Kosturz, Pritge Kostwurz
India: Jamlakhuti (Assamese), Keu, Orop, Kenw, Kemuk, Kewa (Bengali), Pakarmula (Gujerati), Keu, Keukand Kebu, Keyu, Kust, Mahalakri (Hindi), Aarathi Kundige, Benne Kundige, Cangalakoshta, Changal Kostha, Changalakoshta, Changala Koshta, Chikey, Chikke, Cikke, Korikattu, Korikottu, Korikuttu, Kundige Gida Niraja, Neeraja, Padmapatra, Pushkaramoola, Pushkaramula, Pushkarmoola, Vyaadi (Kannada), Channakkoova (Kerala), Anakkuva, Anappu, Canna, Cannakkilannu, Cannakkuva, Cannakkuvva, Channa, Channak-Koova, Channakkuva, Channakuva, Koshtam, Kottam, Marujanna, Narikkurampu, Narumcanna, Narunchana, Maruncanna, Marunchanna, Nariccanna, Narikarambu, Naruncana, Onapoovu, Patimukam, Pushkaramulam, Tjanakua, Tsjana-Kua, Tsjanakua (Malayalam), Khongbam Takhelei (Manipuri), Naagaali, Penva, Pinnga, Pinnaga, Pushkarmoola, Pushkarmula (Marathi), Sumbul (Mizoram), Kevukanda, Sumbul (Oriya), Bramhatirtha, Canda, Kashmeera, Kashmira, Kasmira, Kemuka, Kottam, Kushtha, Kushthabheda, Padmakarna, Padmapatra, Padmapatramulira, Padmapunya, Padmavarnaka, Paushkara, Pushkara, Pushkarajata, Pushkaramula, Pushkaramulaka, Pushkarashifa, Sagara, Shulaghna, Shura,

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Shvasari, Subandhu, Virapushkaravhaya, Vrkisharuha (Sanskrit), Cancamancam, Catikostam, Cetamakam, Cikarappati, Cikarappatikam, Cilatarattinam, Cirakapali, Cirakapati, Cirakapatiakm, Ciram, Itapavanati, Kacumiram, Koestam, Kostam, Kosthum, Kottam, Kottilam, Kudavam, Kugaimanjal, Kukaimancal, Kumam, Kupam, Kuperam, Kura, Kurampai Kuravam, Kurutupalam, Kuttaiyidukki, Kutavan, Kutcim Kutikam, Kuttam, Kuttamam, Kuttapam, Kuttarokovakkini, Kuttiyitukki, Kutti, Kuttu, Malaivacampu, Malaivacapancam, Malaivasambu, Mukkili, Oli, Palakam, Palkostam, Panpakappu, Pappayam, Pari, Paripaviyam, Perunkurumpai, Pillaikkocam, Pulakkaram, Pulkkaram, Punakkam, Putkaram, Tattan, Tatti, Tomapalam, Tuttai, Ubariyavi, Urpalam, Vamananitam, Vappiyam, Vappuyam, Vayinarutatayam, Vellaikkostam, Vengottam, Venkostam, Vintiyavacani, Vintiyavacini, Viranari, Viyacitam, Viyappirayam, Viyappiyam, Viyati (Tamil), Bhangalkoshta, Bogachchikadumpalu, Bommakachchika, Bommakachhika, Bommakaccika, Bommakachika, Cengalvakoshtu, Chengalvakoshtu, Kaashmeeremu, Kashmeeramu, Kashmiramu, Kasmiramu, Kevukinna, Kimuka, Koshtamu, Kushthamu, Paaribhavyamu, Paribhavayamu, Paribhavyamu, Pushkaramoolam, Pushkaramulam, Pushkaramulamu, Vana Vaasa (Telugu)

Indonesia: Kelachin, Tebu Tawar (Bangka), Statjing, Tabar-Tabar (Java), Setawar, Tawa-Tawa (Sumatra), Paching, Paching Tawar, Tepung Tawar (Sundanese)

Kwara'ae: Okaoka, Wakawaka

Laos: Uangz, Uang

Malaysia: Sempulang Padi (Iban), Pejujot, Jujut (Bidayuh), Tawar-Tawar (Kedayan), Setawar, Setengteng, Tawar, Tawar-Tawar, Teng

Nepali: Kayew

Palauan: Isebsab

Philippines: Tabubungiau (Bisaya), Alusani, Tubong-Usa, Tiuasi

Thailand: Kushta, Uang-Phetma, Uang-Yai, Uang-Maina

Sri Lanka: Thebu

Swedish: Spiralkostus

Vietnam: Cát Lồi, Chóc, Đót Đắng, Đọt Hoàng, Mía Dò, Sẹ Vàng

Yapese: Sauer

Origin/Distribution

The species is indigenous to Peninsular Malaysia in Southeast Asia. It has been introduced and naturalized elsewhere in the tropics and also cultivated in subtropical areas. It is found in India, Antilles, Bhutan, Nepal west to south China (Guangdong, Guangxi, Taiwan, Yunnan), Indo-China, New Guinea, Australia, Hawaii and the Pacific islands.

Agroecology

In its native range, it grows wild in wet places in forest margins, mountainous regions, valleys and roadsides from near sea level to 1,700 m. It thrives in a tropical climate in areas of high humanities under partial shade on moist fertile soils.

Edible Plant Parts and Uses

The young, tender leafy shoot and young leaves are eaten as vegetables. The tender shoots when boiled in coconut milk makes a good vegetable (Burkill 1966). In Sarawak, they are fried with anchovies and 'belachan' (Voon et al. 1988; Voon and Kueh 1999). The outer part of the stem is peeled before cooking. The flowers are edible (Chan 1998) in salad or as garnish.

Rhizome of *C. speciosus* is edible (Burkill 1966) and used after cooking and are used for making syrup, and the young shoots are used as vegetable by tribals (Singh 2011). The rhizome is cooked in curies with salt, chilli, tamarind and turmeric powder and the stem crushed to yield a juice by the tribal communities in the Parambikulam Wildlife Sanctuary, Kerala, India (Yesodharan and Sujana 2007).

Botany

Erect, perennial herb growing to 1–3 m high with slightly woody base, stem slender and reddish and apex branched and spirally twisted when old. Rhizome stout, creeping horizontally. Leaves lower part surrounding the stem, tomentose, arranged in a spiral when young (Plate 1). Petiole 5–7 mm; leaf blade oblong or lanceolate, 15–20×6–10 cm, abaxially densely sericeous, base subglobose, apex acuminate or caudate-acuminate, green (creamy-white coloured in variegated cultivar) (Plate 4). Inflorescences terminal paniculate spikes, ellipsoid or ovoid, 8–15 cm; bracts bright red, ovate, 2 cm, leathery, pubescent, bracteoles pale red (Plate 2) with white flowers. Calyx tubular, red, 1.8–2 cm, apex 3 lobed. Corolla tube funnel shaped, 1 cm; lobes oblong-elliptic, 5 cm, apex white or red. Labellum white, trumpet shaped, 6.5–9 cm, apex toothed and crisped, with edges overlapping (Plate 3). Stamen petaloid, white with orange-yellow base, urceolate, pubescent. Ovary glabrous. Capsule red, globose, 1.5 cm, slightly woody with accrescent calyx. Seeds numerous black, glossy.

Nutritive/Medicinal Properties

Leaf Nutrients and Phytochemicals

The proximate nutrient composition of the leaves of *Costus speciosus* per100 g edible portion based on analyses made in Sarawak (Voon et al. 1988; Voon and Kueh 1999) was water 80.7 %, energy 69 kcal, protein 2.3 %, fat 1.9 %, carbohydrates 10.6 %, crude fibre 2.3 %, ash 2.2 %, P 15 mg, K 587 mg, Ca 114 mg, Mg 44 mg, Fe 2.6 mg, Mn 151 ppm, Cu 22.2 ppm and Zn 4.3 ppm. *C. speciosus* leaves were found to contain 18 % protein, 46 mg Fe, 81 mg ascorbic acid, 660 μg β-carotene,

Plate 1 Sessile leaves spirally arranged

Plate 2 Terminal inflorescence with red bracts and white flower

Plate 3 Close-up of flower

Plate 4 Variegated cultivar

149 mg α-tocopherol, 75 mmol of GSH (glutathione), 4.4 g total phenols and 0.848 mg/g extract of flavonoids (Vishalakshi Devi and Urooj 2010). α-amyrinsterate, β-amyrin and lupeol palmitates were isolated from the leaves (Pai and Kulkarni 1997). The leaves of *C. speciosus* were found to accumulate phytoalexins glyceollin II and II when inoculated with a nonpathogenic strain of the fungus *Drechslera longirostrata* (Kumar et al. 1984). Flavonoid contents found in the leaves were rutin 849–1,809 μg/g, quercitrin 874–3,719 μg/g and quercetin 0—308 μg/g (Chang et al. 2012).

Flower Phytochemicals

Chang et al. (2011) developed a surface -assisted pressurized liquid extraction for determination of flavonoids in the flowers. Flavonoid contents found in the flowers were rutin 3,476–4,251 μg/g, quercitrin 5,375–8,475 μg/g and quercetin 127–374 μg/g (Chang et al. 2012).

Seed Phytochemicals

The fixed oil of seed was found to contain palmitic acid 26.9 %, stearic acid 8.3 %, oleic acid 409.5 %, linoleic acid 20.9 %, arachidic acid 1.7 %, gadoleic acid 0.7 % and behenic acid 2 % (Nainan et al 1979). Seeds were reported to yield 6.0 % of a sweet smelling fatty oil which may find use in perfume industries (Suri et al. 1986). The fatty oil contained 55.97 % palmitic acid and 23.75 % oleic acid besides other fatty acids. The defatted seeds contained 1.91 % diosgenin (an important raw material for synthesis of steroidal hormones) and three sugars, i.e. glucose, galactose and rhamnose. *Costus speciosus* seeds were reported to contain on an average 2.4 % diosgenin on dry weight basis, thereby making the seeds desirable for commercial exploitation (Singh et al. 1982). Gamma-tocopherol was isolated from the seeds (Mahmood et al. 1985). From the seeds, an oil 8.3 % comprising palmitic and oleic acids together with diosgenin and two unidentified triterpenoids were isolated (Dixit and Srivastava 1987).

Two furostanol saponins, of costusoside I and costusoside J, were isolated from the seeds and their structures elucidated as 3-*O*-{β-D-glucopyranosyl (1 → 2)-α-L-rhamnopyranosyl (1 → 2) [α-L-rhamnopyranosyl (1 → 4)]-β-D-glucopyranosyl}-26-*O*-(β-D-glucopyranosyl) -22α-methoxy (25 *R*)-furost-5-en-3β, 26-diol and its 22-hydroxy compound, respectively (Singh and Thakur 1982a). β-sitosterol-β-D-glucopyranoside; prosapogenins A and B of dioscin; dioscin; gracillin; 3-*O*-[α-l-rhamnopyranosyl (1 → 2)-β-D-glucopyranosyl]-26-*O*-[β-D-glucopyranosyl]-22α-methoxy-(25R) furost-5-en-3β,26-diol; protodioscin and methyl protodioscin (Singh and Thakur 1982b). 3-*O*-[α-L-rhamnopyranosyl(1 → 2)-β-D-glucopyranosyl]-26-*O*-[β-D-glucopyranosyl]-22α-methoxy-(25R) furost-5-en-3β,26-diol on complete acid hydrolysis yielded diosgenin (44.8 %), D-glucose and L-rhamnose. Partial

hydrolysis of the same saponin afforded prosapogenin identified as trillin. Methyl hexadecanoate, methyl octadecanoate and tetracosanyl octadecanoate (Singh and Thakur 1984) were isolated from the seeds. In addition to α-tocopherolquinone and 5α-stigmast-9(11)-en-3β-ol, two benzoquinones were isolated from the seeds and characterized as 6-methyl dihydrophytylplastoquinone (2,5,6-trimethyl-3-(3,7,11,15-tetramethylhexadecyl)-1,4-benzoquinone) and dihydrophytylplastoquinone (5,6-dimethyl-3-(3,7,11,15-tetramethylhexadecyl)-1,4-benzoquinone), respectively (Mahmood et al. 1984).

Rhizome/Root Nutrients and Phytochemicals

Nutritive composition of the rhizome was reported as energy 286.52 g cal, moisture 89.91 %, total carbohydrate 44.51 %, crude protein 19.2 %, oil 3.52 %, fibre 12.77 %, starch 31.65 %, ascorbic acid 22.5 mg/100 g, N 3.14 %, P 0.06 %, K 1.42 %, Na 0.28 %, Mg 0.19 % and Ca 1.72 % (Singh 2011). Phenolic acid contents in the rhizomes were salicylic acid 1.79 μg/g, vanillic acid 4.79 μg/g and ferulic acid 2.34 μg/g. Diosgenin content from five different localities ranged from 0.138 to 2.73 %. Antinutrient contents in the rhizome were tannins 0.03 %, phenols 0.65 % and oxalate 0.03 %.

The rhizomes were found to contain alkaloids, flavonoids, cardiac glycosides, saponins, sterols and tannins anthra-glycosides, arbutin, bitter principle, essential oils, coumarins, phenols, carboxylic acids, valepotriates, anthraquinones, steroids and sterols (Saraf 2010).

Rhizomes were found to contain 2.12 % free diosgenin in 3.86 % of total sapogenins and also tigogenin (Dasgupta and Pandey 1970). Rhizomes were found to contain lanosterol and stigmasterol and the stem callus diosgenin (Rathore and Khanna 1979); gracillin and dioscin (Tschesche and Pandey 1978). Gupta et al. (1981a) found diosgenin to be distributed in all parts of the plant besides the rhizomes. Methyl triacontanoate, diosgenin, sitosterol and two aliphatic hydroxyketones characterized as 24-hydroxyhentriacontan-27-one and 24-hydroxytriacontan-26-one (Gupta et al. 1981b), a sterol 5α-stigmast-9(11)-en-3β-ol (Gupta et al. 1981c), 8-hydroxytriacontan-25-one and methyl triacontanoate (Gupta et al. 1982), β-sitosterol-β-D-glucoside, dioscin, gracillin and prosapogenins A and B of dioscin (Gupta et al. 1986) were isolated from the roots. The rhizome was found to contain an antifungal principle identified as the methyl ester of *p*-coumaric acid (Bandara et al. 1988). Methylprotodioscin (furostanol saponin) (Agrawal et al. 1984) and curcumin (Gaitonde and Sapre 1989) were isolated from the rhizome. Five compounds were isolated from the rhizomes and characterized as tetradecyl 13-methylpentadecanoate, tetradecyl 11-methyltridecanoate, 14-oxotricosanoic acid, 14-oxoheptacosanoic acid and 15-oxo-octacosanoic acid together with triacontanol, 5α-stigmast-9(11)-en-3β-ol, triacontanoic acid, sitosterol and diosgenin (Gupta et al. 1986). Bis(2-ethylhexyl)phthalate was isolated from the rhizomes (Farooqui and Shukla 1987). Five steroidal saponins were isolated from the rhizome and elucidated as daucosterin; diosgenin-3-*O*-α-L-rhamnopyranosyl (1 → 2)-β-D-glucopyranoside; diosgenin-3-*O*-α-L-rhamnopyranosyl (1 → 2) [α-L-rhamnopyranosyl (1 → 4)]-β-D-glucopyranoside; diosgenin-3-*O*-α-l-rhamnopyranosyl (1 → 2) [β-D-glucopyranosyl (1 → 3)]-β-D-glucopyranoside; and C22-methoxyl, C26-β-D-glucopyranosyl, C22-methoxyl-25 (R)-furost-5-ene-3β and 26-diol-3-*O*-α-L-rhamnopyranosyl (1 → 2) [β-D-glucopyranosyl (1 → 3)]-β-D-glucopyranoside (Chen and Yin 1995).

Eight steroid glycosides were isolated from a methanol extract of underground parts (Inoue et al 1995). Six of them were known glycosides prosapogenin-B of dioscin, dioscin, gracillin, methyl protodioscin, methyl protogracillin and protogracillin, and the remaining two comprised a furostanol monoglycoside, 26-*O*-β-D-glucopyranosyl-(25R)-furost-5-ene-3β, 22ζ, 26-triol, and the other a glycoside diosgenin 3-*O*-β-D-glucopyranosyl (1 → 3)-β-D-glucopyranoside. Six compounds were isolated from the rhizome and elucidated as diosgenin, prosapogenin B of dioscin, diosgenone, cycloartanol, 25-en-cycloartenol and octacosanoic acid (Qiao

et al. 2002). Jahfar et al. (2008) found the steroidal sapogenin, diosgenin, in the rhizomes and costunolide was isolated from the hexane extract of *C. speciosus* root (Eliza et al. 2009).

Furostanol glycoside 26-*O*-β-glucosidase, dimeric with a native apparent molecular weight of 110,000, was purified from the rhizome (Inoue and Ebizuka 1996). This enzyme was highly specific for cleavage of the C-26-bound glucose moiety of furostanol glycosides. They found that glucono-1,5-lactone, a typical β-glucosidase inhibitor, and diosgenin, an aglycone of spirostanol glycosides, strongly inhibited the enzyme activity. Flavonoid contents found in the rhizomes were rutin 2,387–3,942 μg/g, quercitrin 934–9,064 μg/g and quercetin 180–283 μg/g (Chang et al. 2012).

Plant Phytochemicals

A close relationship was found between chlorophyll, soluble nitrogen, total nitrogen and reducing sugar contents with diosgenin content; however, nonreducing sugar decreased with the increase in above parameters as well as diosgenin and other metabolites (Mandal and Chatterjee 1985). Zinc inhibited whereas iron and molybdenum promoted the content of diosgenin in *Costus speciosus.* Studies found that squalene metabolized into 5α-stigmast-9(11)-en- 3β-ol (I) via $\Delta^{9(11)}$lanosterol rather than $\Delta^{8(9)}$lanosterol in *C. speciosus* (Akhila et al. 1987). Radioactive-labelled studies by Akhila and Gupta (1987) found that diosgenin was biosynthesized in leaves and then translocated to all the parts of the plant. Glycosidation of diosgenin occurred in all the parts of the plant and diosgenin glycosides were stored in rhizomes, seeds and flowers. Deglycosidation of saponin was observed only in the rhizomes indicating that some enzymes present in the rhizome were responsible for the hydrolysis. 3-*O*-[β-D-glucopyranosyl-(1″ → 2′)-β-D-glucopyranosyl], 27-*O*-β-D-glucopyranosyl-(25R)-spirost-5-ene-3β,27-diol was isolated from cell suspension cultures of *Costus speciosus,* following incubation with diosgenin (Indrayanto et al. 2001). *Costus speciosus* was reported to produce large quantity of steroidal glycosides derived from the sole aglycone, diosgenin and cycloartenol; a product of oxidosqualene cyclase (OSC) was postulated to be a common intermediate for phytosterols of primary metabolism and diosgenin of secondary metabolism (Kawano et al. 2002).

Antioxidant Activity

In the DPPH assay, the benzene plant extract showed maximum activity with $IC_{50} = 15.30$ μg/ml and no significant change when compared with standard ascorbic acid, which had IC_{50} of 16.14 μg/ml (Nehete et al. 2010). In the total antioxidant capacity test, the methanol and benzene extract showed maximum activity with IC_{50} values of 13.43 and 12.58, respectively. The total antioxidant capacities of extracts were calculated based on the formation of phosphomolybdenum complex that was measured spectrophotometrically at 695 nm. In nitric oxide radical scavenging activity, the benzene extract showed maximum activity with $IC_{50} = 12.56$ μg/ml. In the iron chelating activity, benzene extract showed maximum activity with $IC_{50} = 13.41$ μg/ml as compared with ascorbic acid $IC_{50} = 6.9$ μg/ml. In the hydroxyl radical activity assay, the benzene extract showed maximum activity with $IC_{50} = 13.46$ μg/ml compared with 4.63 μg/ml of ascorbic acid. The phenolic content of the benzene extract showed good correlation coefficient (R^2) for all antioxidant methods. The chloroform leaf extract was shown to have free radical scavenging activity (Chakraborthy 2009). Extracts of various parts of *C. speciosus* showed significant antioxidant activity, which was partially related to its high polyphenolic content (Vijayalakshmi and Sarada 2008).

The total antioxidant capacity of the rhizome was 82.88 mg ascorbic acid equivalent/g plant extract g, total phenols 93.95 mg GAE/g plant extract and total flavonoids 9.32 mg/g quercetin/g plant extract (Jha et al. 2010). IC_{50} values of *C. speciosus* rhizome methanol extract and ascorbic acid were 50.38 and 33.32 μg/ml, respectively, in the DPPH scav-

enging assay. In the NO scavenging assay, IC_{50} value for the methanol rhizome extract was 97.74 µg/m and the IC_{50} values for ascorbic acid and quercetin were higher, 18.63 and 15.97 µg/ml, respectively. Administration of either costunolide (20 mg/kg day) or eremanthin (20 mg/kg day) from *C. speciosus* rhizome, for 60 days, caused a significant reduction in thiobarbituric acid reactive substances (TBARS) level and a significant increase in reduced glutathione (GSH) content along with increased enzymatic activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) in the treated streptozotocin (STZ)-induced diabetic rats when compared to untreated diabetic rats (Eliza et al. 2010). Acute toxicity test revealed the non-toxic nature of the compounds. The results indicated the protective effect of costunolide and eremanthin from oxidative stress.

Antidiabetic Activity

Studies showed that *C. speciosus* rhizome has no significant effect in the fasting or postprandial state when freeze-dried rhizome juice was fed simultaneously with glucose in non-diabetic rats; however, when fed 30 minutes before the glucose load, it showed hypoglycaemic effect (Mosihuzzaman et al. 1994). In NIDDM (non-insulin-dependent diabetes mellitus) rats, *C. speciosus* showed significant hypoglycaemic effect when the juice was fed with simultaneous glucose load. *Costus speciosus* root extract was found to possess antihyperglycaemic, antihyperlipaemic and antioxidative effects (Bavarva and Narasimhacharya 2008). Oral administration of 300 and 450 mg/kg BW of the ethanol root extract to alloxan-diabetic rats produced a reversal of diabetes and its complications. Both doses significantly lowered blood glucose concentration (26.76, 34.68 %), increased glycogenesis and decreased gluconeogenesis, reverting glucose metabolism towards normalcy. Both doses also reversed the hyperlipidaemia by reducing plasma total lipid (12.87, 178.24 %), cholesterol (21.92, 30.77 %) and triglyceride (25.32, 33.99 %) and improved hepatic antioxidant enzyme activities. The high dose (450 mg/kg BW) was found to have more potential antioxidant activities compared with glibenclamide. Another study showed that the hexane rhizome extract had antihyperglycaemic and hypolipidaemic activity and was able to ameliorate the diabetic state of STZ-induced male diabetic Wistar rats (Daisy et al. 2008). Oral administration of hexane extract significantly decreased plasma glucose level; glycosylated haemoglobin (HbA_{1c}), serum total cholesterol and triglyceride levels; urea; uric acid; and creatinine and at the same time markedly increased plasma insulin, tissue glycogen, serum protein and high-density lipoprotein (HDL) cholesterol levels. The hexane crude extract also restored the altered plasma enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and acid phosphatase (ACP) levels to near normal. The hexane crude extract was found to be more active in comparison with the ethyl acetate and methanol rhizome extracts. Oral administration of costunolide from *C. speciosus* roots to streptozotocin-induced diabetic male Wistar rats significantly reduced plasma glucose in a dose-dependent manner when compared to the control (Eliza et al. 2009). In addition, oral administration of costunolide (20 mg/kg bw) significantly decreased glycosylated haemoglobin (HbA(1c)), serum total cholesterol, triglyceride and LDL cholesterol and at the same time markedly increased plasma insulin, tissue glycogen, HDL cholesterol and serum protein. Costunolide restored the altered plasma enzyme (aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphatase and acid phosphatase) levels to near normal. The results indicated that costunolide possessed normo-glycaemic and hypolipidaemic activity.

In a separate study, administration of chloroform, methanol and aqueous extracts of *C. speciosus* rhizomes to overnight-fasted, streptozotocin-induced diabetic rats significantly reduced blood glucose level (Rajesh et al. 2009). Similar studies conducted with oral

glucose tolerance test (OGTT) confirmed the above findings, suggesting that aqueous extract and methanol extracts of *C. speciosus* were highly effective in lowering blood glucose level comparable to glibenclamide. Results from multiple dose studies wherein the drug was administered for 14 days also confirmed the above findings, and the serum lipid profiles high-density lipoproteins (HDL), low-density lipoproteins (LDL) and very low density lipoproteins (VLDL) were found to be optimum in aqueous or methanol extracts on par with normal healthy rats or standard drug glibenclamide-treated rats.

Antihypercholesterolaemic Activity

Supplementation of the rat diet with diosgenin for a week inhibited cholesterol absorption as determined by the serum isotope ratio technique, as well as by measuring in the faeces the amount of unabsorbed radioactivity from orally administered [3H]cholesterol (Cayen and Dvornik 1979). Diosgenin suppressed the serum and liver uptake of radioactivity from co-administered [3H]cholesterol as well as the accumulation of liver cholesterol in the cholesterol-fed rat and was substantially more active than cholestyramine or β-sitosterol. Diosgenin decreased the elevated cholesterol in serum LDL and elevated cholesterol in the HDL fraction of cholesterol-fed rats but had no effect on serum cholesterol in normocholesterolaemic rats. In contrast to cholestyramine, diosgenin markedly increased neutral sterol excretion without altering bile acid excretion; in-vitro, diosgenin had no effect on bile acid binding. Diosgenin treatment increased hepatic and intestinal cholesterol synthesis as well as the activity of hepatic HMG CoA reductase. Diosgenin had no effect on cholesterol synthesis when added to normal rat liver homogenates. The increased unabsorbed cholesterol together with enhanced secretion of cholesterol into bile resulted in enhanced excretion of neutral sterols without affecting the biliary and fecal discharge of bile acids.

Anticancer Activity

All the tested plant extracts showed significant antioxidant and antiproliferative activities in human colon adenocarcinoma cell lines (COLO 320 DM) in a concentration- and time-dependent manner in the following descending order: *Asclepias curassavica* > *Cynodon dactylon* > *Costus speciosus* root > *Amaranthus tristis* > *Merremia emarginata* > *Ophiorrhiza mungos* > *Tabernaemontana heyneana* > *Blepharis maderaspatensis* > *Aegle marmelos* > *Achyranthes aspera* (Baskar et al. 2012).

Diosgenin, a steroidal sapogenin with oestrogenic and antitumour properties, was found to inhibit human chronic myelogenous leukaemia K562 cells proliferation via cell cycle G2/M arrest and apoptosis, with disruption of Ca2+ homeostasis and mitochondrial dysfunction playing vital roles (Liu et al. 2005). The antiapoptotic Bcl-2 and Bcl-xL proteins were downregulated, whereas the proapoptotic Bax was upregulated.

Hepatoprotective Activity

The rhizome extract exhibited significant hepatoprotective activity (Verma and Khosa 2009b). Administration of an ethanolic rhizome extract to carbon tetrachloride-treated rats resulted in a significant decrease in serum glutamic oxaloacetic acid transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (ALKP), serum bilirubin (SBLN) and liver inflammation. This was supported by histopathological studies on the liver.

Antiinflammatory/Antiarthritic Activity

Studies showed that costunolide, from *Costus speciosus* root, inhibited proinflammatory cytokines and iNOS in activated murine BV2 microglia stimulated with lipopolysaccharide (Rayan et al. 2011). Costunolide attenuated the expression of tumour necrosis factor-alpha, interleukin-

1,6, inducible nitric oxide synthase, monocyte chemotactic protein 1 and cyclooxygenase 2 in activated microglia. Further, costunolide suppressed MAPK pathway activation by inducing MKP-1 production. The results suggested that costunolide exhibited an ability to inhibit expression of multiple neuroinflammatory mediators attributable to its inhibition of NFkappaB and MAPK activation and may have potential in the treatment of neuroinflammatory diseases.

The ethanolic rhizome extract of *Costus speciosus* was found to possess antiinflammatory activity (Binny et al. 2010). Significant anti-inflammatory effect was found against carrageenan-induced oedema formation in rats at a dose of 800 mg/kg and against cotton pellet granuloma formation in rats at doses of 400 and 800 mg/kg. It showed slight antipyretic property at 800 mg/kg dose in yeast-induced pyrexia in rats. *Costus speciosus* was found to have significant anti-arthritic properties in Freund's adjuvant-induced arthritis test in adult Albino rats (150–200 mg) (Srivastava et al. 2012). The methanol extract of aerial plant parts in doses of 400 and 800 mg/kg showed 75.50 and 68.33 % protection against increase in rat paw oedema, respectively.

Antinociceptive Activity

The aqueous and ethanol rhizome extracts of *C. speciosus* exhibited significant peripheral antinociceptive actions against acetic acid-induced writhing in Swiss albino mice (Bhattacharya and Nagaich 2010). The aqueous extract significantly inhibited writhes at the dose of 75 and 150 mg/kg body weight, while ethanol extract produced significant protection at the dose of 150 mg/kg body weight. However, in the tail-flick method, only the ethanol extract showed significant central analgesic action, while the aqueous extract was totally ineffective.

Antimicrobial Activity

Among the plants tested, *Costus speciosus* and *Calendula officinalis* showed the highest antidermatophytic activity of 0.24 and 0.27 mg/ml, respectively, against *Trichophyton rubrum* and *Trichophyton mentragrophytes* obtained from patients having skin diseases (Malabadi and Kumar 2005). Ethanol extracts of plants exhibited more activity than water extracts. Hexane and methanol extracts of leaf and rhizome extracts of *C. speciosus* but not the water extracts exhibited antibacterial activity against pathogens isolated from infected burn patients (*Shigella, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas, Bacillus subtilis* and *Salmonella* sp.) (Malabadi 2005). The results were comparable to the conventional antibiotic cream, namely, silver sulphadiazine. *p*-coumaric acid methyl ester was found in the rhizome of *C. speciosus* as a constitutive principle with antifungal activity against plant pathogenic fungi *Cladosporium cladosporioides, Colletotrichum gloeosporioides, Curvularia* sp. and *Penicillium* sp. (Bandara et al. 1988). Antifungal activity of steroid saponins and sapogenins from *C. speciosus* was investigated by Singh et al. (1992) on six species of plant pathogenic fungi at different concentrations. Saponin B was found to be highly effective against conidial germination of *Botrytis cinerea* and *Alternaria* sp.

The water extract of *C. speciosus* rhizome was found to inhibit the growth of *Staphylococcus aureus* (Swarnkar and Katewa 2009). *Costus speciosus* (stem and flower) extract exhibited antituberculosis activity with MIC of 800 µg/ml against *Mycobacterium tuberculosis* H37Rv (Mohamad et al. 2011). The aqueous rhizome extract showed antibacterial activity against *Staphylococcus aureus* (Saraf 2010).

C. speciosus rhizome extract was found to be active against pathogenic strains of Gram-positive (*Staphylococcus aureus*, *Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa, Salmonella typhimurium*) bacteria, and its activity was compared to the standard antibiotic gentamicin (Ariharan et al. 2012). Antimicrobial activities were observed in hexane, chloroform, ethyl acetate and methanol extracts of *C. speciosus* rhizome (Duraipandiyan et al. 2012). The methanol rhizome extract inhibited the growth of *Staphylococcus aureus*, *Staphylococcus*

epidermidis and *Bacillus subtilis*. Two sesquiterpenoid compounds were isolated (costunolide and eremanthin) from the hexane extract. Both compounds inhibited the tested fungi but not tested bacteria. The compound costunolide showed significant antifungal activity. The MIC values of costunolide were 62.5 µg/ml against *Trichophyton mentagrophytes*, 62 µg/ml against *Trichophyton simii*, 31.25 µg/ml against *Trichophyton rubrum* isolate 296, 62.5 µg/ml against *Trichophyton rubrum* isolate 57, 125 µg/ml against *Epidermophyton floccosum*, 250 µg/ml against *Scopulariopsis* sp., 250 µg/ml against *Aspergillus niger*, 125 µg/ml against *Curvularia lunata* and 250 µg/ml against *Magnaporthe grisea*.

Uterine Stimulant Activity

Studies found that the ethanol rhizome extract (10 mg/100 ml) increased spontaneous rat uterine contraction (Lijuan et al. 2011). They found that *C. speciosus* stimulated phasic activity in the rat uterus. It was able to increase contraction via calcium entry on l-type calcium channels and sarcoplasmic reticulum (SR) calcium release. Their data suggested that the uterotonic effect was due to nonoestrogenic effects and not those of diosgenin. They suggested that *C. speciosus* rhizome extract may be a useful uterine stimulant. This uterine activity of the plant supported its use as an ecbolic in the indigenous system of medicine.

Spasmolytic Activity

An alkaloid extracted from *C. speciosus* rhizomes was found to have papaverine-like smooth muscle relaxant and antispasmodic activities (Bhattacharya et al. 1973).

Anticholinesterase Activity

C. specious alkaloids exhibited anticholinesterase activity in both in-vitro and in-vivo tests, elucidating earlier observed potentiation of acetylcholine responses on frog rectus muscle and dog blood pressure (Bhattacharya et al. 1972). The use of the plant in eye diseases and as a depurative may be due to the anticholinesterase activity of the plant alkaloids.

Oestrogenic Activity

Saponins isolated from the rhizomes of *Costus speciosus* exhibited oestrogen-like action on spayed albino rats (Singh et al. 1972). They significantly increased the uterine weight and uterine glycogen concentration and produced proliferative changes in the uterus and vagina. The results were comparable with those produced by stilboestrol. Administration of the methanol rhizome extract at two different doses (250, 500 mg/kg body weight) for 10 days to Gonado-intact female adult mice elicited a significant decrease in ovarian weight and increase in uterine weight in comparison to normal control (Najma et al. 2012). Phytochemical screening revealed the presence of secondary metabolites, i.e. alkaloids and flavonoids. Tewari et al. (1973) reported the oestrogenic activity of 1,600 µg diosgenin isolated from *C. speciosus* rhizome was approx. equal to that of 150 µg neoclinestrol.

Adaptogenic Activity

The alcoholic rhizome extract was found to possess normalizing activity against cold immobilization stress-induced changes in norepinephrine (NE), dopamine (DA), 5-hydroxytryptamine (5-HT), 5-hydroxy indole acetic acid (5-HIAA) and enzyme monoamine oxidase (MAO) in Wistar albino rats (Verma and Khosa 2009a). The results provided biochemical evidence for the antistress activity of the tested extract Tewari et al. (1973).

Antifertility Activity

A mixture of saponins isolated from *C. speciosus* rhizomes effectively protected against pregnancy in rats, when fed at 5–500 µg/100 g body weight for 15 days (Tewari et al. 1973).

Traditional Medicinal Uses

Costus speciosus is an ayurvedic drug plant of repute used to treat various ailments (Bhogaonkar et al. 2012), possessing astringent, aphrodisiac, purgative, anthelmintic, depurative, febrifuge and expectorant properties (Srivastava et al. 2011). All plant parts of the plant are used in folk medicine in various parts of India; its extracts are used for treatment of fever, snake bites and jaundice and as a purgative, astringent and antibacterial agent (Nehete et al. 2010). This plant is widely used for fertility control in women by the rural people of Rangia Subdivision of Kamrup District, Assam (Najma et al. 2012). The plant is referred in the Kama Sutra as a cosmetic ingredient to be used on women's eyelashes to increase sexual attractiveness. In ayurveda, the rhizomes are ascribed to be bitter, astringent, acrid, cooling, aphrodisiac, purgative, anthelmintic, depurative, febrifuge, expectorant, tonic and aphrodisiac; useful in vitated conditions of khapa and pitta, burning sensation, flatulence, leprosy, skin diseases, catarrhal fever, colds, worm infections, pneumonia, rheumatism, dropsy, urinary diseases, jaundice bronchitis, inflammations, coughs, dyspepsia rash, asthma and anaemia (Burkill 1966; Warrier et al. 1995; Singh 2011). The plant is administered for gout; the leaves are given in mental disorders and crushed leaves are applied in fever; decoction of stem is used in fever and dysentery. Hexane, methanol and water extracts of leaf and rhizome extracts of *C. speciosus* are used by Indian traditional healers for treating skin diseases, diabetes, jaundice, snake bites and/or antiinflammatory properties (Malabadi 2005).

According to Burkill (1966), in Peninsular Malaysia, the juice of the rhizome is used as a purgative and for syphilis and after confinement in Java and the stem is given for dysentery. The juice from the shoot or pith is squeezed into the eyes for eye complaints. The Malays eat the rhizome with betel for cough but used it to a greater extent externally. In Peninsular Malaysia and Sarawak, the plant or rhizome is boiled in water for use in bathing to treat high fever (Burkill 1966; Chai 2006). The leaves are crushed and use as poultice on the head; the stem is scraped and the scrapings applied to leprous skin and decoctions of stem scrapings are used as lotions for small pox and fever (Burkill 1966). The plant is cooling and sudorific. The Malays regard it when used medicinally, as exorcising evil spirits which have taken possession of the body. In Java, the rhizome is used for treating nephritis–beriberi–oedema due to hardening (sclerosis) of the liver, difficulty in urination and pricking pain in the urinary tract (Stuart 2012). A decoction of dried or fresh material decoction may be used as external application for nettle rash. A decoction of the dried rhizome is taken for stomachache and dyspepsia. In Visayas, juice of stems is used for dysentery. The juice from the stem is employed for diarrhoea.

Other Uses

Commonly grown as an ornamental. The whole plant has medicinal properties due to the presence of diosgenin, a steroid which is used as a precursor for the preparation of steroidal drugs (Singh 2011). *C. speciosus* rhizome is used to stupefy fish by the Gond tribe of Kawal Wildlife Sanctuary, Andhra Pradesh, India (Murthy et al. 2010).

The plant also has insecticidal property. Diosgenin from *C. speciosus* was found to have a low contact and ovicidal activity but a potent insect growth regulator (IGR) and high oviposition deterrent activity of diamondback moth, *Plutella xylostella* (Pipithsangchan and Morallo-Rejesus 2005). It caused larval and pupal deformities, reduced fecundity and partial sterility. Based on the ED*50*, crude diosgenin was more active than purified diosgenin. The diamondback moth parasitoid, *Cotesia plutellae*, was 14 times less sensitive to diosgenin compared to diamondback moth.

Comments

The plant is easily propagated from rhizome divisions and stem cuttings.

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Costus barbatus

Scientific Name

***Costus barbatus* Suessenguth**

Synonyms

None recorded

Family

Costaceae

Common/English Names

Hawaiian Torch Ginger, Red Tower Ginger, Red Velvet Ginger, Spiral Ginger

Vernacular Names

Spanish: Apagafuego, Cana De Jabali, Sangrafu

Origin/Distribution

The species is a native of Costa Rica, Central America.

Agroecology

The plant grows well in full sun or partial shade in fertile, moist, well-drained, organic matter-rich soils. It blooms year round in the warm humid tropics. It tolerates cold temperatures but not frost. It is found from 600 to 1,600 m altitude in its natural habitat in Costa Rica.

Edible Plant Parts and Uses

Yellow flowers are edible (Carle 1995) and have a delightful sour lemony flavour. Flowers can be eaten straight off the plant and are excellent in a salad.

Botany

An erect, clumping herbaceous terrestrial with subterranean rhizome, growing to 1.5–2.5 m high. Ligule 10–30 mm, obtuse and lobed encircling the stem. Leaves spirally arranged with narrowly elliptic dark green lamina, 13–30 cm by 4.5–10 cm wide, simple, entire margin with a glabrous upper surface and slightly villose beneath (Plate 1). Inflorescence terminal ovoid to fusiform 4–10 cm by 2.5–4.5 cm across with numerous mucronate, bright red appendaged

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Plate 1 Flowers, inflorescences and foliage

bracts each bearing 1–2 tubular flowers in their axils (Plate 1). Flowers with short calyx tube 13–17 mm, corolla yellow, densely pubescent with tubular labellum 26 by 24 mm.

Nutritive/Medicinal Properties

In 'Suriname's traditional medicine', an extract of the stem is used against gonorrhoea, common cold and eye problems and as a laxative.

Other Uses

It is a common cultivated *Costus* species and a very popular ornamental and provides beautiful cut flower.

Comments

The plant is readily propagated from division of the rhizomes or from stem cuttings.

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Costus erythrophyllus

Scientific Name

***Costus erythrophyllus* Loes.**

Synonyms

Costus claviger Benoist

Family

Costaceae

Common/English Names

Blood Red Spiral Costus, Oxblood Ginger, Violet Spiral Flag

Vernacular Names

German: Rotblättriger Spiralingwer, Rotblättriger Zieringwer

Origin/Distribution

The species is a native of Amazonian Peru and Ecuador.

Agroecology

The plant thrives in a tropical/subtropical climate. It grows in a humus-rich, well-drained, friable, moist soil in partial or fully shaded position.

Edible Plant Parts and Uses

The flowers have been reported edible (Carle 1995; King 2007).

Botany

An unbranched rhizomatous perennial 0.3–1 m with leaves spirally disposed and mostly crowded at the apex, shortly petiolated, glabrous, obovate-oblong, 1.5–2.5 dm by 5.5–10 cm, upper surface green, lower surface burgundy, glabrous to sparsely puberulous, base cuneate, apex acute to acuminate, margin entire (Plates 1 and 2). Sheath is green glabrous with deeply 2 unequally lobed ligule. Inflorescence a sub-capitate spike, terminal on leafy shoot arising from the rhizome, all bracts dark red, broadly ovate with reflexed apices and foliaceous, green appendages, 2.5–6 cm by 2–4 cm, triangular ovate, foliaceous, bracteole red, puberulous. Flower calyx with red deltoid lobes, puberulous, corolla white glabrous tubular, labellum arched, spreading, middle lobe trilobulate,

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Plate 1 Leaves with distinct green upper and burgundy lower surfaces

Plate 2 Flowers with red, yellow and white streaks and blotches

broadly ovate, white with central yellow zone, reddish streaks, 6–6.5 cm, stamen 4–5 cm long, with pinkish white anther, 9–10 mm long (Plate 2).

Nutritive/Medicinal Properties

No information has been published on the plant nutritive or medicinal properties.

Costus is traditionally used in Guinean, Brazilian and Trinidadian traditional medicine for various uses, as well as in the Dominican Republic and the United States for diabetes.

Other Uses

A popular ornamental plant for parks, gardens and house gardens.

Comments

The plant is propagated by division of the rhizome.

Selected References

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Costus productus

Scientific Name

***Costus productus* Gleason ex Maas**

Synonyms

None recorded

Family

Costaceae

Common/English Names

Costus, Costus Ginger, Dwarf Orange Ginger, Orange Tulip Ginger, Spiral Ginger

Vernacular Names

None known

Origin/Distribution

The species is indigenous to Peru.

Agroecology

The plant thrives in a warm, humid tropical environment under partial to dappled shade. This plant cannot tolerate dry conditions and requires additional watering during the dry seasons. It prefers acidic to neutral, well-drained fertile sandy-loam soils rich in organic matter.

Edible Plant Parts and Uses

The orangey-yellow flowers are edible with a sweet, subtle fragrance and flavour and make an ideal garnish for salads (Carle 1995; Campbell 2006; NTBG 2013).

Botany

A rhizomatous unbranched evergreen perennial herb, 60–100 cm. Stem arising erect from the rhizome, near base covered with leafless sheaths, leafy higher up. Leaves sessile spirally arranged on the upper quarter of the stem with closed, hirsute ligulate sheaths (Plates 1 and 2). Leaf blade, narrowly obovate to oblong, 20–25 cm by 6–10 cm wide, apex acute to acuminate and base cuneate to obtuse, upper surface glabrous, lower

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Plate 1 Inflorescence and foliage of Orange Tulip Ginger

Plate 2 Sessile spirally arranged leaves and terminal inflorescence

Plate 3 Orange flowers emerging from the red bracts

sparsely pubescent, dark glossy green above, grey green below. Inflorescences terminal on leafy stem (Plate 2), with numerous scarlet, glossy, stiff, appendaged bracts, each bearing a tubular flower with scarlet calyx tube, with tubular yellow orange corolla, labellum and stamen orange fringed with scarlet apex (Plate 3).

Nutritive/Medicinal Properties

Nutritive information of the edible plant parts and/or medicinal properties of the plant have not been published.

Other Uses

Being a low growing plant it makes a great ground cover in outdoor landscape in parks, gardens and houses. It can also be grown in containers.

Comments

The plant can be propagated from division of the rhizomes or from stem cuttings.

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Doryanthes excelsa

Scientific Name

***Doryanthes excelsa* Corrêa**

Synonyms

Agave australis (Haworth) Steudel, *Furcraea australis* Haworth

Family

Doryanthaceae also place in Agavaceae

Common/English Names

Flame Lily, Giant Lily, Globe Spear Lily, Guinea Lily, Gymea Lily, Illawara Lily, Spear Lily

Vernacular Names

None recorded

Origin/Distribution

The Gymea Lily is indigenous to the coastal areas of New South Wales near Sydney, Australia.

Agroecology

The Gymea Lily grows in open dry sclerophyll forests and woodlands in the coastal areas of New South Wales on sandy soils derived from sandstone containing some clay. It thrives in dry climate but prefers well-drained, deep soil and full sun. It is a pyrogenic flowering species and rely on post-bush fire flowering and the production of nondormant seeds to exploit favourable post-fire establishment and growth conditions. Germination of seedlings occurs some 2.5–3 years after the passage of the fire.

Edible Plant Parts and Uses

The Gymea Lily provides a traditional bush food for the aborigines in the coastal areas of New South Wales (Cribb and Cribb 1976; Low 1989). The root, stem and flower spike are edible after some preparation. The stems and roots can be harvested, roasted and eaten or made into a cake. The young flower spikes (about 0.5 m high) can be roasted and eaten. The flowers are soaked in water to produce a sweet, high energy drink.

Botany

A large perennial rosette, clumping plant with a bulbous rhizome and a tussock of long thick, bright green linear, swordlike, glabrous, fibrous,

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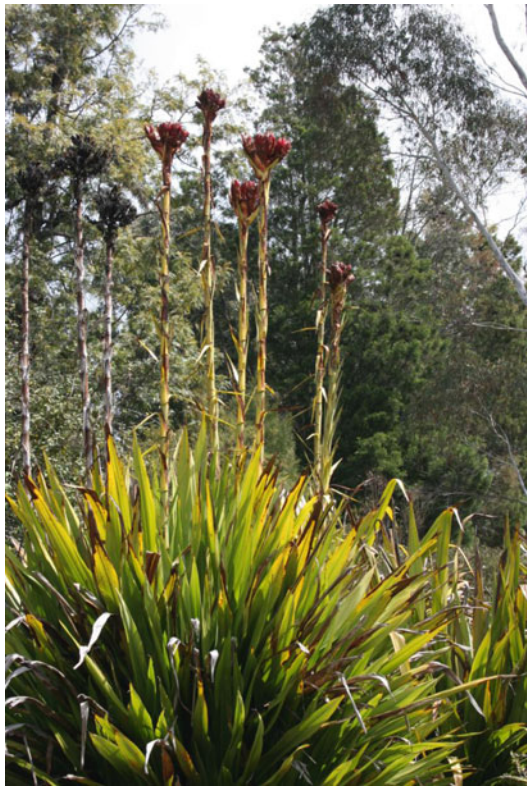

Plate 1 Large clumping plant habit

Plate 2 Flowering spikes with very long peduncles

ensiform leaves up to 1.5 m long and 10 cm wide (Plate 1). It produces a flower spike 2–5 m high, which at its apex bears a large compact terminal head of bright red trumpetlike flowers, each 10 cm across (Plates 2 and 3). Each flower has 6 narrow, lanceolate-oblong tepals 6–12 cm long by 0.6–0.9 cm wide fused at the base and surrounded by deep red bracts; anthers 27–38 mm long, green-yellow; filaments to twice as long as anthers; ovary inferior with 3-locules, style furrowed with 3-angled stigmas. Within the central well formed by the tepals, septal nectaries are formed at the base of the tepals at the top of the ovary. These nectaries exude a sweet viscous jellylike fluid that attracts honey eaters and ensures fertilization. Fruit is a dry woody capsule, ellipsoid to ovoid 7–10 cm long, red-brown at maturity containing numerous reddish-brown seeds 15–23 mm long.

Nutritive/Medicinal Properties

No information on the nutrient composition of the edible parts, and medicinal uses or properties of the plant have been published.

Other Uses

A good rockery landscape plant. The massive flower spikes that reach up to 8 m are highly sought after for cut-flowers and foliage in the floriculture industry. The commercial value of cut-flower and foliage of *Doryanthes*, currently all cut from harvested from wild natural bush areas, is steadily increasing, as is the export demand for these unique flowers.

Plate 3 Close-up of terminal flower head

The leaves contain fibres and are split and fibres used for brush and string making, and bag and mat weaving.

Comments

The plant is propagated by division of established plants or from seeds.

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Acacia cultriformis

Scientific Name

***Acacia cultriformis* A.Cunn. ex G. Don** (Plate 3)

Synonyms

Acacia cultrata Paxton, *Acacia cultriformis* A. Cunn. ex G. Don var. *albicans* hort. ex Chopinet, *Acacia cultriformis* A. Cunn. ex G. Don var. *glaucescens* hort. ex Chopinet, *Acacia glaucifolia* Meisn., *Acacia glaucophylla* F. Cels, *Acacia glaucophylla* Lemaire, *Acacia papuliformis* A. Cunn. ex Loudon, *Acacia papuliformis* G. Don, *Acacia scapuliformis* A. Cunn. ex G. Don, *Racosperma cultriforme* (G. Don) Pedley

Family

Fabaceae also placed in Mimosaceae

Common/English Names

Dog-Tooth Wattle, Dogtooth Wattle, Half-Moon Wattle, Golden-Glow Wattle, Knife Acacia, Knife Edge Wattle, Knife-Leaf Wattle, Knife-Leafed Wattle, Knife-Leaved Wattle, Knife Wattle

Vernacular Names

None recorded

Origin/Distribution

The species is native to some parts of eastern Australia, in the sub-coastal and inland parts of New South Wales and southern Queensland. It has sparingly naturalized in the Canberra region and naturalized beyond its native range in the coastal districts of northern and central New South Wales. The species has been distributed and cultivated elsewhere and has naturalized in New Zealand, Asia, Africa and North and South America.

Agroecology

The species adapts to a warm temperate climate. The plant is suited to a wide range of soil types provided they are reasonably well drained. However, it becomes chlorotic on exceedingly limey soils. In its native range, it is found on arid rocky ridges along the coasts and inland. A position in full sun or light shade is suitable and the species is highly drought, salt and wind tolerant and moderately tolerant to mild frosts.

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Edible Plant Parts and Uses

The flowers are edible cooked and can be used in fritters (Cribb and Cribb 1976).

Botany

Acacia cultriformis is a medium-sized, erect, spreading shrub up to 2–4 m tall with angled or terete branchlets. A cascading or prostrate form of unknown origin is also cultivated. The phyllodes are glabrous, greyish-green or subglaucous, triangular in shape (Plates 1 and 2), 1–3 cm long by 0.5–1.5 cm wide, apex with a small point (mucro), base asymmetric. Inflorescences 2–25 in an axillary raceme; axis 1–8 cm long; peduncles mostly 2.5–5 mm long, glabrous; heads globose to oblong, 3–7 mm long, 13–40-flowered, bright yellow (Plates 1 and 2). Pods straight to slightly curved, glabrous, sometimes pruinose, flattish, 3–10 cm long, 4–7.5 mm wide, constricted between seeds. Seeds longitudinal with expanded funicle.

Plate 1 Sessile, deltoid, greyish-green phyllodes and globose flower heads

Plate 2 Close view of yellow globose flower heads

Plate 3 Plant label

Nutritive/Medicinal Properties

No nutritive composition of the edible flowers has been published.

Leaves and stems were found to contain 0.02–0.07 % alkaloids including tryptamine and β-phenethylamine; the unripe seed pods and seeds 0.04 % (White 1944, 1951, 1957). An indolealkylamine compound 5-methoxy-*N*,*N*-dimethyltryptamine (5-MeO-DMT) was tentatively identified from the phyllodes, stems and flowers (Appleseed 1996, cited by Trout et al. 2007). The compound 5-methoxy-*N*,*N*-dimethyltryptamine (5-MeO-DMT) belongs to a group of naturally-occurring psychoactive indolealkylamine drugs (Shen et al. 2010). It acts as a nonselective serotonin (5-HT) agonist and causes many physiological and behavioural changes.

Seed globulins of *A. cultriformis* were found to have varying proportions of amino acids glutamic acid, isoleucine, threonine and valine (Pettigrew and Watson 1975).

Seeds were reported to contain S-carboxyethylcysteine, S-carboxyethylcysteine sulphoxide, S-carboxyisopropylcysteine, α-amino-β-acetylaminopropionic acid, albizzine, djenkolic

acid, djenkolic acid sulphoxide, γ-glutamyl-djenkolic acid, pipecolic acid, 4-hydroxy-pipecolic acid and 5-hydroxy-pipecolic acid (Evans et al. 1977). Studies by Falade et al. (2012) reported that S-carboxyethylcysteine negatively affected casein protein utilization by rats.

The heartwood was found to contain flavan-3 4-diols: flavan-3,3′,4,4′,7-pentaols (mollisacacidins) of (2*R*,3*S*,4*R*)- and (2*R*,3*S*,4*S*)-configurations, and stereochemically analogous pair of flavan-3,4,4′,7-tetraols (guibourtacacidins) and the 8-*O*-methyl derivatives of (2*R*,3*S*,4*R*)-flavan-3,4,4′,7,8-pentaol (teracacidins) and (2*R*,3*S*,4*S*)-flavan-3,3′,4,4′,7,8-hexaol (melacacidins) (Du Preez and Roux 1970).

Other Uses

Acacia cultriformis is one of the most widely cultivated wattles because of its attractive, unique, triangular foliage and bright yellow blooms. The flowers and foliage are much used in floral arrangements. The flowers are attractive to bees and other pollinators. A yellow dye is extracted from the flowers and green dye extracted from the seed pods (Grae 1974). Plants are heavily armed with thorns and make a good highway screen barrier or protective hedge in residential gardens in warm temperate areas.

Comments

The plant is readily established from seeds following pretreatment by soaking in boiling water or by scarification. Cuttings may be successful but this is less employed. Propagation of the prostrate form would need to be carried out from cuttings in order to retain the prostrate habit.

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Acacia longifolia

Scientific Name

***Acacia longifolia* (Andrews) Willd.**

Synonyms

Acacia longifolia (Andrews) Willd. var. *typica* Benth., *Mimosa longifolia* Andrews, *Mimosa macrostachya* Poir., *Phyllodoce longifolia* (Andrews) Link. *Racosperma longifolium* (Andrews) C. Mart

Family

Fabaceae, also placed in Mimosaceae

Common/English Names

Acacia Trinervis, Aroma Doble, Golden Wattle, Coast Wattle, Sallow Wattle and Sydney Golden Wattle Golden Wattle, Long-Leaved Wattle, Sallow Wattle, Sydney Golden Wattle

Vernacular Names

None recorded

Origin/Distribution

The species is indigenous to native to south-eastern Australia, from the extreme southeast of Queensland, eastern New South Wales, eastern and southern Victoria. It is now widely cultivated in subtropical areas globally.

Agroecology

In its native range, it is found in heath and sclerophyll forest and on coastal headlands, sand dunes, riparian habitats and adjacent alluvial flats up to 150 m.

Edible Plant Parts and Uses

Flowers are edible, cooked or eaten in fritters (Cribb and Cribb 1976).

Acacia species used by the bushfood industry in Australia for the edible wattle seeds, ground seed products and occasionally flowers include *A. longifolia* var. *sophorae* (elegant wattle, coast wattle) (Plate 3) (Hegarty et al. 2001). Well-roasted, high-quality wattleseed will have a coffee, chocolate and hazelnut characteristics (Cherikoff 2011). Typical uses of wattleseed include ground, extract and paste (Cherikoff

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2011). Ground wattle seeds are used in pancake batter, desserts (mousse, creme brulee, anglaise) and baked products e.g. muffins, breads and shortbread. Wattle seed extracts are added to sweet or savoury sauces, dairy desserts and as a coffee substitute.

Botany

A spreading and unarmed shrub or small tree, 2–7 m tall, with a smooth or shallowly fissured, greyish bark; branchlets angled towards the tips and with bright green, phyllodes instead of leaves. Phyllodes simple, flat, glabrous, linear-lanceolate to oblanceolate, 8–20 cm long by 1–2.5 cm wide, with 2–5 prominent longitudinal veins. Inflorescence, 1 or 2 in axil of phyllodes. Flowers yellow in a cylindrical brush like flower heads, 2–5 cm by 7 mm. Fruit 5–15 cm by 3-6 mm, straight to slightly twisted, cylindrical, constricted between seeds with a curved beak, green turning brown, containing 6–8 longitudinal seeds, each with funicle folded into a large aril (Plates 1 and 2).

Nutritive/Medicinal Properties

The following flavonoids were identified in the flowers: naringenin and 5-β-D-glycosyl-naringenin (Kerber and Silva 1993), naringenin (0.018 %w/w), a flavonone, and two of its glycosides, naringenin-5-β-D-galactoside (0.582 % w/w) and naringenin-5-β-D-glucoside (0.2 % w/w) (da Silvia and Keber 2003). An aurone, identified as auteusidin-4-galactoside, was isolated from the ethanol extract of the flowers (Peitz and Keber 2003). *Acacia longifolia* seeds were found to contain 6–10 % water content, 12–13 % dwb protein and 19–20 % dwb in the embryo (Murray et al. 1978). The globulin protein designated G6, of molecular weight c. 250,000, comprised subunits of molecular weight 72,000, 61,000, 45,000, 36,000, 31,000, 16,000 and 11,000.

Small amounts of phenethylamine were found in the leaf, stem and flower (White 1944a, b, 1951). Flower spikes had minor alkaloid (White 1957), tryptamine itself found in some flowers (White 1951). *N*-*N*-Dimethyltryptamine (DMT) 0.2–0.3 % and histamine were also identified in *A. longifolia* (Hegnauer 1994).

Leaf, bark and pod extracts of *Acacia longifolia* yielded two major histamine alkaloids:

Plate 1 Leaves and flower heads

Plate 2 Close up of brush-like flower heads

Plate 3 Tree label

N-(2-imidazol-4-yl-ethyl)-*trans*-cinnamamide and *N*-(2-imidazol-4-yl-ethyl)-deca-*trans*-2, *cis*-4-dienamide in variable amounts and trace amounts in the seeds (Repke 1975). The lipidic fraction extracts of the *Acacia longifolia* wood and bark were found to contain fatty acids, fatty alcohols (minor component), sterols, steryl glucosides and steryl esters (Freire et al. 2005). The fatty acids were mainly 16:0, palmitic acid; 18:2, linoleic acid; 18:1, oleic acid; and 18:0, stearic acid. The sterols were predominantly Δ^7 sterols (spinasterol and dihydrospinasterol) and Δ^5 sterols (stigmasterol and β-sitosterol); other free sterols were campesterol, stigmastanol and β-sitostanol as minor components. The steryl glucosides found were spinasteryl glucoside, β-sitosteryl glucoside and dihydrospinasteryl glucoside in the wood and bark; and campesteryl glucoside and stigmasteryl glucoside in the wood.

Antimicrobial Activity

The ethanol leaf extract (1,000 mg), its ethyl acetate fraction and hydroethanol fractions exhibited antibacterial activity against *Staphylococcus aureus*; and moderate growth inhibitory activity against *Fusarium oxysporum* and *Cylindrocladium spathulatum* (Peitz and Keber 2003). The crude ethanol leaf extract, the ethyl acetate and the remaining ethanol fractions showed growth inhibition of *Staphylococcus aureus*, and only the crude ethanol extract showed moderate growth inhibition of *Pseudomonas aeruginosa* and did not inhibit growth of *Escherichia coli* (Peitz et al. 2003). Phytochemical screening indicated the presence of tannins, leucoanthocianidins, flavonoids and triterpene/steroids.

Anticancer Activity

In-vitro studies showed that spinasterol had antitumorigenic potential (Villaseñor and Domingo 2000). Using the mouse skin tumour assay, spinasterol at a concentration of 15 ug/0.2 ml acetone decreased the incidence of skin tumours by 55.6 % and decreased the number of tumours by 65.0 % when applied immediately after croton oil.

Antidiabetic Nephropathy Activity

Studies found spinasterol to have considerable therapeutic potential in modulating the development and/or progression of diabetic nephropathy (Jeong et al. 2004). Spinasterol was found to be a potent inhibitor ($IC_{50} = 3.9 \times 10^{-12}$ g/ml, 9.5 pmol/l) of glomerular mesangial cell proliferation caused by high-ambient glucose, and its inhibitory potency was about 1,000 times higher than that of simvastatin, an HMG-CoA reductase inhibitor used as a positive control. Spinasterol also significantly reduced the increases of serum triglycerides, renal weight and urinary protein excretion in streptozotocin-induced diabetic mice.

Hypocholesterolaemic Activity

Animal studies showed that spinasterol, as well as sitosterol, inhibited cholesterol absorption, resulting in decreases of the plasma and liver cholesterol levels (Uchida et al. 1983). Further, when cholesterol absorption was inhibited, the synthesis of bile acids, especially that of chenodeoxycholic acid, decreased, suggesting that the dietary cholesterol was preferentially metabolized to chenodeoxycholic acid in mice.

Allergy Problem

Pollens are important triggers for allergic asthma and seasonal rhinitis (Hassim et al. 1998; Widmer et al. 2000). Studies showed that *Acacia longifolia* pollens released proteases that were able to cause detachment of murine airway epithelial cells from their substratum in-vitro and may not be effectively inhibited by endogenous antiproteases (Hassim et al. 1998). The intrinsic protease activity of *Acacia* pollen allergens may contribute to sensitization by disrupting the integrity of the airway epithelial barrier. In another study,

Acacia longifolia pollen diffusate was found to release proteases that exhibited high rates of cleavage of arginine and lysine substrates (Widmer et al. 2000). Disruption of epithelial integrity by proteases released following deposition of pollens on mucosal surfaces could promote sensitization and induce inflammation.

Psychopharmacological Activity

N,*N*-Dimethyltryptamine (DMT) is a psychedelic, hallucinogen compound. In a double-blind, saline placebo-controlled, randomized design study, intravenous administration of dimethyltryptamine (DMT) dose-dependently elevated blood pressure, heart rate, pupil diameter and rectal temperature, in addition to elevating blood concentrations of beta-endorphin, corticotropin, cortisol and prolactin in experienced hallucinogen users (Strassman and Qualls 1994). Growth hormone blood levels rose equally in response to all doses of DMT, and melatonin levels were unaffected. Threshold doses for significant effects relative to placebo were also hallucinogenic (0.2 mg/kg and higher). Subjects with five or more exposures to 3,4-methylenedioxymetha mphetamine demonstrated less robust pupil diameter effects than those with two or fewer exposures. In another randomized, double-blind, design study of experienced hallucinogen users, tolerance to 'psychedelic' subjective effects did not occur according to either clinical interview or Hallucinogen Rating Scale scores (Strassman et al. 1996). Adrenocorticotropic hormone (ACTH), prolactin, cortisol and heart rate responses decreased with repeated DMT administration, although blood pressure did not. The data demonstrated the unique properties of DMT relative to other hallucinogens and underscore the differential regulation of the multiple processes mediating the effects of DMT.

Other Uses

The plant is employed to prevent soil erosion and is useful in securing uninhabited sand in coastal areas. The tree's bark has limited use in tanning, primarily for sheepskin. Leaves have been used as fish poison. The green unripe seeds were used as a substitute for soap. The flowers have fungicidal activity. The ethyl acetate fraction (500 ppm) of the ethanol flower extract showed a remarkable antifungal activity, inhibiting growth of *Rhizoctonia* sp. by 30 %, *Colletotrichum acutatum* by 15.9 % and *Fusarium oxysporum* by 10.4 % (da Silvia and Keber 2003).

Allelopathic Activity

The chloroform fraction obtained from the flower ethanol extract exhibited allelopathic activity; it inhibited markedly the germination of *Lactuca sativa* seeds and growth of the radicle and hypocotyl (Peitz and Keber 2003).

Comments

Two subspecies of *Acacia longifolia* have been recognized: *Acacia longifolia* subsp. *longifolia* and *Acacia longifolia* subsp. *sophorae* (Labill.) Court.

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Bauhinia purpurea

Scientific Name

***Bauhinia purpurea* L.**

Synonyms

Bauhinia castrata Blanco, *Bauhinia coromandeliana* DC., *Bauhinia platyphylla* Span., *Bauhinia platyphylla* Zipp ex Span., *Bauhinia purpurea* L. var. *corneri* de Wit, *Bauhinia purpurea* L. var. *violacea* de Wit, *Bauhinia rosea* Corner, *Bauhinia triandra* Roxb., *Bauhinia violacea* Corner, *Caspareopsis purpurea* (L.) Pittier, *Phanera purpurea* (L.) Benth.

Family

Fabaceae also placed in Caesalpiniaceae

Common/English Names

Hawaiian Orchid Tree, Hong Kong Orchid Tree, Pink Butterfly Tree, Purple Butterfly Tree, Purple Camel's Foot, Purple Bauhinia, Purple Orchid Tree, Semki-Gona Gum

Vernacular Names

Afrikaans: Skoenlapperorgideeëboom
Burmese: Mahahlegani, swèý-tau ni
Chinese: Zi Yang Ti Jia, Yang Ti Jia
Eastonian: Purpur-sämplehik
French: Arbre À Orchidées, Bauhinia À Fleurs Pourpres, Bauhinie, Bauhinier
German: Purpurfarbener Orchideenbaum, Purpurrote Bauhinie, Schmetterlings-Bauhinie
India: Kanchanam (Andhra Pradesh), Kurial, Kanchan (Assamese), Devakanchan, Kanchan, Rakta Kanchan, Raktakanchan, Singyara (Bengali), Megong (Garo), Ashta, Gairal, Guiral, Gurial, Jhinjhora, Kachnar, Kaliar, Kandan, Kaniar, Karal, Karial, Khairwal, Koilari, Koinar, Koliar, Kwiryal, Lal Karal, Makkuna, Mawai, Lal Kachnar, Sona (Hindi), Arelu, Akilu, Banne, Basavanapadu, Deva Kaanchana, Kanchivaala, Kanchivala, Kanchuvaala, Kancivala, Kanjivala, Kempu Kanchuvaala, Kempu Mandaara, Kempukanchavala, Kempukancivala, Kempukanjivala, Kempumandara, Kempu Kanchivaala, Kempumandaara, Mandara, Sarul, Uleppe, Ulipe (Kannada), Dieng Long (Khasi), Chovanna-Mandaru, Chovannamandaru, Cuvannamandaram, Mandaram, Suvannamandaram (Malayalam), Chingthao Angangba (Manipuri), Atmatti, Kanchan, Dev Kanchan, Deva, Devana Kanchana, Kanchana, Ragtachandan, Ragthachandan,Rakta Kanchan, Raktha Kaanchan, Tambdo-Apto (Marathi), Vaube, Vaufavang (Mizoram), Borodo, Vaube (Oriya), Camarikah, Kancanarah, Kanchan, Kovidara, Kovidarah, Mahayamalapatrakah, Raktakovidara, Raktapushpakovidara, Swetakancanara, Tamrapuspah, Vanaraja (Sanskrit), Acanomantarai, Acanomantaraimaram, Acuvacam-

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purappu, Arputaveni, Atthi, Cikappu Mantarai, Compucikam, Compucikamaram, Kalavilaccai, Kalavilaichi, Kalarviluti, Kalaviluti, Karuppumantarai, Kattu Mantarai, Mancaltarai, Mancaltaraimaram, Mandarai, Mandari, Mandareh, Mandharai, Mantarai, Mantharai, Mutiraikkali, Nilataru, Nilattiruvatti, Periyavatti, Punkaram, Purapicam, Segappumandarai, Ulittikam (Tamil), Aroe,Bodanta, Bodanta Chettu, Deva-Kasla, Devakaanchanamu, Devakanjanamu, Kaanchanamu,Kanchanam, Kanjanamu, Peddaare, Peddare, Peddari (Telugu)

Indonesia: Bunga kupu-kupu (Malay), suwoto (Javanese), Aroy kupu-kupu (Sundanese)

Japanese: murasaki mokuwan-ju

Malaysia: Tapak Kuda (Peninsular), lupit (Sabah), daun tangkop bedaup (Iban, Sarawak), akah punan, dakun punan, urok punan (Kayan, Sarawak), dahup dahup (Kedayan, Sarawak), ikop (Penan, Sarawak), babayak (Selako, Sarawak)

Nepal: Khwairalo, Koeralo, tanki

Philippines: Alibang-bang (Tagalog)

Portuguese: Pie De Cabra

Singapore: Tapak Kuda

Spanish: Palo De Orquídeas, Pie de cabra

Sri Lanka: Kolar

Swedish: purpurbauhinia

Thai: Chong Kho; Seaw Dok Dang, Sio Dak Dang sieowaan, sieo dok daeng

Tibetan: Go Bi Da Ra, Ko Bi Da Ra, Ko Bid Dri

Vietnamese: Mòng bò tím; Móng bò hoa đỏ; Mòng bò lan

Origin/Distribution

The species is native to South China (which includes Hong Kong), Pakistan, India and Myanmar, southern China, Philippines and Northern Australia.

Agroecology

A tropical/subtropical species but the plant is frost hardy and light demanding. It thrives in well-drained, loamy soils in areas with 500–2,774 mm or more annual rainfall with no dry season and with temperatures of 9–37 °C. It will survive temperatures of −4 or −5 °C. It grows from above sea level to 2,000–3000 m altitude. In its native range it occurs at lower elevations. It has escaped from cultivation and has naturalized in many tropical countries and occurs in savanna, scrub and dry deciduous forest to swamp forest evergreen lowlands, rain forest to mountain forests.

Edible Plant Parts and Uses

The leaves, flower buds, flowers and young pods are eaten as vegetable and pot herb. The flower and buds are often used in curries and pickles and as condiments (Burkill 1966). The flower buds are cooked and eaten as vegetables in Andhra Pradesh (Reddy et al. 2007) and Uttarakhand Himalaya (Namrata et al. 2011). In Thailand, young shoots and leaves are added in curry dishes; the taste is somewhat sour (Jircas 2010). The young pods and mature seeds of kachnar are known to be cooked and eaten by tribes such as the Kathkors and Gondas of India (Rajaram and Janardhanan 1991).

Botany

A shrub to small tree from 4 to 10 m high with grey to dark brown bark (Plate 1) and pubescent young aerial parts. Leaves petiolate, petiole 2.5–5 cm long, lamina 4.5–11 cm long, 4.5–10 cm wide, 9–11 nerved, cleft about halfway down into 2 acute or rounded lobes, minutely pubescent below when young (Plates 1 and 2). Inflorescence few-flowered panicles at the ends of the branches. Flowers on 5–13 mm long pedicels; tomentose, bract 3 mm long, bracteole 2 mm long, pale purple or at least purple-marked and fragrant (Plates 3 and 4). Hypanthium 7–10 mm long. Calyx 2.5–3.0 cm long, usually splitting into two reflexed segments, one emarginate the other 3 toothed. Petals 3.7–5 cm long, oblanceolate, long clawed, spreading, veined. Stamens usually 3 fertile with versatile anthers, staminodes 7. Ovary

Plate 1 Leaves and trunk of *B. purpurea*

Plate 2 Leaves and flower buds

Plate 3 Flowers and foliage

downy, long stalked; style long, stigma oblique. Pod 15–30 cm long by 1.5–2.5 cm broad, flat green on 2 cm long stalk and containing 12–15 seeds. Seed almost round, 1.2–1.3 cm across, brown and smooth.

Plate 4 Close-up of flower

Nutritive/Medicinal Properties

Flower Phytochemicals

The aqueous methanol extract of fresh flower afforded the flavonoid quercetin and flavonoid glycosides isoquercitin, astragalin, kaempferol-3-glucoside, pelargonidin-3-glucoside and 3-triglucoside (Ramchandra and Joshi 1967). The flower volatile oil was found to have monoterpenes α-terpinene, limonene, myrcene, linalool, citronellyl acetate; and a phenylpropanoid (eugenol) (Wassel et al. 1986).

Leaf Phytochemicals

The following flavonoids quercetin, rutin, quercitrin, apigenin and apigenin-7-*O*-glucoside were from the leaves (Abd-El-Wahab et al. 1987). The leaves were found to have diglucosides of quercitrin, kaempferol and isorhamnetin (Salatino et al. 1999).

A mixture of phytol fatty esters (1a, 1b, 1c, 1d, 1e, 1f), lutein, and B-sitosterol was isolated from the leaves (Ragasa et al. 2004). The two dimeric flavonoids, namely, bis [3′,4′-dihydroxy-6-methoxy-7,8-furano-5′,6′-monomethylalloxy]-5-C-5-biflavonyl and (4′-hydroxy-7-methyl 3-C-α-L-rhamnopyranosyl)-5-C-5-(4′-hydroxy-7-methyl-3-C-α-D-glucopyranosyl) bioflavonoid with protein-precipitating property, were isolated from 70 % aqueous acetone extract of *B. purpurea*

leaves (Yadav and Bhadoria 2005). An ursane triterpene α-amyrin caprylate was isolated along with other triterpenoids from petroleum ether fraction of ethanolic extract (95 %) of the leaf of *Bauhinia purpurea* (Verma et al. 2009).

Leaves of *B. purpurea* were found to have anti-nutrient factors: condensed tannins (195.0 mg/g) with protein-precipitating capacity (7.438 mg BSA (bovine serum albumin)/g) and protein-precipitable phenolics (64.94 %) (Yadav and Bhadoria 2001).

Stem/Bark/Wood Phytochemicals

A 6-butyl-3-hydroxyflavanone elucidated 6-(3″-oxobutyl)taxifolin and 3 glycerol derivatives 2, 3-dihydroxypropyl oleate, 2,3 dihroxypropyl linoleate, and 2,3- dihydroxypropyl 16-hyroxy-decanoate were isolated from the heartwood (Kuo et al. 1998). A flavone glycoside 5, 6-dihydroxy-7-methoxyflavone 6-*O*-β-D-xylopyranoside was isolated from the chloroform-soluble fraction of the ethanol extract of the stem (Yadava and Tripathi 2000).

Root Phytochemicals

The dichloromethane extract of root of *B. purpurea* yielded 11 secondary metabolites comprising eight dihydrodibenzoxepins, namely, bauhinoxepin C–J; a dihydrobenzofuran, bauhinobenzofurin A; a novel spirochromane-2,1′-hexenedione, bauhispirorin A; a new bibenzyl bauhinol E; two flavanones (−)-strobopinin and demethoxy-matteucinol and five known bibenzyls which possessed various pharmacological activities, namely, antimycobacterial, antimalarial, antifungal, cytotoxic and antiinflammatory activities (Boophong et al. 2007).

Seed Phytochemicals

Chalcone glycosides, butein 4′-*O*-β-L-arabinopyranosyl-*O*-β-D-galactoside (Bhartiya et al. 1981) and 3,4-dihydroxychalcone 4-*O*-β-L-arabinopyranosyl-*O*-β-D-galactopyranoside (Bhartiya and Gupta 1981) were isolated from the seeds. *N*-hexane extract of kachnar oilseeds was found to be 17.5 % (Ramadan et al. 2006). The amount of neutral lipids in the crude *B. purpurea* seed oil was the highest (about 99 % of total lipids), followed by glycolipids and phospholipids. Linoleic followed by palmitic, oleic and stearic were the major fatty acids in the crude seed oil and its lipid classes. The oil was characterized by a relatively high amount of phytosterols β-sitosterol and stigmasterol. β-tocopherol was the major tocopherol isomer with the rest being δ-tocopherol. A flavone glycoside was isolated; glycoside-6-4′-diahydroxy-3′-prenyl-3,7,5,7′-tetramethoxy flavone-6-*O*-α-L-rhamnopyranoside was isolated from the acetone-soluble faction of the seed ethanolic extract of *B. purpurea* (Yadav and Sodhi 2001).

The seeds of *B. purpurea* and *B. vahlii* contained higher contents of crude protein and crude lipid than those of *B. racemosa* resulting in higher energy values for these two pulses (Rajaram and Janardranan 1991). The seeds of *B. purpurea* were rich in K, whereas those of *B. racemosa* and *B. vahlii* were rich in Ca and Fe. Albumins and globulins constituted the predominant fractions of the seed proteins in *B. purpurea* and *B. vahlii,* whereas glutelins predominated in *B. racemosa*. In all three species the contents of the essential amino acids lysine, tyrosine and phenylalanine were fairly high; the contents of sulphur amino acids were limiting. Isoleucine and leucine were limiting only in *B. vahlii* proteins. Levels of anti-nutritional factors such as free phenols, tannins, L-DOPA and haemagglutinating and trypsin inhibitor activities were not particularly high.

Raw *B. purpurea* seeds were found to contain anti-nutrient factors (per 100 g): total free phenolics 2.75 g, tannins 2.35 g, phytic acid 692 mg and flatulence factors, raffinose 0.54 g, stachyose 1.17 g and verbascose 0.95 g (Vijayakumari et al. 2007). Soaking the seeds in distilled water caused maximum reduction in the phytic acid content (37 %), whereas soaking in $NaHCO_3$ solution reduced significant levels of phenolics and tannins (72 % and 78 %, respectively). Cooking reduced the levels of oligosaccharides (raffinose by 63 %,

stachyose by 42 % and verbascose by 79 %). Of the attempted treatments, autoclaving appeared to be most effective in reducing levels of all the investigated anti-nutrients, except phytic acid, and also improved the in-vitro protein digestibility of *B. purpurea* seeds.

Plant Phytochemicals

Four dibenz[b,f]oxepins (2a, 3–5) named bauhiniastatins 1–4 and related pacharin were isolated from the leaves, stems, pods and roots (Pettit et al. 2006).

Antioxidant Activity

Studies showed that the methanol plant extract of *Bauhinia purpurea* was more effective in scavenging free radical activity than the petroleum ether and ethyl acetate extracts in all the antioxidant tests (Shajiselvin and Muthu 2011). Maximum chelating of metal ions at 1,000 µg/ml for methanol extract was 77.56 % compared to petroleum ether extract 48.27 %, ethyl acetate extract 59.61 % and EDTA 97.90 %. The respective IC_{50} values were 270, 1,030, 610 and 65 µg/ml for EDTA. Maximum total antioxidant activity (using the phosphomolybdic acid method) at 1,000 µg/ml for the methanol extract was 72.46 % compared to petroleum ether extract 41.61 %, ethyl acetate extract 65.70 % and ascorbate 55.23 %. The respective IC_{50} values were 55.23, 490, 1,250 and 410 µg/ml for ascorbate. Maximum reducing ability (FRAP) at 1,000 µg/ml for the methanol extract was 77.98 % compared to petroleum ether extract 37.67 %, ethyl acetate extract 58.50 % and ascorbate 98.07 %. The respective IC_{50} values were 290, 580, 1,430 and 50 µg/ml for ascorbate. The ethanol leaf extract (95 % v/v) exhibited significant free radical scavenging activity and reducing power activity when compared with ascorbic acid (Joshi et al. 2009). The IC_{50} values were determined to be 78.31 and 59.37 µg/ml for the ethanol leaf extract and ascorbic acid, respectively.

The aqueous and methanol, but not chloroform, extracts of *B. purpurea* leaves (20, 100 and 500 µg/ml) exhibited concentration-dependent antioxidant activity only in the superoxide scavenging assay but low to moderate activity in the DPPH radical scavenging assay, which could be associated with their total phenolic contents (Zakaria et al. 2011b). Soxhlet-extracted (SBE), ultrasonicated (UBE) and macerated (MBE) *B. purpurea* leaf extracts exhibited good DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt) radical scavenging as well as potential reducing ability in total antioxidant capacity (TAC) and FRAP (ferric-reducing antioxidant power) methods (Annegowda et al. 2012). UBE possessed significant radical scavenging activity and reducing ability and polyphenolic constituents followed by MBE and SBE.

Anticancer Activity

Bauhiniastatins 1–4 isolated from various *B. purpurea* plant parts were found to be cancer cell growth inhibitors (Pettit et al. 2006). They exhibited significant growth inhibition against a minipanel of human cancer cell lines, and bauhiniastatin 1 was also found to inhibit the P388 (lymphocytic leukaemia) cancer cell line. Among the secondary metabolites isolated from roots, compounds bauhinoxepin C (1), bauhinoxepin D (2), bauhinoxepin F (4), bauhinoxepin H (6), bauhinoxepin I (7), bauhinoxepin J (8) and a known bibenzyl (18) exhibited cytotoxicity towards KB (nasopharyngeal carcinoma) and BC (breast cancer) cell line with IC_{50} values ranging from 10.5 to 72.3 µM (Boophong et al. 2007). The aqueous and chloroform leaf extracts of *B. purpurea* significantly inhibited in-vitro the proliferation of all cancer cells while the methanol extract inhibited the proliferation of most cancer cells except the leukaemic CEMss cells when assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay (Zakaria et al. 2011b). The aqueous extract was effective against human breast cancer lines MCF-7 (IC_{50}=9 µg/ml) and MDA-MB 231

(IC_{50} = 17 μg/ml) and ovarian cancer Caov-3 (IC_{50} = 16 μg/ml); the chloroform extract was highly effective against the CEMss (IC_{50} = 18 μg/ml) and cervical cancer HeLa (IC_{50} = 21 μg/ml) cell lines; and the methanol extract was highly effective only against the HL-60 (= 12 μg/ml) cell lines. All the extracts did not inhibit proliferation of 3 T3 cells suggesting their non-cytotoxic properties.

Antiinflammatory Activity

The aqueous leaf extract of *Bauhinia purpurea* exhibited antiinflammatory activity in the carrageenan-induced paw oedema in rats (Zakaria et al. 2007). The chloroform leaf extract of *B. purpurea* exhibited significant antiinflammatory activity in rats in a non-concentration-dependent manner in the carrageenan-induced paw oedema test (Zakaria et al. 2009). Unexpectedly, the 100 mg/kg extract showed a less remarkable antiinflammatory activity compared to the other doses tested. The chloroform extract of *B. purpurea* was found to contain bioactive flavonoids, saponins, triterpenes and steroids but no alkaloids and tannins. The methanol stem bark extract (300 mg/kg) exhibited antiinflammatory activity as evaluated by the carrageenan induced rat paw oedema, but its activity was lower than the standard drug, diclofenac (Chandrashekar et al. 2009b).

Among the secondary metabolites isolated from roots, compounds bauhinoxepin F (4) and bauhinoxepin I (7) possessed potent antiinflammatory activity inhibiting the COX-2 enzyme with IC_{50} value of 6.9 and 10.1 μM, respectively (Boophong et al. 2007). Ethanol stem extract of *Bauhinia purpurea* displayed significant antiinflammatory activity as determined by carrageenan-induced paw oedema using plethysmometer in albino rats (Shreedhara et al. 2009). Ethanol root extract of *B. purpurea* administered to rats at doses of 200, 400 mg/kg body weight produced significant antiinflammatory activity in the carrageenan-induced paw oedema model and cotton pellet granuloma pouch method (Pais et al. 2012).

Nephroprotective Activity

Studies showed that the ethanol extract of leaves and unripe pods of *B. purpurea* possessed potent nephroprotective activity against gentamicin-induced toxicity in rats (Lakshmi et al. 2009). Gentamicin-induced glomerular congestion, blood vessel congestion, epithelial desquamation, accumulation of inflammatory cells and necrosis of the kidney cells were found to be reduced in the groups receiving the leaf and unripe pods extract of *Bauhinia purpurea* along with gentamicin. The extracts also normalized the gentamicin-induced increase in serum creatinine, serum uric acid and blood urea nitrogen levels. This was also confirmed by the histopathological studies.

Anti-hypothyroidism Activity

Studies showed that daily administration of *B. purpurea* bark extract (2.5 mg/kg body wt.) to female mice for 20 days increased serum triiodothyronine (T3) and thyroxine (T4) concentrations (Panda and Kar 1999). The extract elicited an increase in hepatic glucose-6-phosphatase (G-6-Pase) activity and antiperoxidative effects as indicated either by a decrease in hepatic lipid peroxidation (LPO) and/or by an increase in the activity of antioxidant enzyme. The results suggested that the plant extract was capable of stimulating thyroid function in female mice.

Recent studies found that *B. purpurea* plant extract has the potential to ameliorate metformin-induced hypothyroidism in type 2 diabetic animals (Jatwa and Kar 2009). The researchers reported that dexamethasone (1.0 mg/kg, i.m.) administration caused hyperglycaemia with a parallel increase in renal lipid peroxidation (LPO), relative risk ratio (RR) and the concentrations of serum insulin, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and triglycerides (TG). Dexamethasone decreased serum triiodothyronine, thyroxine and high-density lipoprotein cholesterol (HDL-C) levels as well as renal superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) content. Oral administration

with metformin (150 mg/kg) to dexamethasone-induced diabetic animals reduced renal lipid peroxidation (LPO), relative risk ratio, serum concentrations of insulin, glucose and low-density lipoprotein cholesterol (LDL-C) with a parallel increase in cellular antioxidants, but it further reduced circulating thyroxine level and caused severe hypothyroidism. Oral administration with either *Withania somnifera* (1.4 g/kg) or *Bauhinia purpurea* (2.5 mg/kg) extract along with dexamethasone and metformin elevated the concentrations of circulating triiodothyronine and thyroxine to euthyroid level. The plant extracts also corrected relative risk ratio and serum lipid concentration.

Antimicrobial Activity

The mixture of phytol fatty esters, sillated from the leaves, was found to have low activity against the fungi *Aspergillus niger* and *Candida albicans* and inactive against the bacteria *Psuedomonas aeruginosa, Staphylococcus aureus*, *Bacillus subtilis and Escherichia coli* and the fungus, *Trichophyton mentagrophytes* (Ragasa et al. 2004). The isolated secondary metabolites, isolated from roots, exhibited antimycobacterial activity with MIC values ranging from 24.4 to 740.7 μM. Among all compounds bauhinoxepin J was the most potent antimycobacterial agent having a MIC value of 24.4 μM (Boophong et al. 2007).

Among the secondary metabolites isolated from roots, compounds bauhinoxepin C (1), bauhinoxepin F (4), bauhinobenzofurin A (9), 2 known bibenzyls (15) and (18) exhibited antifungal activity (IC_{50} 49.6–130.1 μM) (Boophong et al. 2007). Soxhlet-extracted (SBE), ultrasonicated (UBE) and macerated (MBE) *B. purpurea* leaf extracts exhibited antibacterial activity, with UBE inhibiting most of the bacteria followed by MBE and SBE (Annegowda et al. 2012).

Antiulcerogenic Activity

Oral administration of the aqueous leaf extract of *B. purpurea* to rats was found to have antiulcerogenic activity in a dose-dependent manner (Zakaria et al. 2011a). The extract at the dose of 5,000 mg/kg did not cause any signs of toxicity to rats. Histological studies supported the observed antiulcer activity of the extract. Further the extract increased gastric wall mucus secretion. The results supported the traditional uses of *Bauhinia purpurea* in the treatment of ulcers.

CNS (Central Nervous System) Activity

The aqueous leaf extract of *Bauhinia purpurea* exhibited antinociceptive activity in mice in the abdominal constriction, hot plate and formalin tests (Zakaria et al. 2007). The chloroform leaf extract of *B. purpurea* was found to possess significant, but concentration-independent, antinociceptive activity in mice when assessed using the abdominal constriction and hot-plate test (Zakaria et al. 2009). Ethanol root extract of *B. purpurea* administered to rats at doses of 200, 400 mg/kg body weight exhibited antinociceptive activity in the tail flick and acetic acid-induced writhing tests (Pais et al. 2012). Ethanol stem extract of *Bauhinia purpurea* exhibited significant analgesic activity as evaluated by the Eddy's hot-plate and acetic acid writhing animal models (Shreedhara et al. 2009). The ethyl acetate stem bark extract (400 mg/kg) exhibited analgesic activity as tested by acetic acid-induced writhing model and hot plate method (Chandrashekar et al. 2009a).

Hepatoprotective Activity

Studies showed that the aqueous, alcoholic and chloroform leaf extracts of *B. purpurea* exhibited hepatoprotective effects against carbon tetrachloride-induced hepatotoxicity in albino Wistar rats (Veena Rani et al. 2011). All the extracts dose-dependently lowered the elevated levels of alkaline phosphatase (ALP), serum glutamic pyruvic transminase (SGPT) serum glutamic oxaloacetic transaminase (SGOT), total protein (TP), acid phosphatase (AP) total bilirubin (TB) and direct bilirubin (DB) induced

by carbon tetrachloride . This was confirmed by histopathological studies. The hepatoprotective activity of the extract was ascribed to its good antioxidant activity. In another study, the results of in-vivo experiments showed that the water bark extract of *B. purpurea* inhibited lipid peroxidation, protected the experimental animals from alcohol-induced hepatic toxicity in rats and maintained the levels of antioxidants in a dose-dependent manner (Chaturvedi et al. 2011). Both methanol and water bark extracts scavenged free radicals equivalent to gallic acid scavenging and were found rich in total phenol content.

Wound Healing Activity

In the excision and burn wound models, rats treated with high doses of methanol and chloroform leaf extracts of *Bauhinia purpurea* showed significant reduction in time taken for epithelialization and wound contraction (50 %) compared to control (Ananth et al. 2010). A significant increase in breaking strength was found in incision wound model with methanol and chloroform extracts compared to their respective carbopol and simple ointment bases. In the dead space wound model, methanol and chloroform extract treatment (100 and 500 mg/kg) orally produced a significant increase in the breaking strength, dry tissue weight and hydroxyproline content of the granulation tissue when compared to control. Among the extracts, methanol extract exhibited more activity followed by the chloroform extract. The study indicated that *Bauhinia purpurea* leaves exhibited wound healing activity.

Antidiabetic Activity

The ethanol stem extract of *B. purpurea* and its fraction-1 exhibited antidiabetic activity in alloxan-induced diabetic rats, as evident from the serum glucose levels (Muralikrishna et al. 2008). The hypoglycaemic activity may be ascribed to the presence of flavonoids. Oral treatment of the ethanol flower leaf and root extracts of *B. purpurea* at doses of 100, 200, 400 mg/kg for 15 days exhibited significant antidiabetic activity in streptozotocin-induced diabetic rats by reducing and normalizing the elevated fasting blood glucose levels as compared to those of streptozotocin control group (Prasanna and Shastry 2012).

Cardiotonic Activity

The F1 fraction of the ethanol stem extract of *B. purpurea* exhibited excellent adrenergic activity (10 mg/ml) in isolated frog's heart (Muralikrishna et al. 2008). This was further confirmed as its action was blocked by an adrenergic β_2-blocker (propranolol) in isolated frog heart. The cardiotonic activity exhibited by the fraction-1 was probably due the presence of flavonoids. The results suggested that the fraction-1 exhibited positive inotropic and chronotropic effect on an isolated frog's heart.

Antipyretic Activity

The aqueous leaf extract of *Bauhinia purpurea* exhibited antipyretic activity in rats in the brewer's yeast-induced pyrexia test (Zakaria et al. 2007).

Anti-diarrhoeal Activity

The ethanol leaf extract of *B. purpurea* exhibited significant anti-diarrhoeal activity in two animal models, viz. castor oil-induced diarrhoea in rats and gastrointestinal motility test by using charcoal meal compared to the control group (Mukherjee et al. 1998).

Antimalarial Activity

Among the secondary metabolites isolated from roots, compounds bauhinoxepin H, bauhinoxepin I, bauhinoxepin J and a known bibenzyl exhibited antimalarial activity with IC_{50} values 5.8–11.2 μM (Boophong et al. 2007).

Immunological Activity

Bauhinia purpurea lectin (BPA), a galactose- and lactose-binding lectin, was found to have nine amino acids and the amino acid sequence: aspartic acid, threonine, tryptophan, proline, asparagine, threonine, glutamic acid, tryptophan and serine (Yamamoto et al. 1991). Studies showed that a chimeric lectin with unique carbohydrate-binding specificities could be formed *Bauhinia purpurea* lectin (BPA) and Lens culinaris lectin (LCA) (Yamamoto et al. 2000). The chimeric lectin can be constructed from BPA by substituting several amino acid residues in its metal-binding region with other amino acid residues from LCA, providing a powerful tool for biochemical, immunochemical and histochemical studies. *Bauhinia purpurea* agglutinin (BPA) a Galbeta1-3GalNAc (T)-specific leguminous lectin had been widely used in multifarious cytochemical and immunological studies of cells and tissues under pathological or malignant conditions (Wu et al. 2004). This lectin possessed a binding specificity to dense cell surface Galbeta1-3GalNAc (T), high-density polyvalent GalNAcalpha1-Ser/Thr (Tn) and Galbeta1-3/4GlcNAc (I/II) glycoconjugates facilitating its future use in biotechnological and medical applications.

Anthelmintic Activity

The aqueous and ethanol *B. purpurea* plant extracts exhibited significant anthelmintic activity at highest concentration of 100 mg/ml against *Pheretima posthuma* (Kumar et al. 2011).

Traditional Medicinal Uses

The bark, root, leaves and flowers of *Bauhinia purpurea* are reputed to have medicinal properties and used in traditional folk medicine in India, Pakistan, Sri Lanka and Malaysia (CSIR 1948; Chopra et al. 1956; Burkill 1966). Flowers are laxative and are used as a purgative in Pakistan, while the leaves are applied externally to the forehead to treat fever. The leaves contain tannin and are used for poulticing sores and boils in Malaysia and India. The dried buds are used in the treatment of piles, dysentery, diarrhoea and worms. In India the bark is used for poulticing treatment of skin diseases, scrofula and ulcers stomach tumour and wounds. A decoction of the bark is taken for diarrhoea. The root is used as an antidote to snake poison and decoction of the root used for dyspepsia.

In Sarawak, Malaysia, the Ibans consume a tea made from the roots for high blood pressure, stomachache and diarrhoea (Chai 2006). Pounded leaves are rubbed on the back to alleviate backache. The Kayan take the root decoction for cough, stomachache and diarrhoea and the solution used as gargle for toothache. The Kedayan boiled the root with fennel and shallot and drink the decoction for stomach-ache and diarrhoea. The Penan drink the root decoction for toothache. The Selako boil the leaves with sea weed and sea shells and drink the decoction to relieve kidney problems and pain when urinating.

B. purpurea have been used to treat stomach tumours, ulcers, wounds, glandular swellings, diarrhoea and fever in traditional medicine (Zakaria et al. 2007). *B. purpurea* known to the Malays as 'pokok tapak kerbau' has been traditionally used by the Indian, Sri Lankan and Pakistani people to treat ailment like ulcer, wound, glandular swelling and stomach tumour. The decoction of the root is used for expelling gases, flatulence and griping pain from the stomach and bowel; the bark of the plant is used as an astringent in the treatment of diarrhoea. Its decoctions are recommended as a useful wash solution for ulcers. Decoction of *B. purpurea* stem administered twice a day as folk remedy was found to be effective against asthma and other respiratory disorders (Patil et al. 2008) The bark or root and flower mixture with boiled rice water is used as maturant for boils and abscesses (Kurian 2004). The decoction of flower is used as a laxative (Wassel et al. 1986). Fresh bark of Kaanchanaara (*B. purpurea*) mixed with Shunthi (dry *Zingiber officinale*), pounded with sour gruel, was prescribed in enlarge cervical glands (Vrindamaadhava) as well as in goitre (Shaarangadhara Samhitaa, Bhavaprakaasha). Over the counter Kaanchanaara

(*B. purpurea*) Guggulu (Shaarangadhar Samhitaa) is used to treat enlarge cervical glands, goitre and scrofulous tumours. The roots are used as carminative and flower buds as laxative and anthelmintic in folkloric medicine in Mangalore, India (Shiddamallayya et al. 2010). Bark sap with honey is taken against leucorrhoea and is also used to treat menstrual problems in Assam (Das et al. 2008).

Other Uses

The plant is often cultivated as an ornamental, roadside, garden plant and shade tree. It is also used for soil improvement and erosion control. The leaves, pods and shoots are used as fodder. The stem yields semki-gona gum and the bark is good as tanning material, dyeing and for fibre. The wood is used for making furniture, agricultural implement and for house building and fuel.

Comments

Bauhinia purpurea can be grown from seeds, stem cuttings or by air layering.

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Bauhinia variegata

Scientific Name

***Bauhinia variegata* L.**

Synonyms

Bauhinia candida Ait., *Bauhinia chinensis* (DC.) Vogel, *Bauhinia decora* Uribe, *Bauhinia variegata* var. *alboflava* de Wit, *Bauhinia variegata* L. var. *candida* (Aiton) Corner, *Bauhinia variegata* L. var. *chinensis* DC., *Phanera variegata* (L.) Benth.

Family

Fabaceae, also placed in Caesalpiniaceae

Common /English Names

Bauhinia, Butterfly Ash, Butterfly Tree, Camel's Foot, Camel's Foot Tree, Mountain Ebony, Orchid Tree, Pink Orchid Tree, Poor Man's Orchid, Purple Orchid Tree, Variegated Orchid Tree, White Bauhinia, White Bauhinia Orchid Tree, White Camel's Foot, White Variegated Orchid Tree

Vernacular Names

Afrikaans: Orgideëboom

Brazil: Mororó, Pata-De-Vaca, Unha-De-Vaca (Portuguese)

Burmese: Bwècheng

Chinese: Zi Jing, Yang Ti Jia, Yang Zi Jing

French: Arbre A Orchidées, Arbre De Saint-Thomas, Bois De Boeuf, Sabot Boeuf

German: Bunte Bauhinie, Buntfarbene Bauhinie

India: Kotora, Kurol (Assamese), Raktakanchan (Bengali), Darichiksam, Migong (Garo), Barial, Dhak, Goriyal, Gurial, Gwiar, Kachnar, Kancanar, Kandan, Kaniar, Karal, Karial, Khwairaal, Khairwal, Khwairai, Koliar, Kural, Papri, Padrian, Plah (Hindi), Arishina Thaega, Arisinantige, Arjuna, Arsantega, Ayata, Ayisha, Bilikanchavala, Bilikanchivala, Bilikancivala, Bilikanjivala, Irkubalitu, Irkumbalithu, Irkumbalitu, Jhinjero, Kaanchanaara, Kanchivala, Kanchivalado, Kanchiyalapada, Kanchvaala, Kancivala, Kanjivala, Karalabhogi, Karalbogi, Kempu Mandara, Kempukanjivala, Mandara, Mandaara, Kempu Kanchivaala, Kempukancivala, Kempukancivalada, Kempumandar, Kempumandara, Kondalka, Kogilepukka, Kondaalka, Kovindaara, Pulikogelapukka, Seyadla, Ulipa,Ulipe, Ulpe,Utipa (Kannada), Dieng Long, Dieng Tharlong (Khasi), Chommandara, Chovanna-Mandaru, Chovannamandaree, Chovannamandaru, Chuvanna-Mandaram, Chuvannamandaram, Chuvanna-mandari, Chuvannamundiri, Cuvannaman-daram, Konnu, Konnumandaram, Kovidaram, Malayakatti, Mandaram, Suvannamandaram,

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Unna, Unnu (Malayalam), Chingthao-Angouba (Manipuri), Kanaraj, Kanchan, Kavidara, Rakta-Kanchan, Raktakanchan, Rakthakanchan Thaur (Marathi), Vau-Favang, Vaube, Vaufawang (Mizoram), Vau-Favang, Vaube, Kachan (Oriya), Ashmantaka, Asphota, Camarika, Chamari, Chamarika, Champavidala, Gandari, Girija, Kacanara, Kanakaprabha, Kancanara, Kancanarah, Kancanaraka, Kanchana, Kanchanala, Kanchanar, Kanchanara, Kanchanarah, Kanchanaraka, Kantar, Karaka, Karbudara, Kovidar, Kovidara, Kovidarah, Kuddala, Kuddalah, Kuddara, Kuli, Kundali, Mahapushpa, Murva, Pakari, Raktakanchana, Raktapushpa, Shonapushpaka, Suvarnara, Svalpakesari, Tamrapushpa, Uddalaka, Yamalachhada, Yamalapatrakah, Yugapatraka, Yugmapatra, Yugmapatrah (Sanskrit), Akatuti, Aranpucaikkerramaram, Aranpucaimaram, Calacacankati, Cekappumantarai, Cemmantarai, Cempuvatti, Cevappumantarai, Cevvarattinam, Civappumantarai, Irattakancanam, Kammukarimaram, Kancanakam, Kantaputpam, Kuni, Kunkumaccemmantarai, Kunkumamantari, Kuntalam, Mandarai, Mandharai, Munthari, Mantarai, Maramantarai, Segappumandrai, Segappumanchori, Segappumandarai Segapu Manchori, Segapu- Semmandarai, Shemmandarai, Sigappu- Kammukari, Malaiyatti, Palukam, Palukamaram, Palupam, Pattumantarai, Periyavatti, Perumantarai, Potattam, Tamiram, Tampiraputpi, Nattumantarai, Vataraci, Vellaippuvatti, Vennatti (Tamil), Boda, Bodanta, Bodantham, Daevakaanchanamu, Daevakanchanamu, Devakanjanamu Deva Kanchanamu, Devakancanamu, Devakanchanam, Devakanchanamu, Kaanchanamu, Kacini, Kancanamu, Kanjanamu, Mandaara, Mandara, Mandarai, Mandare, Madapaku, Mandari, Mundari, Pedama, Peddaare (Telugu)

Malaysia: Akbar Tapak Kĕrbau Kotidaram, Kupu-Kupu, Tapak Kĕrbau

Nepal: Kachnar, Koiralo, Taki

Pakistan: Kachnar

Portuguese: Arvore De São-Thomaz

Spanish: Arbol Orquídea, Flamboyán Orquídea, Palo De Orquídeas, Pata De Vaca

Sri Lanka: Koboleela

Swedish: Orkidébauhinia

Thai: Sio, Sio Daeng

Vietnamese: Hoa Ban, Móng Bò Đổi Màu, Móng Bò Sọc

Origin/Distribution

The plant is indigenous to southern China, the Indian sub-continent (i.e. Bhutan, India, Nepal and Pakistan) and Southeast Asia (i.e. Laos, Myanmar, Vietnam and Thailand). It is now widely cultivated elsewhere in subtropical and tropical regions of the world. It has naturalized elsewhere in the tropics in Queensland and southern United States.

Agroecology

It grows in areas that annually receive between 750 and 2,000 mm of rainfall with temperatures ranging from 21 to 35 °C. The species grows well in soils of medium fertility that are neither droughty nor wet; it is not tolerant of nutrient-poor sites found throughout India, ascending to an attitude of 1,300 m in the Himalayas.

Edible Plant Parts and Uses

Young sour leaves are eaten as a side dish with rice; flowers and flower buds are also reported eaten in India, Southeast Asia, Africa and South America (Facciola, Burkill).

Botany

A small, erect, medium-sized evergreen or deciduous to semi-deciduous tree that reaches 2–8 m in height and up to 20 cm in trunk diameter. The leaves are alternate, variable in size, ranging from 5 to 13 cm across, bilobed less than halfway, cordate base with 5–12 palmate veins and borne on 2–4 cm long petioles (Plates 1, 2, 3, and 4). Flowers 1 or few, in short lateral racemes, showy,

Plate 1 Alternate, bilobed leaves

Plate 2 A white flower variety

Plate 3 Bud and open flowers

large and fragrant; petals obovate, 3–8 cm long, 2–3 cm wide, variable in colour, either pale purple to rose or white, the uppermost one darker, with purple or crimson veins or blotches, or white

Plate 4 Close view of light purple flower

to yellowish, with green veins, and purplish externally, fertile stamens 5, the anthers 5 mm long; staminodes 5 (Plates 2, 3 and 4). Pods long, narrow and pointed at the ends, hard, flat, glabrous, 13–25 cm long, 15–18 mm wide, coiled upon dehiscence to become falcate containing 10–15 seeds. Seeds light brown, rounded, flat, 15–16 mm long by11–13 mm wide.

Nutritive/Medicinal Properties

Flower Phytochemicals

The flavonoids kaempferol, kaempferol-3-galactoside and kaempferol-3-rhamnoside were isolated from the ethanol extract of white flowers (Rahman and Begum 1966).

Seed Phytochemicals

B. variegata seed was found to have the following amino acid profile: linolenic acid 0.55 %, linoleic acid 36.84 %, oleic acid 26.14 %, stearic acid 16.95 %, palmitic acid 19.52 % and myristic acid traces (Zaka et al. 1983). The residual meal after the extraction of oil contained 41 % protein. *Bauhinia variegata* seed oil was found to have the following physicochemical characteristics (Arain et al. 2012): refractive index (40 °C) 1.4589, peroxide value 1.9 meq O^2/kg oil, iodine value 84.5 g I_2/100 g of oil, saponification number

191.3 mg KOH/g oil, free fatty acids 0.6 %, and unsaponifiable matter 0.9 %. The fatty acid profile comprised linoleic acid C18:2 (42.1 %), oleic acid C18:1 cis 9 (13.4 %), stearic acid C18:0 (17.5 %) and palmitic acid C16:0 (22.11 %) as the major fatty acids. Minor amounts of palmitoleic acid C16:1 (0.4 %), oleic acid cis 7 (0.5 %), margaric acid C17:0 (0.3 %), linolenic acid C18:3 n-6 (0.5 %), arachidic acid C20:0 (1.3 %), behenic acid C22:0 (0.5 %), eicosapentaenoic acid C20:5 (0.2 %) and nervonic acid C24:1 (0.6 %) were also detected. Defatted seed residue contained 41.9 %protein, 18 % oil, 4.8 % ash, 6.7 % moisture, 6.9 % fibre and 28.4 % total carbohydrate. The seed was found to have a high protein content of 29.41 % and lipid content of 14.89 (Pinto et al. 2005).

A flavone glycoside, 5-hydroxy7,3′,4′,5′-tetra-methoxyflavone 5-*O*-β-D-xylopyranosyl-(1 → 2)-α-L-rhamnopyranoside, was isolated from the seeds (Yadava and Reddy 2001). A galactose-binding lectin (BvcL) was isolated from *B. variegata* candida seeds (Silva et al. 2007). It consisted of a large content of serine, glycine, threonine, aspartic acid and glutamic acid and low concentrations of methionine, cysteine and histidine. The N-terminal amino acid sequence of 17 residues showed 90 % sequential homology to galactose-specific legume lectins of the subfamily Caesalpiniodeae. They found that the haemagglutination activity of BvcL was not specific for any human blood group trypsin-treated erythrocytes. A dimeric 64-kDa melibiose-binding lectin was isolated from the seeds (Lin and Ng 2008). A galactose-specific lectin, named BVL, was purified from seeds; it had a pattern similar to other lectins isolated from the same genus, *Bauhinia purpurea* agglutinin (BPA) (Pinto et al. 2008).

Trypsin inhibitors were isolated from seeds of two *Bauhinia variegata* varieties namely *Bauhinia variegata* candida trypsin inhibitor (BvcTI) and *B. variegata* lilac trypsin inhibitor (BvlTI) with molecular weights of about 20,000 without free sulfhydryl groups (Di Ciero et al. 1998). Amino acid analysis revealed a high content of aspartic acid, glutamic acid, serine and glycine and a low content of histidine, tyrosine, methionine and lysine in both inhibitors. Three isoforms were detected in both types. Trypsin inhibitor isoform 3 (BvcTI-3) was composed of 167 residues with a calculated molecular mass of 18,529. Homology studies with other trypsin inhibitors showed that BvcTI-3 belonged to the Kunitz family.

Leaf and Non-woody Aerial Parts Phytochemicals

Physiochemical studies revealed that the leaves had 9.42 % total ash, 5.72 % acid-insoluble ash and water-soluble extractive value of 3.30 % and loss on drying at 105 °C was 6.27 % (Modh et al. 2011). The following flavonoids, quercetin, rutin, quercitrin, apigenin and apigenin-7-*O*-glucoside were isolated from the leaves (Abd-El-Wahab et al. 1987). Preliminary phytochemical analysis revealed the presence of alkaloid, tannin, flavonoid, steroid, triterpenoid and saponin in different extracts. HPTLC fingerprinting for flavonoids revealed presence of two flavonoids rutin and kaempferol. Two long-chain compounds, heptatriacontan-12,13-diol and dotetracont-15-en9-ol, were isolated from the leaves (Singh et al. 2006). A new triterpene saponin, named as 23-hydroxy-3α-[*O*-α-L-1C4-rhamnopyranosyl-(1″ → 4′)-*O*-α-L-4C1-arabinopyranosyl-oxy]olean-12-en-28-oic acid *O*-α-L-1C4-rhamnopyranosyl-(1‴′ → 4‴)-*O*-β-D-4C1-glucopyranosyl-(1‴ → 6″)-*O*-β-D-4C1-glucopyranosyl ester, plus six flavonoid compounds along with two cinnamic acid derivatives were isolated from the leaves (Mohamed et al. 2009).

Six flavonoids, namely, kaempferol (1), ombuin(2),kaempferol7,4′-dimethylether3-*O*-β-D-glucopyranoside (3), kaempferol 3-*O*-β-D-glucopyranoside (4), isorhamnetin 3-*O*-β-D-glucopyranoside (5) and hesperidin (6), together with one triterpene caffeate, 3β-*trans*-(3,4-dihydroxycinnamoyloxy)olean-12-en-28-oic acid (7), were isolated from the nonwoody aerial parts (Rao et al. 2008).

Stem Phytochemicals

Hentriacontane, octacosanol, *β*-sitosterol and stigmasterol (Prakash and Khosa 1976) were isolated from the stem bark. 5,7-Dihydroxy flavonone-4′-*O*-α-L-rhamnopyraonosyl-β-D-glucopyranosides (Gupta et al. 1979), *β*-sitosterol, lupeol and naringenin 5,7-dimethyl ether 4′-rhamnoglucoside were isolated from the stem (Gupta et al. 1980). A phenanthraquinone, named bauhinione isolated from *Bauhinia variegata* stem was elucidated as 2,7-dimethoxy-3-methyl-9,10-dihydrophenanthrene-1,4-dione (Zhao et al. 2005). Rhamnocitrin, a flavonoid, and other compounds 4-*O*-β-D-glucosylbenzoic acid, 5,3′-dihydroxy-6,7,4′-trimethoxyflavanone and 2,4,8,9,10-pentahydroxy-3,7-dimethoxy-anthracene-6-*O*-α-L-rhamnopyranoside were isolated from the stem bark (Surendra et al. 2012).

Root Phytochemicals

A flavonol glycoside 5,7,3′,4′-tetrahydroxy-3-methoxy-7-*O*-α-L-rhamnopyranosyl (1 → 3)-*O*-β-galactopyranoside was isolated from the roots (Yadava and Reddy 2003). A flavanone, 5,7-dimethoxy-30,40-methylenedioxyflavanone, and a dihydrodibenzoxepin, 5,6-dihydro-1,7-dihydroxy-3,4-dimethoxy-methyldibenz oxepin were isolated from the roots (Reddy et al. 2003).

Recent studies reported that *B. variegata* possess chemopreventive, antitumour, cytotoxic, hepatoprotective, antibacterial and antiinflammatory activities.

Antioxidant Activity

The ethanol leaf extract of *Bauhinia variegata* exhibited significant in-vitro antioxidant activity with IC_{50} value of 38.5 μg/ml for DPPH radical scavenging activity, IC_{50} of 70 μg/ml for nitro oxide radical and IC_{50} of 48.5 μg/ml for hydroxyl radical (Saraswathy et al. 2011). The level of oxidation products like lipid peroxides and hydroperoxides decreased significantly in leaf extract incubated neutrophils. Likewise, the antioxidants like reduced glutathione (GSH), catalase and superoxide dismutase (SOD) levels were increased significantly in leaf extract incubated neutrophils when compared to activated neutrophils. The methanol bark extract of *B. variegata* and its polar fractions n-butanol, ethyl acetate and remaining extract showed greater in-vitro DPPH and reducing power antioxidant activity (EC_{50} 44.07, 58.09, 69.68 and 51.81 μg/ml, respectively) in comparison to non-polar fractions (hexane and chloroform) (Sharma et al. 2011a). However, all the fractions effectively protected pBR322 plasmid DNA from hydrogen peroxide-induced damage.

The methanol leaf, bark and flower of *Bauhinia variegata* were found to have hydroxyl radical scavenging activity (Pandey et al. 2012). All the extracts exhibited different level of in-vitro antioxidant activity which was concentration dependent. The percent inhibition (TBARS—thiobarbituric acid reactive substance) at concentration of 10–30 μg/ml was 20.86–62.58 % for the leaf extract, 19.42–60.07 % for the stem extract, 21.58–65.46 % for the bud extract and for ascorbic acid (reference standard) 25.89–70.50 %. Methanol extract was found to be good solvent for extraction and in having good antioxidant activity. The antioxidant IC_{50} values for leaf, stem bark and floral buds were 17.9, 19.5 and 17.2 ug/ml respectively.

Anticancer Activity

Treatment of ethanol *B. variegata* (EBV) extract to Dalton's ascitic lymphoma-bearing Swiss albino mice, enhanced mean survival time with respect to the untreated tumour-bearing mice (Rajkapoor et al. 2003b). The treatment also enhanced peritoneal cell counts. After 14 days of inoculation, EBV was able to reverse the changes in the haemotological parameters, protein and PCV caused by the tumour. Similarly they found that oral administration of EBV was effective in reducing solid tumour mass development induced

by Ehrlich ascites carcinoma (EAC) cells in Swiss albino mice (Rajkapoor et al. 2003c). Further, studies using animal models showed that ethanol extract of *Bauhinia variegata* exhibited significant chemopreventive and cytotoxic effect against *N*-nitrosodiethylamine (DEN)-induced liver tumour and human cancer cell lines (Rajkapoor et al. 2006). Oral administration of ethanol extract of *Bauhinia variegata* (EBV) (250 mg/kg) effectively suppressed liver tumour induced by DEN as revealed by decrease in DEN induced elevated levels of serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total bilirubin, gamma glutamate transpeptidase (GGTP), lipid peroxidase (LPO), glutathione peroxidase (GPx) and glutathione S-transferase (GST). The extract produced an increase in enzymatic antioxidant (superoxide dismutase and catalase) levels and total proteins when compared to those in liver tumour-bearing rats. The histopathological changes of liver samples were compared with respective controls. EBV was found to be cytotoxic against human epithelial larynx cancer (HEp2) and human breast cancer (HBL-100) cells. The dimeric melibiose-binding lectin from the seeds inhibited proliferation in hepatoma HepG2 cells and breast cancer MCF7 cells with an IC_{50} of 1.4 μM and 0.18 μM, respectively (Lin and Ng 2008).

A significant reduction of skin papilloma, with delayed appearance and reduction in the cumulative number of papillomas was observed in the DMBA (7,12-dimethylbenz[α]anthracene) + Kachanar (*Bauhinia variegata* bark extract) + croton oil-treated mice as compared to the DMBA + croton oil-treated mice (Agrawal and Pandey 2009; Pandey and Agrawal 2009). C57 bl mice which received a 50 % methanol extract of Kachanar extract at the doses of 500 and 1,000 mg/ kg body weight for 30 days showed increase in life span and significant reduction in tumour size as compared to controls. In another study they showed that the methanol flower extract had a chemopreventive role against DMBA-induced skin carcinogenesis in mice (Pandey and Agrawal 2010a).

Antimutagenic Activity

In antimutagenicity studies, a single application of Kachanar (*Bauhinia variegata* bark) extract at doses of 300, 600 and 900 mg/kg dry weight, 24 hours prior to the i.p. administration of cyclophosphamide (at 50 mg/kg), significantly prevented micronucleus formation and chromosomal aberrations in bone marrow cells of mice in a dose-dependent manner (Agrawal and Pandey 2009; Pandey and Agrawal 2010b).

Antimicrobial Activity

The alcoholic extract of *B. variegata* was found to have antimicrobial activity against *Bacillus subtilis, Pseudomonas aeruginosa*, *Salmonella typhi*, *Shigella dysenteriae*, *Staphylococcus aureus* and *Vibrio cholera* (Pokhrel et al. 2002). The most sensitive bacterium was *B. subtilis* and the minimum bactericidal concentration (MBC) of the crude extract for this bacterium was 0.39 mg/ml. The extract was found to be more effective against Gram-positive than Gram-negative bacteria.

The antibacterial activity of defatted extracts of *Bauhinia variegata* bark powder was higher than those without defatting (Parekh et al. 2006). Maximum activity was observed at highest concentration i.e. 10 mg/ml. Defatted acetone and methanol extracts of *Bauhinia variegata* were most active as compared to other extracts against all the studied microorganisms – Gram-positive bacteria (*Bacillus cereus* and *Staphylococcus aureus*) and Gram-negative bacteria (*Klebsiella pneumoniae, Escherichia coli,* and *Pseudomonas pseudoalcaligenes*). Petroleum ether extracts were inactive against all microorganisms. Ethanol stem bark extract of *B. variegata* exhibited antimicrobial activity at concentration range of 50–300 μg/ml in a concentration-dependent manner against *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, Candida albicans* and *Aspergillus niger* (Mali et al. 2008).

The ethanol leaf extract of *Bauhinia variegata* showed maximum inhibitory activity against

Salmonella typhi, followed by *Vibrio cholera, Klebsiella pneumonia*, *Escherichia coli* and *Staphylococcus aureus* (Gunalan et al. 2011). For fungi, the leaf extract was very effective against dermatophyte, *Trichophyton mentagrophytes* and against the plant pathogen *Mucor hiemalis*. The alcoholic leaf extract of leaves of *Bauhinia variegata* showed higher antimicrobial activity against Gram-positive species *Staphylococcus aureus* and *Bacillus subtilis* and Gram-negative species *Escherichia coli* and *Pseudomonas aeruginosa* than the petroleum ether and chloroform extracts (Dhale 2011). Phytochemical analysis indicated the presence of alkaloids, oil, fat glycoside, carbohydrates, phenolics, tannins, lignin, saponins, flavonoids and terpenoids in the leaf and bark extracts.

Antidiabetic Activity

The leaves of *Bauhinia variegata* were found to have insulin-like proteins (Azevedo et al. 2006). The activity of this insulin-like protein (0.48 mg/ml) on serum glucose levels of four-week-old Swiss albino (CF1) diabetic mice was similar to that of commercial swine insulin used as control. Further characterization of this molecule by reverse-phase hydrophobic HPLC chromatographic analysis as well as its antidiabetic activity on alloxan-induced mice showed that it has insulin-like properties. This finding supported the use of the plant as anti-diabetic agent in traditional Brazilian medicine. Studies showed that administration of the stem bark extract for 7 days suppressed the elevated blood glucose levels in alloxan-induced hyperglycaemic rats (Kumar et al. 2012). The antihyperglycaemic effect of the extract was comparable to metformin. It was found that the bark extract (200 and 400 mg/kg) and metformin did not influence blood glucose in normal rats.

The crude ethanol leaf extract and its major metabolite (6 S,7 E,9 R)-9-hydroxymegastigma-4,7-dien-3-one-9- β-glucopyranoside (roseoside) exhibited insulinotropic activity (Frankish et al. 2010). The crude extracts and the major metabolite were found to enhance insulin release from the beta-cell lines INS-1in a dose-dependent manner.

Antiinflammatory Activity

A flavonol glycoside 5,7,3′,4′-tetrahydroxy-3-methoxy-7-*O*-α-L-rhamnopyranosyl(1 → 3)-*O*-β-galactopyranoside isolated from the roots showed antiinflammatory activity (Yadava and Reddy 2003). Six flavonoids, namely kaempferol (1), ombuin (2), kaempferol 7,4′-dimethyl ether 3-*O*-β-D-glucopyranoside (3), kaempferol 3-*O*-β-D-glucopyranoside (4), isorhamnetin 3-*O*-β-D-glucopyranoside (5) and hesperidin (6), together with one triterpene caffeate, 3β-*trans*-(3,4-dihydroxycinnamoyloxy)olean-12-en-28-oic acid (7) isolated from the nonwoody aerial parts significantly and dose-dependently inhibited lipopolysaccharide (LPS) and interferon (IFN)-gamma-induced nitric oxide (NO) and cytokines [tumour necrosis factor (TNF)-alpha and interleukin (IL)-12] (Rao et al. 2008). The concentration causing a 50 % inhibition (IC_{50}) of NO, TNF-alpha and IL-12 production by compounds 1, 2 and 7 was approximately 30, 50 and 10 μM, respectively, while at 50, 200 and 40 μM compounds 3, 4 and 5, 6 showed 15–30 % inhibition, respectively. In contrast, compounds 3 and 7 showed no inhibitory effect, while compounds 1, 4–6 reduced by around 10–30 % the synthesis of NO by macrophages, when inducible NO synthase was already expressed with LPS/IFN-gamma for 24 hours. The findings supported the use of the plant for management of inflammatory conditions.

A triterpene saponin, isolated from the leaves, named as 23-hydroxy-3α-[*O*-α-L-1C4-rhamnopyranosyl-(1″ → 4′)-*O*-α-L-4C1-arabinopyranosyl-oxy]olean-12-en-28-oic acid *O*-α-L-1C4-rhamnopyranosyl-(1‴′ → 4‴)-*O*-β-D-4C1-glucopyranosyl-(1‴ → 6″′)-*O*-β-D-4C1-glucopyranosyl ester was found to be nontoxic (LD_{50}) and to have significant antiinflammatory and antinociceptive activities (Mohamed et al. 2009). It also showed slight antischistosomal activity.

Effect of ethanol stem extract of *Bauhinia variegata* exhibited antiarthritic activity on complete Freund's adjuvant (CFA)-induced arthritis in rat (Rajkapoor et al. 2007). Oral administration of the extract effectively inhibited rat paw oedema volume. The extract significantly lowered the

elevated levels of serum aspartate transaminase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) induced by arthritis. The extract also altered the increase in superoxide dismutase (SOD), glutathione peroxidase and decreased catalase level in liver and kidney observed in adjuvant-induced arthritis and normalized the antioxidant levels.

Hepatoprotective Activity

Alcoholic stem bark extract (SBE) at different doses (100 and 200 mg/kg) administered orally to male Sprague-Dawley rats intoxicated by carbon tetrachloride exerted significant hepatoprotective activity (Bodakhe and Ram 2007). A new phenanthraquinone, named bauhinione, 2,7-dimethoxy-3-methyl-9,10- dihydrophenanthrene-1,4-dione was isolated from the stem. Similarly, Sahu et al. (2011) found that oral administration of an ethanol leaf extract to Wistar albino rats intoxicated by paracetamol had a hepatoprotective effect. The leaf extract elicited a significant reduction in level of serum glutamic oxaloacetic transaminase (53.26 %), serum glutamic pyruvic transaminase (41.64 %), serum alkaline phosphatase (72.30 %) and bilirubin (68.18 %) and prevented liver histopathological changes in rats induced by paracetamol.

Nephroprotective Activity

Administration of *B. variegata* ethanol stem extract at dose levels of 400 and 200 mg/kg (bw) to cisplatin-intoxicated rats for 14 days attenuated the biochemical and histological signs of nephrotoxicity of cisplatin in a dose-dependent fashion (Pani et al. 2011). Ethanol extract at 400 mg/kg decreased the serum level of creatinine and urea associated with a significant increase in body weight and urine volume output as compared to the toxic control group. The ethanol stem extract of *B. variegata* at 400 mg/kg (bw) exhibited significant and comparable nephroprotective potential to that of the standard polyherbal drug, cystone. In another study, both extracts ethanol and aqueous root extracts of *B. variegata* exerted significant nephroprotective activity in gentamicin-induced nephrotoxic rats as evident by decrease in elevated serum creatinine, serum urea, urine creatinine and blood urea nitrogen levels, which was further substantiated by histopathological study (Sharma et al. 2011b). In gentamicin-induced glomerular congestion, blood vessel congestion and epithelial desquamation, accumulation of inflammatory cells and necrosis of the kidney cells were found to be reduced in the groups receiving the root extract with gentamicin. Both extracts exhibited significant DPPH, nitric oxide and superoxide radical scavenging activity.

Antihyperlipidaemic Activity

Studies showed that alcoholic and aqueous extracts of *B. variegata* stem and roots could effectively decrease plasma cholesterol, triglyceride, LDL and VLDL and increase plasma HDL levels in Triton WR-1339 (iso-octyl polyoxyethylene phenol)-induced hyperlipidaemic albino rats (Rajani and Ashok 2009). Further, the alcoholic and aqueous extracts exhibited significant antioxidant activity in scavenging DPPH, superoxide, nitric oxide and hydrogen peroxide radicals and reducing power. Its antihyperlipidaemic activity may be attributed to its antioxidant activity.

Immunomodulatory Activity

Different fractions of *B. variegata* seed proteins (albumin, globulin, prolamin, acid glutelin and alkaline glutelin) demonstrated haemagglutinating activity against native and enzyme-treated rabbit erythrocytes with the globulin fraction showing the highest specific haemagglutinating activity (Pinto et al. 2005). Acid glutelin and albumin exhibited higher specific haemagglutinating activity against trypsin-treated and papain-treated rabbit erythrocytes, respectively.

On oral administration, the ethanol stem bark extract of *Bauhinia variegata* elicited a significant increase in the primary and secondary humoral antibody responses, by increasing the haemagglutinating antibody titre at doses of 250 and 500 mg/kg/p.o, in mice (Ghaisas et al. 2009). There was a significant increase in the phagocytic index and percentage neutrophil adhesion at doses of 250 and 500 mg/kg/p.o. The study suggested that the ethanol extract of the stem bark of *Bauhinia variegata* Linn may have promise as an immunomodulatory agent, acting probably by stimulating both the specific and nonspecific arms of immunity. In another study, pretreatment with aqueous and ethanol bark extracts caused dose-dependent and significant reduction in the total leucocyte and eosinophil counts in albino mice with milk-induced leukocytosis and eosinophilia (Mali and Dhake 2011). The results suggested that *Bauhinia variegata* possessed antieosinophilic activity.

Haematinic Activity

The ethanol stem bark extract of *Bauhinia variegata* exerted a haematinic activity on haemolytic anaemic rats (Dhonde et al. 2007).

Antiulcerogenic Activity

Oral administration of alcoholic extract of *B. variegata* to rats with ulcers induced by pyloric ligation and aspirin, decreased the volume of gastric secretion, total, free acidity and ulcer index with respect to control (Rajkapoor et al. 2003*a*). The alcoholic extract of *B. variegata* exhibited significant ulcer protective activity.

Anticataract Activity

In ovine and chick embryo lens model, rhamnocitrin isolated from the stem bark showed significant protection against cloudiness in lenses induced by hydrogen peroxide and hydrocortisone in a dose-dependent manner (Surendra et al. 2012). The findings suggested rhamnocitrin possessed significant anticataract activity which was most likely due to its antioxidant property.

Antiviral Activity

The dimeric melibiose-binding lectin from the seeds inhibited HIV-1 reverse transcriptase activity with an IC_{50} of 1.02 μM.

Mitogenic Activity

The dimeric melibiose-binding lectin from the seeds and concanavalin A (Con A) evoked maximal mitogenic response from mouse splenocytes at similar concentrations, but the maximal response to *B. variegata* lectin was only 1/5 of that induced by Con A in magnitude (Lin and Ng 2008).

Anthelmintic Activity

Ethanol stem bark extract of *B. variegata* exhibited anthelmintic activity in dose-dependent manner, giving shortest time of paralysis and death at 100 mg/ml concentration, for *Pheretima posthuma* and *Ascardia galli* worms (Mali et al. 2008).

Traditional Medicinal Uses

Various parts of the tree have been used in local folk medicine for various ailments in Nepal, India, Sri Lanka and Malaysia especially in the Ayurveda medicine system (CSIR 1959; Chopra et al. 1956; Burkill 1966; Kapoor and Kapoor 1980; Mali et al. 2007; Kumar et al. 2012; Sahu and Gupta 2012). In Sri Lanka, the plant is used for diarrhoea, dropsy, renal problems, dyspepsia, fistula, glandular enlargement, leprosy, piles, skin diseases and for slimming. Different parts of the plant have been used to suppress the oedema, dysentery, ulcers, eye disease, skin diseases, piles and haemorrhoids. Kachnar is widely used in Ayurveda as tonic to the liver (Bodakhe and Ram 2007). The plant juice is used in bath after

childbirth. The bark is alterative, anthelmintic, astringent and tonic. In Nepal, the juice of the bark is used in the treatment of amoebic dysentery, diarrhoea and other stomach disorders. Powdered bark is traditionally used for tonic, strains, ulcers and skin diseases. A paste of the bark is useful in the treatment of cuts and wounds, skin diseases, scrofula and ulcers.

The root is used as an antidote to snake poison and a root decoction is used to treat dyspepsia (Yadava and Reddy 2003; Agrawal and Pandey 2009). The flowers and dried flower buds are used in the treatment of piles, dysentery, diarrhoea, intestinal worms and stomach disorders and as a laxative (Malhotra and Moorty 1973; Badhe and Pandey 1990).

Other Uses

It is a very popular ornamental tree in landscaping and as a hedge plant in subtropical and tropical regions, grown for its showy fragrant flowers and unusual bilobed leaves. The bark is used for dyeing. The wood is used for the production of furniture and agricultural implements.

Comments

Distinct differences between *B. variegata* and *B. purpurea* occur in stamen number and the following characters:

B. purpurea. Flower buds 4 or 5 angled or winged; petals pale purple, shading to pinkish proximally, oblanceolate, 3–6 cm long, not more than 2 cm broad; fertile stamens 3; staminodes 7; leaf blades elliptic to suborbicular, 6–19 cm long and broad, rounded to cordate at base, lobed 1/2-1/4 their length, the lobes rounded to acute.

B. variegata. Flower buds not angled or winged; petals pale purple or rose or white or yellow, obovate 4–6 cm long, 2–3 cm broad, the uppermost one broader; fertile stamens 5; staminodes 5, about half as long as stamens; leaf blades broadly ovate to suborbicular, 5–14 cm long and broad, cordate to truncate at base, lobed about 1/3 their length or less, the lobes rounded.

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Caesalpinia pulcherrima

Scientific Name

***Caesalpinia pulcherrima* (L.) Sw.**

Synonyms

Caesalpinia pulcherrima var. *flava* Bailey and Rehder, *Poinciana bijuga* Lour., *Poinciana elata* Lour., *Poinciana pulcherrima* L.

Family

Fabaceae also in Caesalpiniaceae

Common/English Names

Barbados Flower-Fence, Barbados Pride, Barbados-Pride, Bird-Of-Paradise Flower, Dwarf Poinciana, Flower Crest, Flower-Fence, Flowerfence, Paradise Flower, Paradise-Flower, Peacock Flower, Peacock Tree, Poinciana, Poincillade, Pride of Barbados, Pride-Of-Barbados, Red Bird of Paradise, Spanish Carnation

Vernacular Names

Argentina: Chivato Chico
Brazil: Barba-De-Barata
Bolivia: Pajarillo; Chamorro: Caballero, Kabayeros
Burmese: Daungsop
Chuukese: Simmata, Simota, Warepik
Cook Islands: ʻŌvaʻI, ʻŌvai, Pī Tiare (Maori)
Czech: Sapan Nádherný
Danish: Påfuglebusk, Påfuglehale
German: Stolz Von Barbados
French: Aigrette, Poincillade, Faux Flamboyant, Orgueil De Chine, Petit Flamboyant
Hawaiian: Ohai Alii
India: Krishnachura (Assamese), Krishnachura, Krishanchura (Bengali), Guletura, Gul-Tora, Torai, Gulu Tora (Hindi), Kenjige, Komari, Ratnagandhi, Ratnaganhi, Kenjige Mara, Keneige, Kendge, Kenji Gida, Kanjage, Kenchige, Kencige, Ratnagandi, Channa-keshava Gida, Eejimullu, Hote Seege, Kenjigemara, Kenjuga, Komaari, Nalligaane (Kannada), Settimandaram, Techimandaram, Tsjetti-Mandarum, Cekkimandaram, Chekki-mandaram, Chettimandaram, Teccimandaram, Tsettimandaram (Malayalam), Krishanchura (Manipuri), Sankeshvara (Marathi), Tarra (Oriya), Krishnachuda, Krishnachura, Ratanagandhi, Sidhakhya, Sidhanasha, Sidheshwara (Sanskrit), Mayirkonrai, Mayuram, Nalal, Sirumayirkonrai, Mayilkonnai, Mayil-Konai, Cemmayirkkonrai, Cirontakam, Cirontakamaram, Cittimantarai, Cittimantaram, Irattinakanti, Kittimantaram, Kotinalal, Maikkonrai 1, Mancika 2, Mayikonnai, Mayilkonrai, Mayirkkonrai 1, Mayirpelavam, Mayirpelavamaram, Mayurakonnai, Mayuram 3, Mayuramaram, Perumayirkonrai, Pillicarikai, Pillicarikaimaram, Pirayakacceti,

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Piriyakam 2, Ponmayirkkonrai, Puccilakkonnai, Pumalekkinam 2, Tuccimam, Tuccimamaram, Mucuppira, Mucuppiramaram, Muyarcevitakkonnai, Muyarcevitam, Nalal2, Narikkonrai2, Vatamatakki 2 (Tamil), Pamiditangedu, Ratnagandhi, Sinnaturayi, Turayi, Pamidi Tangedu, Peydi-Tangedu, Ratna Gandhi, Kapura Maddi, Chinaturayi, Cinnaturayi, Paidithangedu, Pamidithangedu, Rathnagandhi, Sinnathuraayi, Thuraayi (Telugu)

Indonesia: Bunga Merak, Kembang Merak, Kembang Patra

Khmer: Dok Fang, Kan Gok Meas, Fang Ham

Kosraean: Rapotin, Repawtin

Malaysia: Chana, Cuban Haji, Bunga Cina, Hambul Merak

Marshallese: Emenawa, Jeimata, Jeimota, Jeimõta, Jemata

Mexico: Maravilla, Siikim; Mokilese: Shimatada

Niuean: Fisihetau, Fitihetau, Clavellina

Philippines: Bulaklak Ng Paraiso, Caballero (Tagalog)

Pingelapan: Seh Muatah

Pohnpeian: Sehmwida, Sem Tah, Semutha

Samoan: Lau Pa, Lau Pā

Satawalese: Waripik

Spanish: Flor De San Francisco, Caballero, Guacamaya; Macata, Francillade, Carzazo, Tabachín

Swedish: Påfågelsträd

Thailand: Khwaang Yoi (Eastern), Som Pho (Northern), Haang Nok Yuung Tai, Nok Yung Tai (Central)

Ulithian: Warapig

Vietnam: Diep Ta, Diep Cung, Kim Phuw Owng

Origin/Distribution

The plant is a native of the West Indies and Mexico and Central America. It is widely distributed and naturalized in the tropics.

Agroecology

A tropical tree species, adapted to temperatures of 15–35 °C in full sun to partial shade, from sea level to 1,000 m altitude or higher but is adapted to semi-drought conditions and tolerate extreme heat. It grows in a wide range of well-drained soils, from alkaline to acidic. It is moderately tolerant of saline conditions and is frost sensitive.

Edible Plant Parts and Uses

The flowers and young pods and seeds are eaten (Tanaka 1976; Pongpangan and Poobrasert 1985; Facciola 1990). Green seeds are sweetish and eaten raw in Thailand or cooked.

Botany

An erect, smooth much-branched shrub or small tree, 1.5–6 m high, branches unarmed or with a few straight prickles. The leaves are alternate, paripinnate, rachis 10–40 cm long, with 5–9 pairs of pinnae, stipules subulate, minute, caducous, leaflets opposite (Plates 1, 2 and 3), apetiolate, 6–12 pairs per pinnae, base unequal, rounded, apex rounded to retuse. Inflorescence in axillary and terminal raceme or panicle, 20–50 cm long; flowers bisexual, red, reddish-pink, orange, orangey-yellow, orange, bright yellow or creamy white; sepals 10–15 × 5–7 mm; petals crisped and clawed, 10–25 × 6–8 mm; stamens very long and very far exserted; ovary with 8–12 ovules (Plates 1, 2, 3, 4, 5 and 6) . The pod is nearly straight, flat, smooth, 6–12cb by1.5–2 cm wide with 6–8 rectangular, brown or black seeds.

Plate 1 Reddish-pink flowers, young pods and pinnate leaves

Plate 2 Close view of reddish-pink flowers

Plate 3 Orangey-yellow flowers, pods and leaves

Plate 4 Orange and orangey-yellow flowers with long exserted stamens

Plate 5 Bright yellow flowers, pods and leaves

Nutritive/Medicinal Properties

Analyses carried out in Nigeria (Yusuf et al. 2007) on the proximate composition of whole seeds and seed nuts (dehulled and dried) are % dry weight basis: moisture 9.5 %, 7.3 %; dry matter 90.95 %, 92.7 %; ash 4.5 %, 6.22 %; carbohydrates 39.1 %, 18.3 %; crude lipid 6.6 %, 5.65 %; crude fibre 9.06 %, 5.98 %; crude protein 48.08 %, 42.97 %; energy 312.15 kcal/100 g, 217.47 kcal/100 g; mineral composition per 100 g : Na 49.5 mg, 40.5 mg; K 39.5 mg, 31 mg; Ca 37.5 mg, 30.5 mg; Mg 58.5 mg, 69.5 mg; Fe 21 mg, 15 mg; P 56 mg, 124 mg; respectively. The results of another analysis conducted in Nigeria (Omole 2003) revealed that the crude protein and crude fat of the seeds were 33.50 and 16.80 %, respectively. The fatty acid profile indicated that the glycerides of oleic, linoleic and linolenic acid accounted for 82.46 % of the total glycerides. Iodine value and saponification number were 104.09 and 195.0, respectively, while the unsaponifiable matter showed a high value of 20 %.

Various scientific studies reported that *Caesalpinia pulcherrima* had antiviral, antiinflammatory, antitumorous, antiulcerogenic and antimicrobial properties.

Plate 6 Creamy-white flowers

Antiviral Activity

One study showed that aqueous extracts of *C. pulcherrima* and its related quercetin possessed a broad-spectrum antiviral activity against herpes viruses (HSV-1, HSV-2) and adenoviruses (ADV-3, ADV-8, ADV-11). Among them, the strongest activities against adenovirus ADV-8 were fruit and seed (EC_{50} = 41.2 mg/l, SI = 83.2), stem and leaf (EC_{50} = 61.8 mg/l, SI = 52.1) and flower (EC_{50} = 177.9 mg/l, SI = 15.5), whereas quercetin possessed the strongest anti-ADV-3 activity (EC_{50} = 24.3 mg/l, SI = 20.4). In conclusion, some compounds of *C. pulcherrima* which possess antiviral activities may be derived from the flavonoid of quercetin. The mode of action of quercetin against HSV-1 and ADV-3 was found to be at the early stage of multiplication and with SI values greater than 20, suggesting the potential use of this compound for treatment of the infection caused by these two viruses.

Antiinflammatory Activity

The following homoisoflavonoids, (*E*)-7-methoxy-3-(4′-methoxybenzylidene) chroman-4-one and (*E*)-7-hydroxy-3-(3′,4′,5′-trimethoxybenzylidene) chroman-4-one, (*Z*)-7-hydroxy-3-(4′-methoxybenzylidene) chroman-4-one (isobonducellin), (*E*)-7-hydroxy-3-(4′-methoxybenzylidene) chroman-4-one (bonducellin) and (*E*)-7-hydroxy-3-(2′,4′-dimethoxybenzylidene) chroman-4-one, were isolated from the whole plant of *Caesalpinia pulcherrima.* Five flavonoids, namely, 5,7-dimethoxyflavanone (1), 5,7-dimethoxy-3′,4′-methylenedioxyflavanone (2), isobonducellin (3), 2′-hydroxy-2,3,4′,6′-tetramethoxychalcone (4) and bonducellin (5), exhibited significant antiinflammatory activity. They significantly and dose-dependently inhibited the inflammatory mediators: nitric oxide (NO) and cytokines [tumour necrosis factor (TNF)-alpha and interleukin (IL)-12]. According to their inhibitory results, the order of antiinflammatory potency was compounds 3>5>4>2>1. Furthermore, peritoneal macrophages were pre-activated with lipopolysaccharide LPS/IFN-gamma (interferon-gamma) for 24 hours and determined the inhibitory effects of the above-mentioned isolates on the production of NO after a further 24 hours. The findings supported the use of *Caesalpinia pulcherrima* for the treatment of inflammatory diseases in traditional medicine. Two new flavonoids, 5,7-dimethoxy-3′,4′-methylenedioxyflavanone and isobonducellin along with 2′-hydroxy-2,3,4′,6′-tetramethoxychalcone, 5,7-dimethoxyflavone and bonducellin, were isolated from the aerial parts of *Caesalpinia pulcherrima*. Both flavonoids also exhibited antimicrobial activity.

Antimicrobial Activity

A new cassane-type diterpene isovouacapenol E (1) was isolated from the leaves of *Caesalpinia pulcherrima,* together with the known compounds caesaldekarin A (3), spathulenol (4), caryophyllene oxide (5), phytol and sitosterol. Four new cassane-type furanoditerpenoids (1–4) were isolated from the air-dried leaves of

Caesalpinia pulcherrima. The exocyclic methylene compound 1 readily isomerized and oxidized to the benzofuran 4. Benzyl 2, 6-dimethoxybenzoate (5) was also identified in this study. Antimicrobial tests on 1–5 indicated that they were active against several bacteria (*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Bacillus subtilis*) and fungi (*Candida albicans* and *Trichophyton mentagrophytes*). An ethanolic extract of the dry fruits of *Caesalpinia pulcherrima* exhibited a broad spectrum of antimicrobial activity, particularly against *Escherichia coli* (enteropathogen), *Proteus vulgaris, Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Antitumorous Activity

Cassane diterpenoids: pulcherralpin, pulcherrin A, pulcherrin B, pulcherrin C, neocaesalpin P, neocaesalpin Q and neocaesalpin R, together with eight known compounds: isovouacapenol C, 6-*p*-cinnamoyl-7β-hydroxy-vouacapen-5α-ol, pulcherrimin E, pulcherrimin C, α-cadinol, 7-hydroxycadalene, teucladiol and bonducellin—were isolated from the stem of *Caesalpinia pulcherrima*. Five new cassane diterpenoids (1–5) were isolated from the roots of *Caesalpinia pulcherrima*, along with the known isovouacapenol C (6), pulcherrimin A (11) and 6β-cinnamoyl-7β-hydroxyvouacapen-5α-ol (12). Two cassane-furanoditerpenoids, 6β-benzoyl-7β-hydroxyvouacapen-5 α-ol (1) and 6β-cinnamoyl-7β-hydroxyvouacapen-5α-ol (2), expressed moderate cytotoxic activity towards KB (human oral carcinonoid cancer), BC (human breast cancer) and NCl-H187 (small cell lung cancer) cell lines. Compound 2 showed strong antitubercular activity with a minimum inhibitory concentration (MIC) of 6.25 μg/ml, whereas the benzoyl analogue (1) was less active (MIC 25 μg/ml).

Antiulcerogenic Activity

Caesalpinia pulcherrima also has antiulcerogenic property. Pretreatment of the petroleum ether extract of *Caesalpinia pulcherrima* prevented the formation of gastric lesions in HCI/ethanol model in rats. In the aspirin and pylorus ligation model, the extract was able to significantly reduce the ulcer score and increased mucus content, but had no effect on gastric juice volume or acid content. Thus the results indicated that the extracts' antiulcerogenic effect was attributable to augmentation of gastric defence mechanisms.

Traditional Medicinal Uses

The bark, leaves, flowers, fruits and roots serve medicinal purposes in folkloric medicine. In general a decoction or infusion of roots, bark, leaves or flowers is used as a purgative and emmenagogue. Bark, root and flower have been used in traditional medicines for cutaneous and subcutaneous parasitic infection, febrifuges, pulmonary troubles; leaf especially for nasopharyngeal affections and as laxatives; and leaf and flower as abortifacients and ecbolics. Wood, leaf, root, flower and seed-pod provide tannins and astringents and seeds provide mucilage.

Medicine men in the Amazon Rainforest have long known some of the medicinal uses for *Caesalpinia pulcherrima*, which is known as *ayoowiri*. The juice from the leaves is said to cure fever, the juice from the flower is said to cure sores, and the seeds are said to cure bad cough, breathing difficulty and chest pain. Roots are used as abortifacient. In Papua New Guinea, the roots are used as an abortifacient, whereas the leaves are taken to relieve constipation. In Vietnam, the roots are used as an emmenagogue in folk medicine. In Indonesia, the pounded roots are given to children for convulsions, the bark employed for diarrhoea. The leaves are used with acorn and onions and applied to distended stomach. The leaves are also purgative and used as abortifacient to bring on abortion and used for fever infusion in Indochina. In the West Indies, the leaves and flowers are taken for fever. The flowers are reputed to have purgative, febrifuge and emmenagogue properties. A decoction is a popular remedy for erysipelas and for inflammation of the eyes. They are used also as a tonic.

The flowers are used as vermifuge and a decoction for coughs and chronic catarrh. The fruit is astringent and is employed against diarrhoea and dysentery. The seeds are used as an effective abortifacient.

Other Uses

Peacock flower is a popular ornamental throughout the tropics. It is commonly used for living fences, hedge plant and windbreaks in tropical countries. The flowers, in powder, are used as insecticides. The plant has been used as fish poison. By-products from the leaves include dyes, tannin, stains, inks, tattoos and mordants. The seeds contain galactomannans which can be used as food stabilizers. The firm heartwood serves the production of wooden pegs or tree nails. A yellow-flowering race of this species is used by the Chinese in Malaysia for ritual purposes. It is also the national flower of the Caribbean island of Barbados and is depicted on the Queen's personal Barbadian flag.

Comments

The plant is readily propagated from seeds or stem cuttings.

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Clitoria ternatea

Scientific Name

***Clitoria ternatea* L.**

Synonyms

Clitoria albiflora Mattei, *Clitoria bracteata* Poir., *Clitoria coelestris* Siebert & Voss, *Clitoria parviflora* Raf., *Clitoria philippensis* Perr., *Clitoria pilosula* Benth., *Clitoria ternatea* var. *pilosula* (Benth.) Baker, *Clitoria ternatensium* Crantz, *Lathyrus spectabilis* Forssk., *Nauchea ternatea* (L.) Descourt., *Ternatea ternatea* (L.) Kuntze, *Ternatea vulgaris* Kunth, *Ternatea vulgaris* Kuntze

Family

Fabaceae, also in Papilionaceae

Common/English Names

Asian Pigeonwing, Blue Butterfly Pea, Blue Pea, Butterfly Pea, Butterfly Pea Flower, Cordofan-Pea, Cocos

Vernacular Names

Arabic: Mazariyune-Hindi, Bazrulmazariyune-Hindi (Seeds), Bazrulmazariyunehindi, Buzrula, Mazariyunehindi

Chinese: Die Dou
Brazil: Cunha, Clitória
French: Honte, Pois Tonelle
German: Blaue Klitorie
India: Aparajita (Assamese), Aparajita (Bengali), Aparajit, Aparajita, Aprajita, Kajina, Kalina, Kalizer, Kava-Thenthi, Kavathenthi, Khagin, Kowa, Shobanjan, Wowatheti, Aparjit, Khagtu, Gokarni, Koyalri (Hindi), Girikarniballi, Kantisoppu, Karnikay, Sankhapushpaballi, Shankapushpa, Dhintina, Girikarnike, Satuga, Shankhapushpi, Giri Karnike, Girikarnikaballi, Sanka, Shanka, Shankhapushpa (Kannada), Aral, Kaka-Valli, Kakkanamkoti, Malayamukki, Samkhupuspam, Sankhankuppi, Sankhapushpam, Sankhupuspam, Schanga-Cuspi, Shankapuspam, Sankapushpam, Shankhankuppi, Shankhapushpam, Shlongokuspi, Shunkoopushpa (Malayalam), Aparajita (Manipuri), Gokurna-Mula, Gokaran, Gokarni, Gokurna, Kajli, Sholonga, Gokarana, Gokarni Suphali, Kajili, Supli (Marathi), Vryshapadi (Oriya), Ajita, Andrikarni, Aparajit, Aparajita, Aparaka, Aprajita, Ashphota, Ashvakshurardikarni, Asphota, Bhadra, Bhumilagna, Garani, Gardabhi, Gavadini, Gavakshi, Girikanya, Girikarnika, Girishalini, Gokarna, Gokarna-Mul, Gokarnika, Katabhi, Khurne, Kinihi, Nagaparyayakarni, Neela-Gheriekurnee, Nilaghiria, Nilagirikarni, Romavalli, Sankhapushpi, Sankhapuspi, Sankhini, Shankhapushpi, Shveta, Shvetavarata, Sinhapushpi, Sitapushpa, Supushpi, Suputri, Sveta, Vishnu-Kranta, Vishnukantri,

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Vishnukranta, Vishnukranti (Sanskrit), Girikanni, Kakkanam, Kakkattan, Kannikkodi, Kannikkoti, Karisanni, Karkkurattai, Karudakkovai, Karudattondai, Karuvilai, Kakkanan-Kodi, Kakkananko di-Virai, Kakkankoti, Vellai Kakkattan, Kakkana Ver, Vellai-K-Kakkanam, Canku Puspam, Kakkanam Koti, Kakkanatti, Karuppu-K-Kakkanam-Koti, Kakkanan, Kakkattan-Kodi, Kavachhi, Kodi-Kakkanam, Kuruvilai, Karkakartan Vayr, Kaakkanam, Sankapushpam, Karkakartum, Karkokartun, Venkakkattan, Ancanala, Ancanala, Aral, Atirikarni, Ayittiram, Cankuputpakkoti, Cankuputpam, Kakkam, Kakkana, Kakkanankovvai, Kakkarattan, Kakkorattai, Kakkurattai, Kakkurattai, Karkurattai, Karkurattaikkoti, Karttakakkattan, Karunkakkanam, Karunkakkattan, Karunkakkattankoti, Karunkananko ti, Karunkattan, Karunkattankoti, Karutakanatti, Karutakanattikkoti, Karutakkovai, Karutakkovvai, Karutattontai, Karuttakakkanam, Karuttakakkanan, Karuttappu, Karuttontai, Karuvilaikkakkanam, Karuvilam, Kauri 2, Kaurikkoti, Kavetanam, Kicinikkoti, Kiruttini, Kiruttinikkoti, Kokanni, Kokarni, Kollankovai, Kurattai, Kurokanatti, Kurokanattikkoti, Kurottai, Makanatti, Makanattikkoti, Mayil, Tarukanni, Minni, Muntakkini, Muntakkinikkoti, Nakanatti, Nakanattikkoti, Nilakirikaranai, Nilakkakkanam, Nilakkakkattan, Viranu, Uromavalli, Uyavaikkoti, Vainakanatti, Vainakanattikkoti, Vullay Kakartan Vayr (Tamil), Dintana, Dintena, Gilarnika, Nallavusinitige, Sankapushpam, Sanku-Pushpamu, Gantina, Nall Vusiri, Nallaghentana, Nalladintenatige, Nallavusiniige, Nelladintena, Nullaghentana, Tantiri, Telladintena, Adavichikkudu, Nalla Dintena, Shanku Poolu, Shankupushpamu, Thelladintena (Telugu), Mazeriyunihindi, Mazriyun (Urdu)

Indonesia: Kembang Telang, Mentelang (Java), Kembang Telang (Sundanese)

Japanese: Choumame

Malaysia: Bunga Biru, Kacang Telang, Kacang Puki, Kelang

Persian: Darakhte-Bikhehayat, Tukhme-Bikhehayat (Seeds), Darakhtebikhehayat, Tukhmebikhehayat

Philippines: Giting-Princesa (Bikol), Balog-Balog (Cebu Bisaya), Kalompagi, Samsamping (Iloko), Samsampin (Pangasinan), Kolokanting, Pukingan, Puki-Reyna (Tagalog)

Portuguese: Clitoria-Azul

Spanish: Azulejo, Conchitis, Papito, Zapatico De La Reina, Zapotillo, Conchita Azul, Campanilla, Bandera, Choroque, Lupita, Pito De Parra, Bejuco De Conchitas

Sri Lanka: Katarodu-Wel

Thai: Ang Chan, Daeng Chan, Uegng Chan

Tibetan: A Sa Khu Ra, A-Pa-Ra-Dzi-Ta, Ge Ri Ka Rni Ka Dkar Po, Sra Na Ma Geri Ka Rni Ka, Sve

Vietnamese: Dau Biec

Origin/Distribution

The true origin of the species is obscured by extensive naturalization; it is probable that it originated from South America. It is now distributed pantropically.

Agroecology

The plant grows wild in wasteland, thickets or disturbed areas and on most soil types at low and medium altitudes. It is adaptable to a wide range of soil types from sandy soils to heavy clays including calcareous soils and with a wide pH range from 4.5 to 8.9. It is moderately tolerant to salinity. It thrives in areas with 700–1,500 mm mean annual rainfall but will survive in areas with only 400 mm and dry periods. It tolerates short-term flooding but not prolonged waterlogging. It is tolerant to light frost and will tolerate low temperatures down to 15 °C and high temperature to 35 °C. It prefers full sun but will tolerate partial shading and is used as cover crops in rubber and coconut plantations in the tropics.

Edible Plant Parts and Uses

The flower, fruit and leaves are edible (Burkill 1966; Tanaka 1976; Facciola 1990; Kaisoon et al. 2001; Wetwitayaklung et al. 2008). In Southeast Asia, the flowers are used for colouring rice in puddings and cakes and leaves used for colouring food stuff green. In Thailand, the leaves are used in salad and for frying. Young pods are edible and eaten as vegetable.

Botany

A short-lived, fast-growing climbing perennial, leguminous herb. Stem thin, glabrous or sparsely pubescent, climbing or twining, 2–5 m long. Leaves imparipinnate, arranged in 2–3 pairs, bright green, petiolate (1.5–3 cm long), leaflets elliptic-ovate to elliptic lanceolate, 1.5–5 cm by 0.4–3 cm wide, acute or notched apex and rounded base, margin entire (Plates 1 and 2). Inflorescence axillary bearing several flowers on 4–9 mm long pedicels and with ovate, persistent bracteoles. Flowers—clitoris-like flower shape with large obovate, reflexed, funnel-shaped standard, 5 cm long, light to deep blue, mauve or white and yellow at the inner base (Plates 1 and 2). Pods flattish, linear-oblong, 6–12 cm long by 0.6–1.2 cm wide, beaked with 4–8 flat, rounded, olive-brown to black seeds.

Plate 1 Blue flowers and imparipinnate leaves

Nutritive/Medicinal Properties

Phytochemicals in Flowers

The per cent yield and the amount of total polyphenols in g/100 g calculated as gallic acid on dried flowers and crude methanol extracts basis of *C. ternatea* extract were reported as 10.23 %, 0.55 g dried flower, 2.29 g crude extract (Wetwitayaklung et al. 2008). Among 24 edible flowers tested, the lowest TEAC value was obtained from the extract of *Clitoria ternatea* (TEAC = 0.01, IC_{50} = 1.08 mg/50 µl) and *Sesbania grandiflora* (TEAC = 0.01, IC_{50} = 1.32 mg/50 µl) (Wetwitayaklung et al. 2008).

Clitoria ternatea flowers were found to contain little calcium (1.9 mg/100 g) compared to common vegetables as determined *via* inductively coupled

Plate 2 Close view of flower

plasma atomic emission spectroscopy (Chin 1992). The soluble phenol acids (per g dry weight) identified in *Clitoria ternatea* flower extract were as follows: gallic acid 33.2 µg, protocatechuic acid 1.8 µg, caffeic acid 10.03 µg, *p*-coumaric acid 11.6 µg, ferulic acid 34.8 µg, sinapic acid 152.8 µg and total phenolic acid 243.5 µg (Kaisoon et al. 2001). The flowers contained 261.5 µg total bound phenolic acid made up of ferulic acid 108 µg and sinapic acid 153.5 µg. The flowers contained 115.5 µg total soluble flavonoid made up of rutin 38.1 µg, myricetin 4.85 µg, quercetin 68.9 µg and kaempferol 3.65 µg; and bound flavonoid 141.4 µg made up of quercetin 113.2 µg, quercetin 11.1 µg and apigenin 17.2 µg. The DPPH radical scavenging activity (% inhibition) of soluble and bound phenolic fraction of the flower was 32.7 and 17.59 %, respectively. The reducing potential of the soluble and bound phenolic fraction of the flower as evaluated by FRAP (ferric-reducing antioxidant power) assay mmol $FeSO_4$/100 g dry weight was 16.37 mmol and 7.7 mmol, respectively. Bound phenolics exhibited lower antioxidant activity than soluble ones.

The anthocyanins, malvidin-3-β-glycoside and deiphinidin-3-β-glycoside were isolated from *C. ternatea* flowers (Srivastava and Pandey 1977). Saito et al. (1985) found that stability of the anthocyanins increased with the degree of acylation with cinnamic and malonic acids as well as with the degree of substitution of hydrogens on the B ring in *C. ternatea.* Other anthocyanins reported were ternatins, polyacetylated delphinidin 3,3′,5-triglucosides that conferred blue colour to the petals *C. ternatea*. Six new stable anthocyanins, named ternatin A1, A2, B1, B2, D1 and D2, were isolated from the blue flowers of *Clitoria ternatea* (Terahara et al. 1989a). The structures of two common components prepared from alkaline deacylation of ternatin mixture yielded two common components: *E*-4-*p*-coumaryl β-D-glucoside (1) and delphinidin 3,3′,5′-tri-β-D-glucoside (2). The structure of ternatin Al was elucidated as 3-*O*-(6-*O*-malonyl-β-D-glucopyranosyl)-3′,5′-di-*O*-(6-*O*-(*E*-4-*O*-(6-*O*-(*E*-4-*O*-β-D-glucopyranosyl-p-coumaryl)-β-D-glucopyranosyl)-*p*-coumaryl)-β-D-glucopyranosyl)-delphinidin (Terahara et al. 1990c). Ternatin D1, an acylated anthocyanin, was elucidated as 3-*O*-(6-*O*-malonyl-β-D-glucopyranosyl)-3′,5′-di-*O*-(6-*O*-(*E*-4-*O*-(6-*O*-E-*p*-coumaryl-β-D-glucopyranosyl)-*p*-coumaryl)-β-D-glucopyranosyl)delphinidin (Terahara et al. 1989b); ternatin A1, the largest ternatin (Terahara et al. 1990b); ternatin B1, a pentaacylated anthocyanin elucidated as 3-*O*-(6-*O*-malonyl-β-D-glucopyranosyl)-3′-*O*-ß-D-glucopyranosyl-*E*-*p*-coumaryl-ß-D-glucopyranosyl-*E*-*p*-coumaryl-ß-D-glucopyranosyl-ß-D-glucopyranosyl-5′-*O*-*E*-*p*-coumaryl-ß-D-glucopyranosyl-*E*-*p*-coumaryl-ß-D-glucopyranosyl ß-D-glucopyranosyl-delphinidin (Kondo et al. 1990). Two acyl moieties, prepared by alkaline deacylation or H2O2 oxidation of ternatin mixture from *C. ternatea* flowers, were identified as *E*-4-*O*-β-D-glucopyranosyl-*p*-coumaric acid and 6-*O*-malonyl-D-glucopyranose and six ternatins A1, A2, B1, B2, D1 from the flowers were partly characterized as highly acylated delphinidin derivatives (Terahara et al. 1990a). Deacylternatin was determined as delphinidin 3,3′,5′-tri-*O*-b-d-glucopyranoside (Terahara et al. 1990b). The structure of ternatin A2 was identified as 3-*O*-(6-*O*-malonyl-β-D-glucopyranosyl)-3′-*O*-(6-*O*-(*E-4-O*-(6-*O*-(*E*-4-*O*-β-D-glucopyranosyl-*p*-coumaryl)-β-D-glucopyraonsyl)-*p*-coumaryl)-β-D-glucopyranosyl)-5′-*O*-(6-*O*-(*E*-4-*O*-β-D-glucopyranosyl-*p*-coumaryl)-β-D-glucopyranosyl)delphinidin (Terahara et al. 1990d). Anthocyanins ternatins A1, A2, B1, B2, D1 and D2 were isolated from double blue flowers (Honda et al. 1991). Five anthocyanins, namely, ternatins A3, B4, B3, B2 and D2, were isolated from *Clitoria ternatea* flowers (Terahara et al. 1996). Eight new anthocyanins 1–8 (ternatins C1, C2, C3, C4, C5 and D3 and preternatins A3 and C4) were isolated from *Clitoria ternatea* flowers (Terahara et al. 1998). The structures of 1–6 were postulated as delphinidin 3-malonylglucoside having 3′-GCGC-5′-G, 3′-GCGCG-5′-G, 3′-GC-5′-G, 3′-GCG-5′-G, 3′-G-5′-G and 3′-GC-5′-GC, and compounds 7 and 8 as delphinidin 3-glucoside having 3′-GCG-5′-GCG and 3′-GCG-5′-G as side chains, respectively, in which Dp=delphinidin, G=D-glucose and C=*p*-coumaric acid.

The following flavonol glycosides were isolated from the petals of *Clitoria ternatea* cv Double Blue: kaempferol 3-*O*-(2″-*O*-*α*-rhamnosyl-6″-*O*-malonyl)-β-glucoside; quercetin 3-*O*-(2″-*O*-*α*-rhamnosyl-6″-*O*-malonyl)-β-glucoside; myricetin 3-*O*-(2″,6″-di-*O*-α-rhamnosyl)-β-glucoside; kaempferol 3-(2(G)- rhamnosylrutinoside 3-(2(G)-rhamnosylrutinoside; quercetin 3-(2(G)- rhamnosylrutinoside; kaempferol 3-neohesperidoside;quercetin3-neohesperidoside; myricetin 3-neohesperidoside; kaempferol 3-rutinoside; quercetin 3-rutinoside; myricetin 3-rutinoside; kaempferol 3-glucoside; quercetin 3-glucoside; myricetin 3-glucoside; and myricetin 3-*O*-(2″-*O*-α-rhamnosyl-6″-*O*-malonyl)-β-glucoside (Kazuma et al. 2003b). Delphinidin 3-*O*-(2″-*O*-*α*-rhamnosyl-6″-*O*-malonyl)-β-glucoside; 2, delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside; 3, delphinidin 3-neohesperidoside; and 4, delphinidin 3-*O*-β-glucoside were isolated from the petals of a mauve line (WM) (Kazuma et al. 2003a). Ternatins, a group of 15 (poly)acylated delphinidin glucosides, were identified in all the blue petal lines (WB, BM-1, 'Double Blue' and 'Albiflora'), WM accumulated delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside instead. The white petal line (WW) did not contain anthocyanins. The change in flower colour from blue to mauve was not due to a change in the structure of an anthocyanidin from delphinidin but to the lack of (polyacylated) glucosyl group substitutions at both the 3′- and 5′-positions of ternatins implying glucosylation at the 3′- and 5′-positions of anthocyanin to be a critical step in producing blue petals in *C. ternatea*. Among the ternatins, blue anthocyanins found in the petals of *Clitoria ternatea*, ternatin C5 (delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside-3′,5′-di-*O*-β-glucoside) was found to have the structure common to all the ternatins, i.e. characterized by its glucosylation pattern: a 3,3′,5′-triglucosylated anthocyanidin (Kazuma et al. 2004). An intermediate in the biosynthesis of ternatin C5 in the blue petals, delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside-3′-*O*-β-glucoside, was also identified. In *C. ternatea*, a blue flower cultivars (DB) and mauve flower variety (WM) accumulated polyacylated anthocyanins (ternatins) and delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside (Kogawa et al. 2007*b*). Further, WM accumulated minor delphinidin glycosides—3-*O*-β-glucoside, 3-*O*-(2″-*O*-*α*-rhamnosyl)-β-glucoside and 3-*O*-(2″-*O*-*α*-rhamnosyl-6″-*O*-malonyl)-β-glucoside of delphinidin. These glycosidic patterns for minor anthocyanins in WM were also found among the minor flavonol glycosides in all the varieties including a white flower variety (WW) although the major flavonol glycosides were 3-*O*-(2″-*O*-*α*-rhamnosyl)-β-glucoside,3-*O*-(6″-*O*-*α*-rhamnosyl)-β-glucoside, 3-*O*-(2″,6″-di-*O*-α-rhamnosyl)-β-glucoside of kaempferol, quercetin and myricetin. A UDP-glucose: anthocyanin 3′,5′-*O*-glucosyltransferase (UA3′5′GT) was purified from the petals of *Clitoria ternatea* which accumulated polyacylated anthocyanins named ternatins (Kogawa et al. 2007a). In the biosynthesis of ternatins, delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside (1) was first converted to delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside-3′-*O*-β-glucoside (2). Then 2 was converted to ternatin C5 (3), which was delphinidin 3-*O*-(6″-*O*-malonyl)-β-glucoside-3′,5′-di-*O*-β-glucoside. UA3′5′GT was responsible for these two steps by transferring two glucosyl groups in a stepwise manner. Its substrate specificity revealed the regioselectivity to the anthocyanin's 3′- or 5′-OH groups. The presence of alkaloids, flavonoids, saponins, tannins, carbohydrates and proteins were reported in the methanol extract of the flowers (Uma et al. 2009).

Phytochemicals in Seeds

Sinha (1960a) identified yellow fixed oil (yield 18.78 %) from the seeds and isolated γ-sitosterol. Gupta and Lal (1968) reported hexaconazole, β-sitosterol and an anthoxanthin glucoside from the seeds; on acid hydrolysis, the anthoxanthin glucoside yielded quercetin and glucose. They also identified the following amino acids in the seed: lysine, valine, methionine, phenylalanine, isoleucine, aspartic acid, serine, glycine, alanine, glutamic acid, tyrosine, proline, arginine and histidine. Kulshrestra and Khare (1968) isolated six crystalline compounds in the seeds: adenosine,

kaempferol-3-rhamnoglucoside, *p*-hydroxycinnamic acid and ethyl-α-D-GALACTOPYRANOSIDE, and two remaining compounds a polypeptide and a phenylglycoside.

Clitoria ternatea seed was found to contain 1.75 % moisture, 10.2 % oil, 38.4 % protein, 44.8 % total sugars, 3.75 % ash and energy 500.5 cal/100 g (Joshi et al. 1981). The seed oil was found to contain palmitic, stearic, oleic, linoleic and linolenic acids in the weight ratio of 18.5, 9.5, 51.4, 16.8 and 3.8 %, respectively. The oil had a specific gravity of 0.884 at 30 °C, refractive index at 39 °C of 1.459, saponification value of 187.7, iodine value of 70.4, acid value of 0.25 and unsaponifiable matter of 1.8 %. Protein constituted 38.4 % comprising 18 amino acids. Essential amino acid profile was (%) lysine (6.40–6.55), histidine (2.03–2.15), threonine (3.13–3.2), phenylalanine (3.2–3.30), methionine (1.06–1.04), serine (6.7–6.86), tyrosine (2.05–2.17), cystine (0–0.11), arginine (7.13–7.16), glutamic acid (23.9–24.03), aspartic acid (12.5–12.7), alanine (4.6–6.8), valine (5.8), proline traces, γ-aminobutyric acid traces and leucine plus isoleucine (15.51–15.8).

The seeds were found to contain 4.79 % oligosaccharides (Revilleza et al. 1990).

Three trypsin inhibitors were isolated from the seeds (Macedo and Xavier-Filho 1992). *C. ternatea* seeds were found to contain antifungal proteins, homologous to plant defensins (Osborn et al. 1995). Low levels of condensed tannins (0–2.48 mg catechin/g) and protein precipitable polyphenols (0.16–0.77 mg tannic acid/g) were detected in the raw mature seeds (Laurena et al. 1994).

Finotin a small basic antimicrobial and insecticidal protein was isolated from the seeds (Kelemu et al. 2004). A β-D-galactoside-specific lectin, designated *C. ternatea* agglutinin (CTA), purified from *Clitoria ternatea* seeds was found to compose of two identical subunits of molecular weight 34.7 kDa associated by non-covalent bonds and belonged to Gal/Gal NAc-specific group (Naeem et al. 2007a, b). CTA agglutinated trypsin-treated human B erythrocytes and may probably exhibit sugar uptake activity. This lectin could be used as valuable tool for glycobiology studies in biomedical and cancer research since it binds β-D-galactosides. The content of lectin was found to be 30 mg/30 g dry weight of pulse. The yield was 2.8 % as compared to 0.3 % obtained on fetuin column.

Phytochemicals in Leaves

Leaf mucilage was reported to contain anhydrogalactose, anhydropentosan and methyl pentosan (Sinha 1960b). Aiyar et al. (1973) reported 3 glycosides of kaempferol from the leaves: kaempferol-3-monoglucoside, kaempferol-3-rhamnosyl (1 → 6) glucoside and kaempferol-3-rhamnosyl (1 → 6) galactoside. The light petroleum ether and ether extracts yielded waxy material, chlorophyll and β-sisterol. Four kaempferol glycosides, I, II, III and IV, were isolated from *Clitoria ternatea* leaves and identified as kaempferol 3-glucoside (I), 3-rutinoside (II) and 3-neohesperidoside (III) and IV was characterized as kaempferol-3-*O*-rhamnosyl-(1 → 2)-*O*-[rhamnosyl-(1 → 6)]-glucoside and named clitorin (Morita et al. 1977). Stigmast-4-ene-3,6-dione was isolated from the dried leaves of *C. ternatea* (Ripperger 1978). The leaves were reported to have 12.5 % moisture content, 13.2 % total ash, 4.8 % acid insoluble ash, 5.3 % water soluble ash, water soluble extractive value 25.2 % and alcohol soluble extractive value 18.4 % (Taur et al. 2010).

Phytochemicals in Aerial Parts

Phytoconstituents such as propane 1,1-diethoxy- (4.73 %), 1,6,10-dodecatriene, 7,11-dimethyl-3-methylene-, (*Z*)- (1.18 %), 1,2,3,5-cyclohexanetetrol (1à,2á,3à,5á)- (3.55 %), myo-inositol, 4-C-methyl- (31.07 %), hexadecanoic acid, ethyl ester (2.66 %), phytol (1.18 %), 9,12-octadecadienoic acid, methyl ester (*E,E*)- (0.89 %), 7,11-hexadecadienal (1.18 %), octadecanoic acid, ethyl ester (0.59 %), isoparvifuran (5.33 %), 6H-benzofuro[3,2-c][1]benzopyran, 6a,11a-dihydro-3,9-dimethoxy- (6a*Rcis*)- [synonym:

homopterocarpin] (10.66 %), petrocarpin (15.68 %) and 1H-cycloprop[e]azulene, 1a,2,3,5,6,7,7a,7b-octahydro-1,1,4,7- tetramethyl-, [1a*R*-(1aà,7à,7aá,7bà)]-[synonym: varidiflorene] were found in *C. ternatea* aerial part extract (Sarumathy et al. 2011).

C. ternatea had been reported to have cyclotides, plant-derived proteins with a unique cyclic cystine knot topology and to play a role in host defence as well as to have a diverse range of pharmaceutically important activities, including uterotonic activity and antimicrobial and anti-HIV activity and had attracted recent interest as templates in drug design (Poth et al. 2011a). The scientists confirmed the expression and correct processing of the cyclotide encoded by the Cter M precursor gene transcript following extraction from *C. ternatea* leaf. Seven additional cyclotide sequences were also identified from *C. ternatea* leaf and flower, five of which were unique. Cter M displayed insecticidal activity against the cotton budworm *Helicoverpa armigera* and bound to phospholipid membranes, suggesting its activity to be modulated by membrane disruption. Further they found 12 novel cyclotides in the seeds (Poth et al. 2011b).

Phytochemicals in Roots

Taraxerone and taraxerol were isolated from *C. ternatea* roots (Banerjee and Chakravarti 1963, 1964). The concentration of taraxerol was found to be 12.4 mg/g w/w in the hydroalcoholic extract of *C. ternatea* root (Kumar et al. 2008).

Agrobacterium rhizogenes-transformed root cultures of butterfly pea were found to produce up to fourfold more yield of taraxerol, the anticancer triterpenoid compound compared to that in natural roots (Swain et al. 2012).

Phytochemical studies reported that the root-bark contained starch, taraxerol, tannin and resins; the seeds contained a fixed oil, bitter acid resin, tannic acid and 6 % ash and an alkaloid. The flowers were found to anthocyanins such as ternatins and preternatins and flavonol glycosides; kaempferol 3-*O*-(2″-*O*-α-rhamnosyl-6″-*O*-malonyl)-β-glucoside; quercetin 3-*O*-(2″-*O*-α-rhamnosyl-6″-*O*-malonyl)-β-glucoside; myricetin 3-*O*-(2″,6″-di-*O*-α-rhamnosyl)-β-glucoside; kaempferol and quercetin 3-(2(G)-rhamnosylrutinoside); kaempferol, quercetin and myricetin 3-neohesperidosides, 3-rutinosides and 3-glucosides; and myricetin 3-*O*-(2″-*O*-α-rhamnosyl-6″-*O*-malonyl)-β-glucoside.

Antioxidant Activity

Terahara and Nishiyama (2000) considered ternatins as good radical-scavenging type antioxidants. Crude pigment extract from blue flowers of butterfly pea, containing ternatins (delphinidin 3-malonylGs connected with a series of 3′, 5′-GC… side chains (G: D-glucose, C: p-coumaric acid)), was reported to have potential as new multifunctional natural pigment for a food colourant, cosmetic and disease-preventing food material. Some reasons stipulated were the relatively high antioxidative activity of ternatin B and D groups, the stable colour of ternatins in aqueous solution and the safe traditional usage of the crude pigments as food colourant in Southeast Asia. The leaves and blue and white flowers of *Clitoria ternatea* exhibited significant antioxidant activity with the blue flower-bearing plant showing higher scavenging activity (Sivaprabha et al. 2008). Aqueous *C. ternatea* flower extracts were shown to have stronger antioxidant activity (as measured by DPPH scavenging activity) than ethanol extracts (IC_{50} values were 1 mg/ml and 4 mg/ml, respectively) (Kamkaen and Wilkinson 2009). Aqueous extracts incorporated into an eye gel formulation were also shown to retain this activity; however, it was significantly less than a commercial anti-wrinkle cream included for comparison. The total phenolic content was 1.9 mg/g extract as gallic acid equivalents.

Methanol root extracts of blue- and white-flowered varieties of *C. ternatea* showed more potent antioxidant activity in DPPH radical-

scavenging assay than the pet ether or chloroform extracts (Patil and Patil 2011). The methanol root extracts also showed significant reductive ability as well as hydroxyl radical scavenging activity. The antioxidant activity of *C. ternatea* methanol leaf extract was 67.85 % at a concentration of 1 mg/ml and was also concentration dependent, with an IC_{50} value of 420.00 µg/ml (Nithianantham et al. 2011). The amount of total phenolics and flavonoids were estimated to be 358.99 mg/g gallic acid equivalent and 123.75 mg/g catechin equivalent, respectively.

Antidiabetic Activity

Oral administration of aqueous extract of *C. ternatea* leaves (400 mg/kg body weight) and flowers (400 mg/kg body weight) for 84 days significantly reduced serum glucose, glycosylated haemoglobin, total cholesterol, triglycerides, urea, creatinine and the activity of gluconeogenic enzyme glucose-6-phosphatase, but increased serum insulin, HDL-cholesterol, protein, liver and skeletal muscle glycogen content and the activity of glycolytic enzyme glucokinase (Daisy et al. 2009). For all the above biochemical parameters investigated, *C. ternatea* leaves treated rat showed a little better activity than *C. ternatea* flowers treated diabetic rats. In another study, the ethanol seed extract of *C. ternatea* at 400 mg/kg body weight dose significantly decreased blood glucose, cholesterol, alkaline phosphatase, aspartate amino transferase and alanine amino transferase in diabetic rats when compared to streptozotocin-induced diabetic control (Kalyan et al. 2011). Ethanol extract showed the presence of various phytoconstituents, namely, sterols, alkaloids, glycosides, saponins, tannins, carbohydrates, proteins, phenolic compounds and flavonoids. Dried plant extracts of roselle, chrysanthemum, mulberry, bael and butterfly pea were found to have in-vitro inhibitory effects on intestinal α-glucosidase and pancreatic α-amylase (Adisakwattana et al. 2012). They reported that the use of plant-based foods and their combinations with inhibitory effects on intestinal α-glucosidase (maltase and sucrase) and pancreatic α-amylase could help prevent the onset of diabetes by controlling postprandial hyperglycaemia resulting in aggressive delay of carbohydrate digestion to absorbable monosaccharide. Phytochemical analysis revealed that the total phenolic content of the dried plant extracts were in the range of 460.0–230.3 mg gallic acid equivalent/g dried extract. The dried extracts contained flavonoid in the range of 50.3–114.8 mg quercetin equivalent/g dried extract. It was noted that the IC_{50} values of chrysanthemum, mulberry and butterfly pea extracts were 4.24, 0.59 and 3.15 mg/ml, respectively. Further, the IC_{50} values of chrysanthemum, mulberry and butterfly pea extracts against intestinal sucrase were 3.85, 0.94 and 4.41 mg/ml, respectively. In addition, the IC_{50} values of roselle and butterfly pea extracts against pancreatic α-amylase occurred at concentration of 3.52 and 4.05 mg/ml, respectively. Combining roselle, chrysanthemum and butterfly pea extracts with mulberry extract showed additive interaction on intestinal maltase inhibition.

Antimicrobial/Insecticidal Activity

The aqueous, methanol and chloroform extracts of *C. ternatea* flowers exhibited activity against uropathogenic *Escherichia coli*, enteropathogenic *Escherichia coli*, enterotoxigenic *Escherichia coli, Salmonella typhimurium, Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (Uma et al. 2009). However, the petroleum ether and hexane extracts did not exhibit any activity. The methanol leaf extract of *C. ternatea* was found to possess a more potent inhibitory activity effect against *Bacillus cereus, Staphylococcus aureus, Klebsiella pneumonia, Proteus vulgaris* and *Salmonella typhi* when compared to the petroleum ether and ethyl acetate extracts (Anand et al. 2011).

Finotin a small basic protein was isolated from the seeds was found to be antimicrobial and insecticidal (Kelemu et al. 2004). It exhibited broad and potent inhibitory effect on the growth of various important fungal pathogens of plants, namely, *Rhizoctonia solani, Fusarium solani, Colletotrichum lindemuthianum, Lasiodiplodia*

theobromae, Pyricularia grisea, Bipolaris oryzae and *Colletotrichum gloeosporioides*. It also inhibited the common bean bacterial blight pathogen *Xanthomonas axonopodis* pv. *phaseoli.* Finotin also had powerful inhibitory properties against the bean bruchids *Zabrotes subfasciatus* and *Acanthoscelides obtectu*s. *Clitoria ternatea* leaf extract showed a favourable antifungal activity against *Aspergillus niger* with a minimum inhibition concentration 0.8 mg/ml and minimum fungicidal concentration 1.6 mg/ml (Kamilla et al. 2009). The leaf extract exhibited considerable antifungal activity on hyphal growth of *A. niger*. There was loss of cytoplasm in fungal hyphae and the hyphal wall, and its diameter became markedly thinner and distorted and resulted in cell wall disruption. In addition, conidiophore alterations were also observed.

Central Nervous System Activity

The alcoholic extracts of aerial and root parts of *C. ternatea* at 300 and 500 mg/kg doses administered orally to rats were capable of attenuating electroshock-induced amnesia (Taranalli and Cheeramkuzhy 2000). Extracts at 300 mg/kg dose produced significant memory retention, and the root parts were found to be more effective. They found that *C. ternatea* extracts increased rat brain acetylcholine content and acetyl cholinesterase activity in a similar fashion to the standard cerebroprotective drug pyritinol. Jain et al. (2003) reported *Clitoria ternatea* to possess nootropic, anxiolytic, antidepressant, anticonvulsant and antistress activities. A methanol extract of *Clitoria ternatea* was found to impact on the central nervous system. The extract decreased time required to occupy the central platform (transfer latency, TL) in the elevated plus maze (EPM) and increased discrimination index in the object recognition test, indicating nootropic activity. The extract was more active in the object recognition test than in the EPM. The extract increased occupancy in the open arm of EPM by 160 % and in the lit box of the light/dark exploration test by 157 %, indicating its anxiolytic activity. It decreased the duration of immobility in tail suspension test (suggesting its antidepressant activity), reduced stress-induced ulcers and reduced the convulsing action of PTZ and MES. The extract exhibited tendency to reduce the intensity of behaviour mediated via serotonin and acetylcholine. Recent studies by Malik et al. (2011) also showed that *C. ternatea*, commonly used as a component ingredient in the well-known Ayurveda herbal drug Shankhpushpi, exhibited nootropic, anxiolytic and CNS-depressant activity.

Neonatal rat pups (7 days old) intubated with either 50 mg/kg body weight or 100 mg/kg body weight of aqueous root extract of *Clitoria ternatea* for 30 days resulted in memory enhancement (Rai et al. 2001). There was improvement in retention and spatial learning performance at both time points of behavioural tests in neonatal rat pups, indicating the memory enhancing property of the extract which implicated a permanent change in the brain of extract treated rats. Another study showed that the plant extract enhanced memory. Treatment with 100 mg/kg of *Clitoria ternatea* aqueous root extract, for 30 days in neonatal and young adult age groups of rat, significantly increased acetylcholine (ACh) content in their hippocampi as compared to age matched controls (Rai et al. 2002). Increase in ACh content in their hippocampus may be the neurochemical basis for their improved learning and memory. Further Rai et al. (2005) found that the significant improvement in dendritic arborization of amygdaloid neurons correlated with the increased passive avoidance learning and memory in the extract treated rats. The results suggested that *Clitoria ternatea* aqueous root extract enhanced memory by increasing the functional growth of neurons of the amygdala.

Antiinflammatory, Analgesic and Antipyretic Activities

Clitoria ternatea also has antiinflammatory, analgesic and antipyretic attributes (Devi et al. 2003). Its methanol root extract when given by oral route to rats was found to inhibit both the rat paw oedema caused by carrageenan and vascular permeability induced by acetic acid in rats.

Moreover, the extract exhibited a significant inhibition in yeast-induced pyrexia in rats. In the acetic acid-induced writhing response, the extract markedly reduced the number of writhing at doses of 200 and 400 mg/kg (p.o.) in mice. The methanol root extract at doses of 200, 300 and 400 mg/kg body wt. p.o. produced significant reduction in normal body temperature and yeast-provoked elevated temperature in a dose-dependent manner. The effect extended up to 5 hours after the drug administration. The antipyretic effect of the extract was comparable to that of paracetamol (150 mg/kg body wt., p.o.), a standard antipyretic agent.

Antiplatelet Aggregating Activity

Anthocyanins ternatins (A1, A2, B1, B2, D1 and D2) isolated from *Clitoria ternatea* (double blue) were found to have blood platelet aggregation-inhibiting (Honda et al. 1991) and vascular smooth-muscle-relaxing activities.

Antihyperlipidaemic Activity

Oral administration of the hydroalcoholic extract of the roots and seeds of *C. ternatea* resulted in a significant reduction of serum total cholesterol, triglycerides, very low-density lipoprotein cholesterol and low-density lipoprotein cholesterol levels (Solanki and Jain 2010a). The atherogenic index and the HDL/LDL ratio were also normalized after treatment in diet-induced hyperlipidaemic rats. The effects were compared with atorvastatin (50 mg/kg, p.o.) and gemfibrozil (50 mg/kg, p.o.), reference standards. The authors attributed the cholesterol-lowering effect of *C. ternatea* to increased biliary excretion and decreased absorption of dietary cholesterol.

Hepatoprotective Activity

The results of the paracetamol-induced liver toxicity studies showed that mice treated with the methanol extract of *C. ternatea* leaf (200 mg/kg) showed a significant decrease in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin levels, which were all elevated in the paracetamol group (Nithianantham et al. 2011). *C. ternatea* leaf extract therapy also had protective effects against histopathological alterations. In another study, *C. ternatea* seed extract significantly decreased SGOT, SGPT, ALP and total bilirubin in both acetaminophen and CCl_4-intoxicated rats (Solanki and Jain 2011). The *C. ternatea* root extract showed similar results only in CCl_4-intoxicated rats. Hepatic collagen content as evident from decreased hydroxyproline levels and hepatic mast cell infiltration were significantly decreased in extracts pretreated animals. In addition, *C. ternatea* seed extracts significantly reduced hepatic lipid peroxidation as evident from the decreased MDA and increased antioxidant enzyme activities and GSH levels in the liver tissues. They suggested that the hepatoprotective activity of *C. ternatea* could be attributed to antioxidant properties and prevention of pre-inflammatory changes. They suggested that the hepatoprotective action was likely related to its potent antioxidative activity.

Nephroprotective Activity

Oral administration of the ethanol extract of *C. ternatea* plant elicited nephroprotective activity against acetaminophen-induced nephrotoxicity in male albino rats (Sarumathy et al. 2011). Biochemical studies showed that there was an increase in the levels of serum urea and creatinine along with an increase in the body weight and reduction in the levels of uric acid in acetaminophen-induced animals. These values were reverted significantly by treatment with *Clitoria ternatea* extracts at two different doses of 250 and 500 mg/kg body weight. The antioxidant studies revealed that the levels of renal SOD, CAT, GSH and GPx in the APAP-treated animals are increased significantly along with a reduced MDA content in ethanol extract of *Clitoria ternatea-treated* groups. Further, histopathological changes also revealed the protective nature of the *Clitoria ternatea* extract against

acetaminophen-induced necrotic damage of renal tissues.

Immunomodulatory Activity

C. ternatea seed and root extracts showed significant immunosuppressive effects as evident from significant decrease in primary and secondary antibody titres in SRBCs-sensitized rats, paw thickness in delayed type hypersensitivity (DTH) response and neutrophil adhesion and in-vitro phagocytosis (Solanki and Jain 2010b). They attributed the immunomodulatory effects of *C. ternatea* on humoral, cell-mediated and nonspecific immune response to decreased immune cell sensitization, immune cell presentation and phagocytosis. They also asserted that the antiinflammatory and antioxidant properties of plant might be playing major role in immunomodulatory activity.

Wound Healing Activity

C. ternatea seed and root extracts significantly improved wound healing in excision, incision and dead-space models in rats when administered orally by gavage as well as applied topically as ointment (Solanki and Jain 2012). These effects were comparable to that of cotrimoxazole ointment. The findings suggested that *C. ternatea* affected all three phases—inflammatory, proliferative and remodelling phases of wound healing. The plant extracts were found to contain phenolic compounds and seed extract was containing flavonol glycosides.

Antinutrient Activity

Three trypsin inhibitors with molecular weights of 20, 12 and 7 kDa and with one-chain molecule were isolated from the seeds (Macedo and Xavier-Filho 1992). The 20-kDa inhibitor had arginine in the reactive site, the 12-kDa had lysine in the reactive site, and both belonged to the Kunitz and Bowman–Birk families, respectively. The small molecular weight inhibitor (7 kDa) also had an arginine in the reactive site and was probably of the Bowman–Birk type. The seeds were found to have oligosaccharides which could be completely removed by 2 minutes roasting; germination resulted only in 30–40 % of total oligosaccharide (Revilleza et al. 1990).

Anthelmintic Activity

Clitoria ternatea was found to have an anthelmintic activity (Khadatkar et al. 2008). A crude alcoholic extract and its ethyl acetate and methanol fractions significantly demonstrated paralysis and also caused death of worms (*Pheretima posthuma*) especially at higher concentration of 50 mg/ml, as compared to standard reference piperazine citrate.

Antihistaminic Activity

The ethanol extract of *Clitoria ternatea* root was found to have antihistaminic activity using clonidine- and haloperidol-induced catalepsy in mice (Taur and Patil 2011b).

Antiasthmatic Activity

The ethanol extract of *Clitoria ternatea* root significantly decreased milk-induced leukocytosis and eosinophilia, protected egg albumin-induced degranulations of mast cells in mice and inhibited area of blue dye leakage in passive cutaneous anaphylaxis in rats at (100–150 mg/kg, i.p.) (Taur and Patil 2011a). Phytochemical studies observed the presence of steroids, saponin, flavonoids and glycosides. The results suggested that the antiasthmatic activity of ECTR may be due to the presence of flavonoids or saponins.

Mosquito Larvicidal Activity

Among the methanol extracts of *C. ternatea* leaves, roots, flowers and seeds, the seed extract was effective against the larvae of all the three

major mosquito vectors *Aedes aegypti*, *Culex quinquefasciatus* and *Anopheles stephensi* with LC_{50} values 65.2, 154.5 and 54.4 ppm, respectively (Mathew et al. 2009). Among the three plant species (*Saraca indica/asoca*, *Nyctanthes arbor-tristis* and *Clitoria ternatea*) studied, *C. ternatea* showed the most promising mosquito larvicidal activity. The phytochemical analysis of the promising methanol extract of the seed extract was positive for carbohydrates, saponins, terpenoids, tannins and proteins.

Traditional Medicinal Uses

Clitoria ternatea, a traditional Ayurvedic medicine, has been used for centuries for many diseases and disorders. It has been employed as a memory enhancer, nootropic, antistress, anxiolytic, antidepressant, anticonvulsant, tranquilizing and sedative agent and used in the traditional Indian system of medicine as a brain tonic and is believed to promote memory and intelligence (Burkill 1966; Aiyar et al. 1973; Taranalli and Cheeramkuzhy 2000; Mukherjee et al. 2008; Wetwitayaklung et al. 2008; Anand et al. 2011; Malik et al. 2011; Kaisoon et al. 2001; Stuart 2012). The plant parts have been considered cooling, acrid, purgative, laxative, diuretic, antipyretic, antiinflammatory, analgesic and anthelmintic.

The root, leaves and flowers are used in the form of powder and decoction to treat oedema, mental disorder, goitre, vitiligo, snake poisoning, toothache, eye disease, fever, asthma, jaundice, earaches, pile, throat infections, skin diseases (boils and scabies), renal stones and filariasis, and also used as an aphrodisiac. In the Philippines, the leaves were employed as wet dressing for wounds; root decoction taken to treat inflammation of joints, and the seeds used in poultices for swollen joints. In Indonesia, the seeds are considered aperient, the roots are cathartic, the leaves are used as poultices, and juice of white flowers was used for inflamed eyes. In Thailand, the flowers are used as hair tonic, for hair growth, as stimulant and for hair colouring.

Other Uses

Butterfly pea is a multipurpose forage legume. It provides bioactive compounds for medicinal use and it is also an ornamental plant on fence rows, cover crop and green manure crop. Butterfly pea, a highly palatable forage legume, is generally preferred over other legumes by livestock such as sheep, goat and cattle. It has thin stem and large leaves, nil bloat and nontoxic which make it ideal for forage and haymaking. Its vigorous growth, tolerance to frost and dry periods and heavy grazing pressures make this suitable for wasteland development. It is used as a revegetation species on coal mines in central Queensland, Australia. When grown as green manure or ley pasture, it enhances soil fertility to improve yields of subsequent crops like maize, sorghum wheat. It is used as a cover crop in rubber, cocoa and coconut plantations.

The flowers are still widely used for making dye in Southeast Asia because they are rich in blue anthocyanin, a plant pigment. The dye is added to cosmetics, fabrics and shampoo (which helps keep dyed hair dark) and used as a food colourant. The blue dye is also used as a natural pH indicator in the pharmaceutical industry.

Comments

Clitoria ternatea is readily propagated from seed and by cuttings.

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Erythrina variegata

Scientific Name

***Erythrina variegata* L.**

Synonyms

Chirocalyx candolleanus Walp., *Chirocalyx divaricatus* (DC.) Walp., *Chirocalyx indicus* (Lam.) Walp., *Chirocalyx pictus* (L.) Walp., *Corallodendron divaricatum* (Moc. & Sessé ex DC.) Kuntze, *Corallodendron orientale* (L.) Kuntze, *Corallodendron spathaceum* (DC.) Kuntze, *Erythrina alba* Cogniaux & Marchal, *Erythrina boninensis* Tuyama, *Erythrina carnea* Blanco nom. illeg., *Erythrina corallodendron* Linn., *Erythrina corallodendron* var. *orientalis* L., *Erythrina corallodendrum* Lour., *Erythrina divaricata* DC. nom. illeg., *Erythrina humeana* sensu R.Vig., *Erythrina indica* Lam., *Erythrina indica* var. *alba* W. S. Millard & E. Blatter, *Erythrina indica* var. *fastigiata* Guill., *Erythrina lithosperma* Blume ex Miq., *Erythrina lobulata* Miq. *Erythrina loureiri* G. Don, *Erythrina marmorata* Veitch ex Planch., *Erythrina mysorensis* Gamble, *Erythrina orientalis* (L.) Murr., *Erythrina parcellii* W. Bull, *Erythrina phlebocarpa* F.M. Bail., *Erythrina picta* L., *Erythrina rostrata* Ridl., *Erythrina spathacea* DC., *Erythrina variegata* f. *alba* Maheshw., *Erythrina variegata* f. *marmorata* Maheshw., *Erythrina variegata* f. *mysorensis* Maheshw., *Erythrina variegata* f. *orientalis* Maheshw., *Erythrina variegata* f. *parcellii* Maheshw., *Erythrina variegata* f. *picta* (L.) Maheshw., *Erythrina variegata* var. *orientalis* (L.) Merr., *Gelala alba* Rumphius, *Gelala litorea* Rumph., *Tetradapa javanorum* Osbeck

Family

Fabaceae, also placed in Papilionaceae

Common/English Names

Coral Tree, East Indian Coral Tree, East Indies Coral Tree, Indian Bean Tree, Indian Coral Bean, Indian Coral Tree, Lenten Tree, Mochi Wood Tree, Tiger's Claw

Vernacular Names

Bangladesh: Mandar
Burmese: Penglay-Kathit
Chinese: Hai Tong Pi, Hoi Tong Peh
Chuukese: Paar, Weeku
Cook Islands: Gatae
Fiji: Drala, Drala Dina, Rara, Rara Damu, Rarawai, Segar
French: Arbreau Corail, Arbre Corail À Feuilles Panachées, Arbre Corail De L'inde, Arbre Immortel, Bois Immortel, Bois Immortel Vrai, Pignon D'inde
German: Indischer Korallenbaum
Hawaiian: Wiliwili-Haole

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India: Madaar, Modar, Ranga (Assamese), Deo, Deuya, Kanda Mathar, Maadaara, Madar, Mandaara, Palte Madar, Tepalte Madar (Bengali), Paanarvo (Gujerati), Dadap Pharhad, Dhobi-Palas, Jangli-Sem, Mahamed, Mandara, Palas, Pangara, Pangra, Panjira, Paribhadra, Parijat, Phārahaḍa, Raktamadar (Hindi), Bilee Vaarjipe, Bili Vaarjipae, Bilivarijapa, Haalivaana, Haaravaana, Haaru Vaana, Hongara, Hongarike, Kempu Vaari Jaapa, Kempuvarijapa, Mandaara, Mullu Murige, Mullumurunji, Murige, Muruku, Paarijaathaka, Pongaara, Vaarjipe Mara, Warjipe. (Kannada), Pongero (Konkani), Mandaram, Mullumurikku, Mulmurikk, Mulmurukku, Murikk, Murikku, Paribhadram, Penmurikk (Malayalam), Korou Angangba (Manipuri), Mandar, Paangaara, Pangara, Pangaru, Paringa, Phandra (Marathi), Fartuah (Mizo), Salotonoya (Oriya), Bahupushpah, Kantakipalasa, Mahamedah, Mandar, Mandara, Mandarak, Mandaravah, Mandaruh, Mazndatah, Paribhadra, Páribhadrah, Parijata, Pravalashmantakah, Raktapuspa, Sushpah, Sutikatah, Vyagulikesarah, Vidrumah (Sanskrit), Civappu-Moccai, Kaliyana, Kaliyana Murukku, Kaliyāṇa Murukkuvakai, Kaliyana Murunkai, Kannalamurukku, Kiñcukam, Muḷḷu-Murukku, Muṇmurukku Murukku, Murungu, Navir, Palacam, Paricatam, Savusayam, Veḷḷaikkavi (Tamil), Baadida Chettu, Baadidapu Chettu, Baadis Chettu, Baadisa, Baaditha, Baaditi, Baanditha Chettu, Baarjapu Chettu, Badida, Badidepuchettu, Baridamu, Mahaameda, Muchchekarra, Muchikatta, Paaribhadrakamu, Paaribhvyamu, Parijatamu, Rohinamu, Wngiram (Telugu)

Indonesia: Dadap Ayam, Dadap Laut (Javanese), Belendung, Dadap Belendung (Sundanese), Thethek (Madurese)

Japanese: Deigo, Deiko, Kaitohi

Khmer: Roluŏhs Ba:Y

Korean: Haedongp'i

Laotian: Do:K Kho, Th'o:Ng Ba:Nz

Malaysia: Dedap, Deap Batik, Cengkering

Marquesas: Natae, Netae

Nepalese: Mandar, Phalledo

Niue: Gate

Papua New Guinea: Ivini (Hula, Central Province), Ialawa (Wagawaga, Milne Bay), Balbal (Raval, East New Britain), Bubakai (Kokopo, East New Britain), Lehelehe (Lontis, Buka, North Solomons Province), Valval (Lamekot, New Ireland), Banban (Ugana, New Ireland)

Philippines: Andorogat, Dapdap, Kabrab (Bikol), Dapdap (Bisaya), Sabang (Bontok), Vuvak (Ibanag), Bagbag Dubdub (Ilokano), Dapdap, Sulbang (Pampangan), Dapdap, Karapdap, Kasindak (Tagalog)

Pohnpei: Paripein

Russian: Eritrina Indijskaia, Eritrina PëStraya, Eritrina Raznoobraznaia

Samoan: Gatae

Sri Lanka: Era Badu, Era Mudu, Katu Eramadu, Mandar, Murunga (Sinhalese)

Swedish: Indiskt Koralträd

Tahiti: 'Atae

Thailand: Thong Baan, Thong Phuek (Northern), Thong Laang Laai (Central), Thong Lang Dang (Bangkok)

Tibetan: Man D Ra Ba

Tongan: Ngatae

Vietnam: Hải Đồng Bì, Lá Vông, Thích Đồng Bì, Vông Nem

Yapese: Paar, Raar

Origin/Distribution

It is native to tropical Asia—from Taiwan and southern China through the Philippines, Indonesia, Malaysia, Thailand, Myanmar, India, islands in the Indian Ocean and all the way to tropical East Africa. Introduced and naturalized also in American and African tropical countries.

Agroecology

An adaptable species that grows in the humid tropics, subtropics and semiarid areas, occurring in zones with mean annual temperatures of 20–32 °C and mean annual rainfall of 800–

1,500 mm with 5–6 months of rainy periods. It occurs wild in deciduous forest from the coastal dunes and forests to an elevation of 1,500 m. It thrives best in full sun on a deep, well-drained, sandy loam, but they tolerate a wide range of soil conditions from sands to clays of pH 4.5–8.0. The tree is drought tolerant, fairly fire tolerant, and can tolerate brief periods of waterlogging.

Edible Plant Parts and Uses

Young and old leaves are eaten steamed or stewed as lalab with rice or mixed with other vegetables (Ochse and Bakhuizen van den Brink 1980). In Papua New Guinea, the leaves are eaten cooked (French 1986). The boiled flowers and young leaves are edible, cooked like string beans but in more water (Deane 2002–2012). Seeds are consumed after roasting or boiling but are poisonous when eaten raw (Burkill 1966). In Vietnam, the leaves of *E. variegata* are used to wrap 'nem' (a kind of fermented pork).

Botany

An erect much branched, medium-sized, deciduous tree up to 25 m high and a spread of 8–12 m. Stem smooth, greyish with large scattered conical prickles on the stem and branch. Leaves are alternate, trifoliate, 20–30 cm long, the terminal largest; leaflet-stalk glandular (Plates 1 and 2). Leaflets are triangular to broadly rhomboid-ovate, with acuminate tips and obtuse bases, shining green. Inflorescence in dense axillary and terminal racemes appearing before the leaves (Plates 1 and 3); rachis tomentose; bracts small; flowers bright red; calyx tubular, minutely 5-toothed; corolla long, standard broad, ovate-elliptical, shortly clawed and 7–9 cm long, wings and keel subequal; stamens 10, connate basally, exserted; ovary multi-ovuled, style glabrous, incurved (Plates 3 and 4). Pods are black, cylindrical, long up to 38 cm, dehiscent and constricted between the glossy, reddish brown reniform seeds. Each pod has 5–10 seeds.

Plate 1 Terminal inflorescence and leaves

Plate 2 Trifoliate leaves (Chung GF)

Plate 3 Terminal inflorescence (Chung GF)

Plate 4 Close view of flowers (Chung GF)

Nutritive/Medicinal Properties

Leaf Nutrients/Phytochemicals

Food nutrient value of fresh leaves per 100 g edible portion reported is moisture 78.1 g, energy 69 kcal, protein 5.0 g, fat 0.7 g, carbohydrate 10.6 g, fibre 3.0 g, ash 2.6 g, Ca 639.1 mg, Fe 4.1 mg and P 109 mg (National Institute of Nutrition-University of Central Florida Project 2001–2004).

Erythaline and erythratine were isolated (Folkers and Koniuszy 1940). Leaves were reported to have a total alkaloidal content of 0.11 % constituting alkaloids erysotrine, erysodine, erysovine, erythaline, erysopine, erysopitine, erysonine, erysodienone, orientaline, hypaphorine, hypaphorine methyl ester and also N,N-dimethyltryptophan (Ghosal et al. 1970, 1972). From the leaves were isolated two alkaloids (erysothrine and hypaphorine) (Nguyen et al. 1991); two tetrahydroprotoberberine alkaloids (scoulerine and (+)-coreximine); a benzyltetrahydroisoquinoline alkaloid (L-reticuline); a dibenz[d, f]azonine alkaloid (erybidine); *O*-methylerybidine and *N*-norreticuline (Ito et al. 1973); scoulerine and coreximine (Ito 1999); 10,11-dioxoerythratidine (Herlina et al. 2005); phytol (Herlina et al. 2006); isolate 11 characterized as a triterpene pentacyclic 3b-11a-28-trihydroxy-oleane-2-ene and isolate 17 as a mixture of β-sitosterol and stigmasterol (Herlina et al. 2008); pentacyclic triterpenoid (3,22,23-trihydroxy-oleane-12-ene); pentacyclic triterpenoid (3b,11a-28trihydroxy-oleane-12-ene); and 10,11-dioxoerythratidine (Supratman et al.2010). Kalachaveedu et al. (2011) extracted β-sitosterol (433 mg, 1.445 w/w), oleanolic acid (65 mg, 0.217 % w/w) and β-sitosterol glycoside (108 mg, 0.36 % w/w).

The leaf was found to contain a lectin with molecular weight of 58 kDa, made up of two subunit molecular weights of 30 and 33 kDa (Konozy et al. 2002). The leaf lectin was found to be a glycoprotein with a neutral sugar content of 9.5 %. The leaf lectin was rich in acidic as well as hydrophobic amino acids and totally lacked cysteine and methionine. The N-terminal amino acids were Val-Glu-Thr-IIe-Ser-Phe-Ser-Phe-Ser-Glu-Phe-Glu-Ala-Gly-Asn-Asp-X-Leu-Thr-Gln-Glu-Gly-Ala-Ala-Leu-.

Flower Phytochemicals

The alkaloid, erythratine, elucidated as 11-hydroxyerysotrine, was isolated from the flowers in Egypt (El-Olemy et al. 1978). The flowers were found to contain 7-methoxy 8-(15-OH pentadecyl)-coumarin; phaseollin; 29-norcycloartenol; 3-β-acetoxy- β-norcholest-5-ene; docosanoic and capric acid; flavonoid abyssinone; prenylated isoflavonoids stigmoidins A, B and C, besides isoquinoline alkaloids erythritol; and isoquinoline alkaloid isococcoline, isoflavones alpinumisoflavone, erythrinin A,B and C, osajin and erythrabasin I (Sharma and Chawla 1992; Chawla and Sharma 1993). Two isoquinoline alkaloids designated erythrosotidienone and erythromotidienone plus stigmasterol, cycloartenol and erysotramidine were isolated from the acetone flower extract (Sharma and Chawla 1998).

Seed Phytochemicals

Marañon and Santos (1932) found an alkaloid, a fatty oil, and a saponaceous glucoside from the seeds. The alkaloid isolated had the properties identical with those of hypaphorine. From seeds

erythraline and 'free' and 'liberated' erysovine were isolated (Singh and Chawla 1970). The fatty acid composition of the seed oil was also determined. A prenylated flavone glycoside 5,7,4′-trihydroxy-3′-methoxy-8-C-prenylflavone 7-*O*-β-D-glucopyranosyl-(1 → 3)-α-l-arabinopyranoside (**1**) was isolated from the seeds (Yadava and Reddy 1999). Nitrogen contents of *E. variegata* seeds and deoiled seeds showed good protein content; albumin, globulin, prolamine and glutelin were separated out by fractionation (Samanta and Laskar 2008). Fractionation of protein was done to separate albumin, globulin, prolamine and glutelin. The total protein isolates (TPI) and the fractions isolated contained 17 amino acids, most of which were essential.

A D-galactose-binding glycoprotein lectin was purified from the seeds (Datta and Basu 1981). A mitogenic D-galactosephilic lectin was isolated from seeds (Gilboa-Garber and Mizrahi 1981). Kunitz-type trypsin inhibitors, ETIa and ETIb, and chymotrypsin inhibitor ECI were isolated from the seeds (Kouzuma et al. 1992). The proteins ETIa and ETIb comprised 172 and 176 amino acid residues with molecular weight 19,242 and 19,783, respectively, and shared 112 identical amino acid residues, about 65 % identity. A chymotrypsin inhibitor (ECI) isolated from seeds was found to have 179 amino acid residues with a pyroglutamic acid as the N-terminal residue and has a calculated molecular weight of 19,791 (Kimura et al. 1993). About 60 % of the residues of ECI were identical to those of ETIa and ETIb and the reactive sites, Arg63, in ETIa and ETIb were changed to Leu64 in ECI. A Bowman-Birk family proteinase inhibitor (EBI) isolated from the seeds was found to consist of 61 amino acid residues, the shortest among the Bowman-Birk family inhibitors sequenced to date, and with a molecular weight of 6,689 (Kimura et al. 1994). EBI could be classified as a group II inhibitor, showing the best homology (67 %) to the Bowman-Birk proteinase inhibitor from soybeans. *Erythrina variegata* chymotrypsin inhibitor (ECI) and chymotrypsin molecules were found to undergo aggregation in the complex-forming buffer simultaneously with a binary complex consisting of one ECI and one chymotrypsin molecule in a soluble form (Kimura et al. 1997). ECI comprised two peptides; the N-terminal peptide, ECI-(1-107)-peptide, containing the primary reactive site retained a slight inhibitory activity, while the C-terminal peptide, ECI-(108-179)-peptide, exhibited no inhibitory activity. It was demonstrated that amino acid residues Gln62 (P3), Phe63 (P2), Leu64 (P1) and Phe67 (P3′) in the primary binding loop of *Erythrina variegata* chymotrypsin inhibitor (ECI), a member of the Kunitz inhibitor family, were involved in its strong inhibitory activity towards chymotrypsin (Iwanaga et al. 1998). It was further shown that the intramolecular interaction between the primary binding loop and the scaffold of ECI played an important role in the strong inhibitory activity towards chymotrypsin (Iwanaga et al. 1999).

The purified seed isolectins (EVLI, EVLII and EVLIII) isolated from *E. variegata*, were all specific for galactopyranosides and N-acetylgalactosamine, and their affinities for simple sugars were EVLIII greater than EVLII greater than EVLI (Yamasaki et al. 1992). EVLI and EVLIII were found to be homodimers made up of an A-subunit of molecular mass 36,000 and a B-subunit of molecular mass 33,000, whereas EVLII a heterodimer composed of the A- and B-subunits. They found that there was no structural difference of the sugar chains linked to the two subunits of *E. variegata* galactose-specific isolectins (Yamaguchi et al. 1993). This together with the results of amino acid sequence comparisons indicated that the difference in molecular mass of these two subunits resulted almost wholly from the difference in the number of oligosaccharides linked to them.

Stem/Bark/Wood Phytochemicals

The petroleum ether bark extract was found to compose of wax alcohols and wax acids, alkyl ferulates, alkyl phenolates, stigmasterol, sitosterol, campesterol and citrostadienol/24-methylenelophenol (Singh et al. 1975). The ethanol bark extract yielded chloroform-soluble and water-soluble bases, identified as erysovine

and stachydrine, respectively. From the bark were isolated isoflavones (erythrinins A,B, C, osajin; alpinumisoflavone; and oxyresveratrol and dihydrooxyresveratrol) (Deshpande et al. 1977), alkaloids (erysotine, erythratidine, *epi*-erythratidine and 11-hydroxy-*epi*-erythratidine) (Chawla et al. 1988), three flavonoid phospholipase A_2 (PLA_2) inhibitors(4′-hydroxy-3′,5′-diprenylisoflavonone (abyssinone V) and 3,9-dihydroxy-2,10-diprenyl-pterocarp-6a-ene(erycrystagallin)and4′-hydroxy-6,3′,5′-triprenylisoflavonone) (Hedge et al. 1997), erythrinin B (Kobayahsi et al. 1997), alpinumisoflavone and two prenylated isoflavones (erythrivarones A and B characterized as dihydroalpinumisoflavone and 4′-hydroxy-[6″,6″-dimethyldihydropyrano(2″,3″:5,6)]-[6‴,6‴-dimethyldihy dropyrano(2‴,3‴:7,8)] isoflavone, respectively) (Huang and Yen 1996; 1997) and warangalone (Huang and Tseng 1998). Isoflavonoids, eryvarin A and eryvarin B, were isolated from wood (Tanaka et al. 2000). Two isoflavone derivatives named indicanines D and E together with 11 known compounds including six isoflavones (genistein, wighteone, alpinumisoflavone, dimethylalpinumisoflavone, 8-prenyl erythrinin C and erysenegalensein E), one cinnamate (erythrinassinate B), two pentacyclic triterpenes (oleanolic acid and erythrodiol) and two phytosterols (stigmasterol and its 3-*O*-β-D-glucopyranoside) were isolated from the stem bark (Nkengfack et al. 2001). Huang and Chiang (2004) isolated the following constituents from the methanol stem bark extract: triterpenoids, namely, lup-20(29)-en-3-one; β-amyrin; olean-12-en-3β, 22β-diol; olean-12-en-3β, 28-diol; 22β, 24-dihvdroxvolean-12-en-3-one; oleanonic acid; oleanolic acid; and olean-12-en-3β, 22β, 24-triol along with warangalone and 6,8-diprenylkaempferol.

From the stem bark, three isoflavones (5,4′-dihydroxy-8-(3,3-dimethylallyl)-2″-methoxyisopropylfurano[4,5:6,7]isoflavone (1), 5,7,4′-trihydroxy-6-(3,3-dimethylallyloxiranylmethyl) isoflavone (2) and 5,4′-dihydroxy-8-(3,3-dimethylallyl)-2″-hydroxymethyl-2″-methyl-pyrano[5,6:6,7]isoflavone (3)) and a new isoflavanone, 5,4′-dihydroxy-2′-methoxy-8-(3,3-dimethylallyl)-2″,2″-dimethylpyrano[5,6:6,7] isoflavanone (4), together with seven known compounds, euchrenone b10 (5), isoerysenegalensein E (6), wighteone (7), laburnetin (8), lupiwighteone (9), erythrodiol (10) and oleanolic acid (11), were isolated (Li et al. 2006). Genistein derivatives mainly in the form of prenylgenistein from this extract, including 6-prenylgenistein, 8-prenylgenistein and 6, 8-diprenylgenistein, were isolated from the stem bark (Zhang et al. 2008). Warangalone 8(3,3-dimethyl-allyl)-4′-hydroxy-2‴,2‴-imethylpyran[6,7,b]isoflavon was isolated from the stem bark (Herlina et al. 2009). The following secondary metabolites were isolated from the stem bark: alpinum isoflavone,6-hydroxygenistein,3β,28-dihydroxyolean-12-ene, epilupeol (Rahman et al. 2007) and three isoflavones (scandenone, 4′,5,7-trihydroxy-8-prenylisoflavone and 4′,5,7-trihydroxy-8-methylisoflavone) (Rahman et al. 2010). Liu et al. (2012) isolated erysopine and erysovine from the stem bark.

Root Phytochemicals

The following compounds were isolated from the roots: warangalone (scandenone), 5,7,4′-trihydroxy-6,8-diprenylisoflavone, erycristagallin, erythrabys-sin-II, phaseollin, phaseollidin, isobavachin and a cinnamylphenol, eryvariestyrene (*E*-1-[2, 4-dihydroxy-5-(3-methylbut-2-enyl)]-2-phenylethylene) (Telikepalli et al. 1990); pterocarpans, dihydrofolinin and erythrabyssin II, and the alkyl ester of ferulic acid, octacosyl ferulate (Ahmad et al. 2002); orientanol B (9-hydroxy3-methoxy-2γ, γ, dimethylallylpterocarpan), erycristagallin (3,9-dihydroxy-2,10-di(γ,γ-dimethylallyl)-6α,11α-dehydropterocarpan), cristacarpin, sigmoidin K, 2-(γ,γ-dimethylallyl)- 6α-hydroxyphaseollidin, erystagallin A (3,6α-dihydroxy-9-methoxy-2,10-di(γ,γ-dimethylallyl) pterocarpan) (Sato et al. 2002); two diphenylpropan-1,2-diols, eryvarinols A (1) and B (2) and their structures were elucidated as 1-(4-hydroxy-2-methoxyphenyl)-2-(4-hydroxy-3, 5-dimethoxybenzoyloxy)-3-(4-hydroxyphenyl) propan-1-ol (1) and its 3″-prenyl derivative (2)

(Tanaka et al. 2002a); 3,9-dihydroxy-2,10-di(γ,γ-dimethylallyl)-6α,11α-dehydropterocarpan (erycristagallin) and 9-hydroxy-3-methoxy-2-γ,γ-dimethylallylpterocarpan (orientanol B) (Tanaka et al. 2002b); two 3-phenoxychromones, eryvarins F and G, and their structures were elucidated as 3-(2,4-dihydroxyphenoxy)-7-hydroxy-6,8-di(3,3-dimethylallyl)chromen-4-one and 3-(2,4-dihydroxyphenoxy)-8-(3,3-dimethylallyl)-2,2-dimethylpyrano[5,6:6,7] chromen-4-one, respectively (Tanaka et al. 2003); three isoflavonoids, eryvarins M–O, two 2-arylbenzofurans, eryvarins P and Q, and a 3-aryl-2,3-dihydrobenzofuran, eryvarin R (Tanaka et al. 2004); two isoflavonoids, eryvarins S and T, and a new 2-arylbenzofuran, eryvarin U (Tanaka et al. 2005); a biisoflavonoid, biseryvarin A, was isolated from the roots (Tanaka et al. 2010); and two isoflavonoids, eryvarins V and W, and a chromen-4-one derivative, eryvarin X (Tanaka et al. 2011).

A 3-phenylcoumarin, indicanine A, was isolated from the root bark together with, robustic acid, daidzein and 8-prenyldaidzein (Nkengfack et al. 2000). The structure of the new compound was characterized as 4-hydroxy-5-methoxy-3-(4′-methoxyphenyl)-2″-(1-methylethenyl)dihydrofurano[4″,5″:6,7]coumarin. In addition to two known compounds, 5,4′-di-*O*-methylalpinumisoflavone and cajanin, a new 3-phenylcoumarin metabolite, named indicanine B, and a new isoflavone derivative, named indicanine C, were isolated from the root bark (Waffo et al. 2000). The structures of the new compounds were characterized as 4-hydroxy-3-(4′-hydroxyphenyl)-5-methoxy-2″,2″-dimethylpyrano [5″,6″:6,7] coumarin and 4′-hydroxy-5-methoxy-2″,2″-dimethylpyrano [5″,6″:6,7] isoflavone, respectively.

Antioxidant Activity

The crude methanol stem bark extract, n-hexane, carbon tetrachloride and chloroform soluble fractions showed moderate DPPH antioxidant activity (IC_{50} = 484.4–82.35 μg/ml), while the purified compounds, 4′,5,7-trihydroxy-8-prenyl isoflavone alpinum isoflavone and 6-hydroxygenistein, exhibited high antioxidant activity, having IC_{50} of 6.42, 8.30 and 8.78 μg/ml, respectively (Rahman et al. 2010). At the same time the standard compound, tert-butyl-1-hydroxytoluene (BUT), demonstrated an IC_{50} of 5.88 μg/ml.

Studies showed that the aqueous and methanol leaf extracts exhibited significant DPPH radical scavenging activity with an IC_{50} value of 342.59 and 283.24 μg/ml, respectively (Sakat and Juvekar 2010). The aqueous and methanol extracts significantly scavenged nitric oxide radicals (IC_{50} = 250.12; 328.29 μg/ml, respectively). Lipid peroxidation induced by thiobarbituric acid reactive substances (TBARS) was inhibited by the aqueous extract with low IC_{50} value (97.29 μg/ml) as compared to methanol extract (IC_{50} = 283.74 μg/ml). Both the extracts exhibited similar quantities of total phenolics. Total flavonoids were found to be in higher quantities than total flavonols in aqueous extract as compared to methanol extract.

Antimicrobial Activity

Among the isoflavonoids isolated from *E. variegata*, 3,9-dihydroxy-2,10-di(γ,γ-dimethylallyl)-6α,11α-dehydropterocarpan (erycristagallin) showed the highest antibacterial activity against mutants Streptococci, other oral Streptococci, *Actinomyces* and *Lactobacillus* species with a minimum inhibitory concentration (MIC) range of 1.56–6.25 μg/ml, followed by 3,6a-dihydroxy-9-methoxy-2,10-di(γ,γ-dimethylallyl)pterocarpan (erystagallin A) and 9-hydroxy-3-methoxy-2-γ,γ-dimethylallylpterocarpan (orientanol B) (MIC range: 3.13–12.5 μg/ml) (Sato et al. 2002).

Fourteen out of 16 isoflavonoids isolated from the roots showed antibacterial activity in the concentration range (1.56–100 μg/ml); the MIC values varied significantly among them (Tanaka et al. 2002b). Of the active compounds, 3,9-dihydroxy-2,10-di(γ,γ-dimethylallyl)-6α,11α-dehydropterocarpan (erycristagallin) and 9-hydroxy-3-methoxy-2-γ,γ-dimethylallylpterocarpan (orientanol B) exhibited the highest activity against methicillin-resistant *Staphylococcus aureus* with MIC values of 3.13–6.25 μg/ml. The phytochemical 2′,4′-dihydroxy-8-γ,γ-dimethylallyl-2″,2″-dimethylpyrano[5″,6″:6,7]

isoflavanone (bidwillon B), isolated from *Erythrina variegata*, inhibited the growth of 12 methicillin-resistant *Staphylococcus aureus* (MRSA) strains at minimum inhibitory concentrations (MICs) of 3.13–6.25 mg/l, while MICs of mupirocin, an antibiotic, were 0.20–3.13 mg/l (Sato et al. 2004). The minimum bactericidal concentration (MBC) for bidwillon B and mupirocin against MRSA weas 6.25–25 mg/l (MBC_{90}: 12.5 mg/l) and 3.13–25 mg/l (MBC_{90}: 25 mg/l), respectively. When bidwillon B and mupirocin were combined, synergistic effects were observed for 11 strains of MRSA (fractional inhibitory concentration indices, 0.5–0.75). The MBCs of mupirocin in the presence of bidwillon B (3.13 mg/l) were reduced to 0.05–1.56 mg/l. The results suggested t bidwillon B and mupirocin to be potent phytotherapeutics, and/or their combination may be useful in the elimination of nasal and skin carriage of MRSA.

Eryvarin Q, a 2-arylbenzofuran, isolated from the roots, showed potent antibacterial activity against methicillin-resistant *Staphylococcus aureus* (Tanaka et al. 2004). The isoflavonoid eryvarin U, isolated from the roots, exhibited potent antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) strains (Tanaka et al. 2005).

The crude methanol bark extract showed comparatively strong growth inhibition of *Bacillus subtilis, Escherichia coli* and *Aspergillus niger*, while n-hexane soluble fraction of the methanol extract showed poor activity against most of the test microorganisms (Rahman et al. 2007). The carbon tetrachloride fraction of the methanol extract showed moderate growth inhibition of *Bacillus cereus, B. subtilis, E. coli, Pseudomonas aeruginosa, Shigella dysenteriae* and *Vibrio mimicus*. The chloroform soluble fraction showed strong activity against *B. cereus*, *B. subtilis*, *E. coli*, *P. aeruginosa* and *A. niger*. The aqueous soluble fraction showed significant activity against Gram-positive bacteria, namely, *B. cereus*, *B. subtilis, Sarcina lutea* and the Gram-negative bacteria, *P. aeruginosa*. This fraction also showed strong activity against *A. niger* and *Saccharomyces cerevisiae* and moderate activity against *Candida albicans*.

The isoflavonoid eryvarin W, isolated from the roots, exhibited potent antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) strains (Tanaka et al. 2011). A biisoflavonoid, biseryvarin A, isolated from the roots showed low activity against methicillin-resistant *Staphylococcus aureus* (MRSA) (Tanaka et al. 2010).

Antitumour Activity

The ethyl acetate and n-butanol fraction of the ethanol stem bark extract but not the aqueous fraction promoted proliferation of the rat osteogenic sarcoma (UMR106), osteoblast-like (OB-like) cells (Li et al. 2006). Eleven compounds isolated from the ethyl acetate fraction including 4 new isoflavones and 7 known compounds, euchrenone b_{10}, isoerysenegalensein E, wighteone, laburnetin, lupiwighteone, erythrodiol and oleanolic acid, also stimulated UMR106 cell proliferation at concentrations of 5×10^{-8} to $5 - 10^{-6}$ mol/L but did not promote proliferation at 5×10^{-5} mol/L.

Among the proteinase inhibitors of *E. variegata*, EBI, which belongs to the Bowman-Birk family of inhibitors, was cytotoxic in relatively differentiated cells such as Molt4 and Jurkat derived from acute T lymphoblastic leukaemia (T-ALL) cells specifically, but ETIa and ECI, which are classified into Kunitz family inhibitors, did not (Ohba et al. 1998). The succinylation of lysine residue(s) of EBI led to about 50 % loss of the trypsin inhibitory activity as compared with the authentic EBI. When Molt-4 cells were incubated with this derivative, no significant cytotoxicity was observed, suggesting that the proteinase inhibitory activity might be involved in the cytotoxicity in human tumour cell lines. Erythrina alkaloid derivative, 10,11-dioxoerythratidine from the leaves, showed anticancer activity against breast cancer cell line T47D in vitro used with IC_{50} 1.0 µg/ml (Herlina et al. 2005). The methanol leaf extract of *E. variegata* and its ethyl acetate fraction and two compounds from the fraction isolate 11 and 17 exhibited anticancer activity against breast cancer T47D cell line in vitro

(Herlina et al. 2008). The potency against breast cancer cells ranked in the order of isolate 17 > isolate 11 > ethyl acetate fraction > methanol extract. Isolate 11 was characterized as a triterpene pentacyclic 3b-11a-28-trihydroxy-oleane-2-ene and isolate 17 as a mixture of β-sitosterol and stigmasterol. Rahman et al. (2007) evaluated the lethality of the *n*-hexane, carbon tetrachloride, chloroform and aqueous soluble fractions of the methanol bark extract to brine shrimp on *Artemia salina.* The LC50 were found to be 36.68, 4.67, 7.733 and 14.289 µg/ml, respectively. The cytotoxicity exhibited by the carbon tetrachloride and chloroform soluble fractions was significant and comparable to the positive control (vincristine sulphate). The results suggested that these fractions may be useful as antiproliferative and antitumorous bioactive agents.

Erythrina variegata extract exhibited antitumour effect in-vivo using the Lewis lung cancer mice model (Zhang et al. 2009). It also exhibited in-vitro antitumour effect against liver cancer cells. The methanol stem bark extract of *Erythrina variegata* showed significant anticancer activity against breast cancer T47D cell lines in vitro using the sulforhodamine B (SRB) assay (Herlina et al. 2011). Its bioactive component erystagallin A showed potent anticancer activity against breast cancer T47D cell lines in vitro with IC_{50} 3.3 µg/ml. Xanthoxyletin isolated from *E. variegata* exhibited antiproliferative effects in-vitro against human gastric adenocarcinoma SGC-7901 cells (Rasul et al. 2011). Its inhibitory effects on cells were associated with the DNA damage, apoptosis through mitochondrial dysfunction and cell-cycle arrest at S phase in a dose-dependent manner. Xanthoxyletin also increased the production of reactive oxygen species in SGC-7901 cells.

Studies showed that treatment of Dalton's ascitic lymphoma-induced Swiss Albino mice with methanol root bark extract of *Erythrina variegata* significantly increased the life span and decreased cancer cell number and tumour weight (Baskar et al. 2010). The haematological parameters were also normalized by the extract in tumour-induced mice.

Antiinflammatory Activity

Total alkaloids extracted from the leaves were found to have antiinflammatory activity (Nguyen et al. 1992). Three isoflavones, abyssinone V (1), 4′-hydroxy-6,3′,5′-triprenylisoflavonone (2) and erycrystagallin (3), isolated from the bark, exhibited phospholipase A2 (PLA2) inhibition with IC_{50} values of 6, 10 and 3 µM for 1 – 3, respectively (Hedge et al. 1997). The methanol leaf extract was found to have antiinflammatory activity as observed by reduction of the paw oedema (Verma et al. 2005). It contained indole alkaloids. Studies revealed that ethanol leaf extract of *E. variegata* produced above 90 % protection of the HRBC membrane from lysis due to hyposaline at dose level of 1,600 µg/ml when compared to 100 % lysis induced in control (Balamurugan et al. 2010). The standard drug, diclofenac, produced 95.26 % protection at a concentration of 50 mg/100 ml. The prevention of hypotonicity-induced HRBC membrane lysis was taken as a measure of antiinflammatory activity.

Blood Clotting Activity

Studies indicated that *Erythrina variegata* Kunitz proteinase inhibitors possessed different potency towards serine proteinases in the blood coagulation and fibrinolytic systems, in spite of their high similarity in amino acid sequence (Nakagaki et al. 1996). ETIa and ETIb, two Kunitz family trypsin inhibitors, prolonged the activated partial thromboplastin time (APTT) and also the prothrombin time (PT) of human plasma, but the Kunitz family chymotrypsin inhibitor, ECI, and Bowman-Birk family inhibitor, EBI, from *E. variegata* hardly prolonged these times. Trypsin inhibitors ETIa and ETIb inhibited the amidolytic activity of factor Xa and ETIb but not ETIA-inhibited plasma kallikrein. Neither ETIa nor ETIb exhibited any inhibitory activity towards beta-factor XIIa and thrombin. Furthermore, trypsin inhibitors ETIa and ETIb inhibited plasmin, a serine proteinase in the fibrinolytic system, whereas ECI and EBI did not. Of the two *Erythrina variegata* trypsin inhibitors designated

ETIa and ETIb, ETIa was found to have the ability to inhibit tissue-type plasminogen activator (tPA), while ETIb did not (Kouzuma et al. 1997a). They found that Arg61 and Leu62 residues in ETIa were important in inhibiting tPA and also suggest that beside these two residues, the other amino acid(s) or other structural element may be involved in interaction of ETIa with tPA. They also found that site-specific mutation of Arg63 to Leu (aR63L) or Asp (aR63D) in ETIa resulted in abolition of the inhibitory activities towards both trypsin and tPA (Kouzuma et al. 1997b). The result suggested that Arg61 and Leu62 in ETIa, in addition to Arg63, may play an important role in the interaction with tPA.

Immunomodulatory Activity

A D-galactose-binding glycoprotein lectin agglutinating human erythrocytes was purified from the seeds (Datta and Basu 1981). The lectin possessed leucoagglutinating property. A mitogenic D-galactosephilic lectin isolated from seeds was found to be similar to the soybean lectin in being a glycoprotein of molecular weight around 110,000–120,000 and having D-galactosephilic activity (Gilboa-Garber and Mizrahi 1981). The lectin resembled soybean and *Pseudomonas aeruginosa* lectins, by binding to D-GALACTOSAMINE, N-acetyl-D-galactosamine, alpha-galactoside and beta-galactoside as well as to D-galactose. Like these lectins it absorbed onto either untreated or enzyme (papain or neuraminidase)-treated human red blood cells but exhibited a considerable mitogenic activity towards human lymphocytes (predominantly T cells) only after their treatment with neuraminidase. This lectin was different in regard to the intensity of their agglutinating activity towards erythrocytes obtained from different animals and human donors of diverse ABO blood groups. Li et al. (1990) found that the Gal beta 1-4GlcNAc beta 1-3(Gal beta 1-4GlcNAc beta 1-6)Gal sugar sequence, an I-antigen determinant, was essential for the high affinity binding of the oligosaccharides to the *Erythrina variegata* agglutinin (EVA). The binding affinity of *Erythrina corallodendron* (synonym of *E. variegata*) seed lectin was found to be in the order N-acetyllactosamine > N-acetyl-D-galactosamine > α-galactoside and β-galactoside > D-galactose (Sudakevitz et al. 1991). Its ABO(H) blood group specificity revealed the following order of activity: O(H)I > A2 I > O(H)i adult > A2BI > BI > O(H)i cord > A1I > A1i adult > Bi cord > A1BI > Ai cord > ABi cord > OhI. The *Erythrina indica* (synonym of *E. variegata*) lectin showed a lower differentiation between the agglutination of O(H) and Oh erythrocytes. Both Erythrina seed lectins exhibited H/HI blood group preference.

Erythrina leaf lectin (EiLL) agglutinated all human RBC types, with a slight preference for the O blood group (Konozy et al. 2002). The carbohydrate specificity of lectin was directed towards D-galactose and its derivatives with pronounced preference for lactose. EiLL had pH optima at pH 7.0; above and below this pH lectin lost sugar-binding capability rapidly.

Anti-osteoporotic Activity

Studies by Zhang et al. (2007b) demonstrated that *Erythrina variegata* stem bark extract could suppress the high rate of bone turnover induced by oestrogen deficiency, inhibit bone loss and improve the biomechanical properties of bone in the ovariectomized rats. Daily oral administration of the plant extract at 300 and 600 mg/kg for 14 weeks to rats prevented the ovariectomy-induced increase in the serum osteocalcin, alkaline phosphatase and urinary deoxypyridinoline (DPD) levels. Histomorphometric analysis of the proximal end of the tibia showed that the extract prevented the oestrogen deficiency-induced decrease in trabecular thickness and trabecular area, as well as restoring the increase in trabecular separation in a dose-dependent manner. Also, the extract improved the energy absorption and stiffness of the mid-shaft of the rat femur. In a follow-up study, they isolated genistein derivatives mainly in the form of prenylgenistein from this extract, including 6-prenylgenistein, 8-prenylgenistein and 6, 8-diprenylgenistein (Zhang et al. 2008). They found genistein did not promote cell growth but genistein derivatives

exerted stimulatory effects on osteogenesis in UMR 106 cells. Further animal studies indicated that the protective effects of *E. variegata* stem bark extract on bone properties in ovariectomized rats were likely to be mediated by its inhibitory actions on the process of bone resorption via the suppression of osteoclast differentiation and maturation (Zhang et al. 2010). The extract inhibited the upregulation of cathepsin K mRNA and the downregulation of osteoprotegrin mRNA in the tibia of ovariectomized rats.

Calcium Homeostasis Activity

Oral administration of *Erythrina variegata* extracts could improve the serum Ca level and inhibit urinary Ca excretion in ovariectomized rats and maintain Ca homeostasis, and this might be attributed to the upregulation of the extract on vitamin D receptor mRNA expression in the duodenum and CaBP-9k mRNA expression in the kidney (Zhang et al. 2007a).

β-Glucosidase Inhibitory Activity

In the β-glucosidase inhibitory bioassay, the crude methanol extract, n-hexane, carbon tetrachloride and chloroform soluble fractions of *E. variegata* stem bark revealed 34.75, 95.04, 91.49 and 55.32 %, inhibition, respectively (Rahman et al. 2010).

Hypotensive Activity

The aqueous seed extract elicited a sharp fall in blood pressure and at higher dose completely stopped the heart in guinea pigs (Chatterjee et al. 1981). It also produced a contraction of isolated guinea pig ileum. The fall in blood pressure and contraction of ileum were completely blocked by an antihistaminic agent—diphenhydramine. The extract did not show any CNS activity, since it neither affected the barbiturate-induced sleeping time nor protected the pentylenetetrazol-induced convulsions, although it depressed the respiration at higher doses but stimulate the same in smaller doses in guinea pigs.

Antimalarial Activity

Erythrina alkaloid derivative, 10,11-dioxoerythratidine from the leaves, showed antimalarial activity against both strains of *Plasmodium falciparum* in-vitro used with IC_{50} of 25.5 μg/ml against strain 3D7 and 3.3 μg/ml against K1(Herlina et al. 2005). The methanol leaf extract of *E. variegata* exhibited significant antimalarial activity in-vitro towards *Plasmodium falciparum* (Herlina et al. 2007). Its *n*-butanol fraction gave the most potent activity, exhibiting equipotency against both strains of the parasite with IC_{5O} of 5.1 μg/ml against K1 and 13.2 μg/ml/against 3D7. The methanol bark extract of *E. variegata* showed significant antimalarial activity towards *Plasmodium falciparum* in vitro using the lactate dehydrogenase (LDH) assay (Herlina et al. 2009). Its ethyl acetate fraction showed the highest activity, exhibiting equipotency against both strains of parasite with IC_{50} of 23.8 μg/ml against 3D7 and 9.3 μg/ml against K1. The active component of the fraction isolated was identified as warangalone, 8(3,3-dimethylallyl)-4′-hydroxy-2‴,2‴-imethylpyran[6,7,b]isoflavon which showed significant antimalarial activity against both strains with IC_{50} of 4.8 μg/ml against 3D7 and 3.7 μg/ml against K1. The methanol stem bark extract of *Erythrina variegata* showed significant antimalarial activity against *Plasmodium falciparum* in-vitro using the lactate dehydrogenase (LDH) assay (Herlina et al. 2011). Its bioactive component erystagallin A showed potent antimalarial activity against both strains of parasite in-vitro used with IC_{50} of 0.02 μg/mL against 3D7 and 6.0 μg/mL against K1, respectively. The pentacyclic triterpenoid, 3,22,23-trihydroxy-oleane-12-ene (1); pentacyclic triterpenoid, 3b,11a-28trihydroxy-oleane-12-ene (2); and 10,11-dioxoerythratidine (3) isolated from the ethyl acetate fraction of the methanol extract of dried leaves showed antimalarial activity (Supratman et al. 2010). Compound 3 showed antimalarial higher than compounds 1

and 2 against *P. falciparum* K1 strains resistant to chloroquine due to the presence of epoxy group in pyran ring.

Antihyperlipidaemic Activity

The elevated levels of total cholesterol, triglycerides, low-density lipoprotein and very low-density lipoprotein due to high-fat diet (HFD) was significantly reduced by concurrent treatment with methanol seed extract of *E. variegata* (200 and 400 mg/kg) (Balamurugan and Shantha 2010). A significant reduction in high-density lipoprotein was found in HFD-fed groups; however, a nonsignificant increment was produced by the administration of the extract. The extract reduced the elevated body weight and mesenteric fat pad weight and the enhanced HMG-CoA reductase activity of HFD hyperlipidaemic rats. The extract also significantly reduced antioxidant enzymes such as superoxide dismutase and catalase and lipid peroxidation in HFD rats. Administration of *E. variegata* leaf extract to guinea pigs fed on a high-fat diet reduced TC (33 %), triglyceride (TGL; 39 %) and LDL (36 %), while high-density lipoprotein (HDL) levels remained unaltered demonstrating its marginal hypolipidaemic influence (Kalachaveedu et al. 2011). Atherosclerotic changes in coronary histopathology caused by the high-fat diet were altered beneficially by the leaf extract.

Hypoglycaemic Activity

The methanol leaf extract of *E. variegata* exhibited promising hypoglycaemic action in streptozotocin (STZ)-induced diabetic rats substantiating its ethnomedicinal use (Kumar et al. 2011). The extract administered orally at doses of 300, 600 and 900 mg/kg significantly and dose-dependently reduced and normalized blood glucose levels as compared to that of STZ control rats, the 900 mg/kg dose being the most potent showing complete normalization of blood glucose levels. Serum biochemical parameters including lipid profile were significantly restored towards normal levels in the extract-treated rats as compared to STZ diabetic rats.

Antidiarrhoeal Activity

The ethanol leaf extract significantly modified normal defecation frequency as well as inhibited castor oil-induced diarrhoea in Wistar rats (Sonia et al. 2011). The extract also displayed a significant reduction in gastrointestinal motility in charcoal meal test. The findings suggested that the ethanol extract of leaves of *Erythrina indica* elicited potent antidiarrhoeal effects substantiating its traditional claim as an antidiarrhoeal agent.

Diuretic Activity

The ethanol, chloroform and ethyl acetate leaf extracts exhibited significant diuretic activity as evidenced by increased total urine volume and the urine concentration of Na^+, K^+ and Cl (Jesupillai et al. 2008). The results supported the use of the plant as a diuretic agent in traditional medicine.

Antifertility Activity

Phytol from *E. variegata* leaves exhibited antifertility effects on the spermatozoa of white rats (*Rattus norvegicus)* in-vitro at a concentration of 0.25×10^3 µg/µl (Herlina et al.).

Spasmloytic Activity

Total alkaloidal fraction from bark caused smooth muscle relaxation of isolated rabbit ileum and inhibited spontaneous rhythmic contraction of isolated rat uterus in concentration of 0.5–2.0 mg/ml (Ghosal et al. 1972). *E. variegata* behaved like a spasmolytic agent due to its relaxing activity, thus may have an important role in conditions like diarrhoea or spasm or colic pain. Erythrinin B from *E. variegata* bark significantly

inhibited the Na+/H+ exchange system of arterial smooth muscle cells, with minimum inhibitory concentrations of 1.25 μg (Kobayashi et al. 1997).

CNS (Central Nervous System) Activity

The total alkaloid fraction from the bark showed several characteristic pharmacological effects: neuromuscular blocking, smooth muscle relaxant, CNS depressant, hydrocholeretic and anticonvulsant effects, which were consistent with the reported uses of the plant extracts in the indigenous system of medicine (Ghosal et al. 1972). The ethanol, chloroform and ethyl acetate leaf extracts of leaves showed significant ($P<0.05$) anticonvulsant activity against maximal electroshock (MES) and pentylenetetrazol (PTZ)-induced convulsions in mice (Rajamanickam and Sathyanarayanan 2008). Ethanol extract gave more prominent activity when compared to other extracts.

The aqueous leaf extract showed potent sedative activity but no analgesic effects, as claimed by Sri Lankan Ayurvedic physicians (Ratnasooriya and Dharmasiri 1999). The methanol leaf extract showed mild sedative hypnotic activity when evaluated using pentobarbital (Verma et al. 2005). However, in a later study, the methanol leaf extract was found to have analgesic activity. In acetic acid-induced writhing model, the methanol leaf extract of the leaf of *E. variegata* at a dose of 500 mg/kg showed significant antinociceptive activity with 49.03 % inhibition of writhing response (Haque et al. 2006). In radiant heat tail-flick model, the extract also showed significant increase in the tail-flick latency at a dose of 500 mg/kg body weight with 36.02 % elongation of tail-flick time. As the crude extract appeared to be active in both animal models of nociception, it may possess peripherally and centrally acting compounds for its antinociceptive action.

Marañon and Santos (1932) isolated an alkaloid from the seeds which had properties identical with those of hypaphorine. Hypaphorine had been found to promote sleep in mice (Ozawa et al. 2008).

Toxicity Activity

The leaves and bark were found to contain the toxic alkaloid, erythrinine, a central nervous system depressant with effects similar to the alkaloid cytosine (Greshoff 1890; Nellis 1997). Symptoms reported included vomiting, malaise, lethargy and depression (Nellis 1997). Erythrinine was also isolated from the plant by Ito et al. (1970).

Traditional Medicinal Uses

A wide range of chemical compounds have been isolated, mainly alkaloids, flavonoids, triterpenoids and lectin from *E. variegata*. In Asia and the Pacific Islands, different parts of the plant have been used in traditional medicine for a variety of ailments and as nervine sedative, collyrium in ophthalmia, antiasthmatic, antiepileptic, antiseptic, astringent, febrifuge, anti-bilious, diuretic, laxative, expectorant, anthelmintic, vermifuge and an astringent (Crevost and Petelot 1928; Burkill 1966; WHO 1998; Rahman et al. 2007, 2010; Stuart 2012; Kumar et al. 2010).

The bark is used as a laxative, diuretic, expectorant astringent, febrifuge, anti-bilious and anthelmintic and is useful in ophthalmia and skin diseases. The bark is also employed to facilitate the maturation of boils. Dried bark decoction or infusion in alcohol is used for lumbar and leg pain. The stem bark is used against rheumatism in the form of a decoction, extract or tincture and an infusion used for stomachache. The bark when crushed and pounded is used for curing toothache by inserting into cavities or hollow tooth. The bark is chewed for dysentery. A mixture of bark scrapings and lime is applied to reduce swellings. The inner bark is scraped and mixed with little water; the juice is squeezed and drunk to cure cough with sore throat. The wood is rasped in water and given for haematuria. The bark and leaves are used in 'paribhadra', an Indian preparation as a vermifuge, for treating filariasis, and to relieve joint pain. A decoction of the bark and leaves, sweetened, is considered a good expectorant. The leaves and bark were found to contain the toxic alkaloid, erythrinine, a central nervous

system depressant with effects similar to the alkaloid cytosine (Greshoff 1890; Nellis 1997).

The leaves are employed in fever, inflammation and joint pains and as laxative, diuretic and expectorant. Heated crushed wet leaves are rubbed over the head and body of a person with fever. The juice of the leaves is used in earache, toothache, constipation and cough, and consuming the leaves is held to stimulate lactation, appetite and menstruation. The extract from crushed leaf mixed with water is drunk to relieve cough. Crushed fresh leaves are used externally as a poultice in haemorrhoids and metroptosis. Powdered leaves are topically applied for wounds and ulcers, and a warm poultice is applied externally to relieve rheumatic joints. Leaves are reported to be sedative and are used for the relief of insomnia and anxiety and for treating asthma. Leaves are crushed with seawater and drunk daily to relieve stomachache. Honeyed leaf juice is used as vermifuge for tapeworm and roundworm infestations. Pulverized leaves in the form of snuff are used for infantile convulsion and ascariasis. Leaves mixed with castor oil are used as therapy for dysentery.

The roots and leaves are considered to be febrifuge. The root decoction is used as a gargle for loose and aching teeth and an infusion used for bronchitis. Seeds used internally and externally for cancer and externally for abscesses. Pounded seeds are used as poultice for snake bites and for abscesses and cancerous growths.

Other Uses

Erythrina variegata is a multipurpose tree and an important agroforestry species. The species is simultaneously used as leaf forage and medicinal plant (in Vietnam especially grown for official purposes). It has also proven valuable for fodder production and as sturdy windbreaks. It is a useful plant for soil enrichment as it fixes nitrogen, nodulating readily and prolifically in both acid and alkaline soils and is also a good source of organic matter for green manure. In Asia and other tropical countries, it is a common ornamental tree for landscape, avenue planting and fencing/hedging purposes. It is also used as live support tree for black pepper, betel leaf, jasmine, grapes and yams and as a shade tree for coffee and cocoa. The soft and white timber has been used for making packing cases, floats, picture frames and toys, and recently pulp for the paper industry.

Erythrina variegata has insecticidal activity. Two alkaloids isolated from the stem bark, identified as erysopine and erysovine, exhibited antifeedant activity against maize weevil *Sitophilus zeamais* adults with EC_{50} values of 108.5 and 89.7 ppm, respectively (Liu et al. 2012). The D-galactose binding lectin from *E. indica* seeds significantly reduced egg hatching, pupation and emergence of the melon fruit fly, *Bactrocera cucurbitae* (Singh et al. 2009). Treatment of the larvae with the lectin significantly suppressed the activity of hydrolase enzymes (acid and alkaline phosphatases), one oxidoreductase (catalase) and one group transfer enzyme (glutathione S-transferases), but the esterases increased significantly.

Studies showed that *E. variegata* leaf powder could remove metal pollutant from solution. One study showed *E. variegata* leaf powder could bioadsorb zinc from aqueous solution (Venkateswarlu et al. 2008). There was a significant increase in percentage removal of Zn as pH increased from 2 to 3 and attained maximum at pH 7. In a subsequent study they found that *E. variegata* leaf powder could remove cadmium from solution; a significant increase in percentage removal of cadmium was observed as pH increased from 2 to 4 (Kumar et al. 2009).

Comments

E. variegata is readily propagated from seeds and woody stem cuttings.

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Gliricidia sepium

Scientific Name

***Gliricidia sepium* (Jacq.) Kunth ex Walp.**

Synonyms

Galedupa pungam Blanco, *Gliricidia lambii* Fernald, *Gliricidia maculata* (Kunth) Walp., *Gliricidia maculata* var. *multijuga* Micheli, *Gliricidia sepium* (Jacq.) Kunth ex Griseb., *Lonchocarpus rosea* (Mill.) DC., *Lonchocarpus sepium* (Jacq.) DC., *Millettia luzonensis* A. Gray, *Millettia slendidissima* sensu Naves, non Blume, *Robinia maculata* Kunth, *Robinia rosea* Mill., *Robinia sepium* Jacq., *Robinia variegata* Schltdl.

Family

Fabaceae

Common/English Names

Gliricidia, Glory Cedar, Mexican Lilac, Mother Of Cocoa, Nicaraguan Cacao Shade, Quick Stick, St. Vincent Plum, Tree Of Iron

Vernacular Names

Brazil: Mãe-Do-Cacau, Planta-Mãe-Do-Cacau
Columbia: Matarratón
Creole: Piyon
Cuba: Mata Ratón, Piñón Amoroso, Piñón Florido
Eastonian: Tara-Gliritsiidia
French: Immortelle, Lilas Étranger, Madre De Cacao
Guatemala: Madre De Cacao, Madre Cacao
Honduras: Madreado
India: Saranga (Bengali), Gobbarda Mara (Kannada), Kona, Seema Konna (Malayalam), Seemai Agathi (Tamil), Madri (Telugu)
Indonesia: Gamal, Liriksidia
Laotian: Kh'è: Fàlangx, Kh'è: No:Yz
Malaysia: Bunga Jepun
Mexico: Cacahuananache, Cacahaunantl
Nicaragua: Madero Negro
Nigeria: Agunmaniye
Palauan: Rechesengel
Papiamento: Mata Raton
Philippines: Kakaoati (Bontok), Mandiri-Kakau (Sulu), Kakauati, Kakawate, Madre Cacao, Madre Kakau, Marikadua, Marikakaw (Tagalog), Madre Cacao, Madre De Cacao (Spanish)
Spanish: Almácigo Extranjero, Amory Celos, Bien Vestida, Cacao De Nance, Cacahuananche, Cachanance, Desnodo Florecido, Floresco, Madre De Cacao, Madre Negro, Madriado, Madricacao Mata Ratón, Mata Raton, Palo De Hierro, Palo De Parque, Piñón Amoroso, Piñón De Cuba, Piñón Florido, Varita De San José
Sri Lanka: Kona, Maikona Gaha, Seemakonna
Thai: Kha Farang, Khae-Farang
Venezuela: Ratón
Vietnamese: Anh Dào Gisa, Hông Mai, Sát Thu

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Origin/Distribution

G. sepium is indigenous to the seasonal dry forest areas of Mexico and Central America, namely, Belize, Costa Rica, El Salvador, Guatemala, Honduras and Nicaragua. It is now widely distributed in tropical Americas, the Caribbean, Africa, Asia and the Pacific Islands.

Agroecology

A warm tropical tree species grows in areas with warm, seasonally dry climates with moderate mean annual rainfall (900–1,500 mm). It thrives best in areas with mean annual temperatures of 20–27 °C and tolerates high temperatures of 36–42 °C and low temperatures down to 14 °C (Elevitch and Francis 2006). Night temperature lower than 5 °C is detrimental to the tree. The tree is extremely frost sensitive. The tree grows in climates with summer, winter, bimodal rainfall or uniformly distributed rainfall patterns, with mean annual precipitation of 600–3,500 mm. It is largely deciduous during the dry season but is evergreen in areas with uniformly distributed rainfall as in Kalimantan, Indonesia.

In its native range in Central America, it is often found on highly eroded soils of volcanic origin with pH 4.5–6.2 from near sea level to 1,200 m altitude. It is adaptable to a wide range of soil types—on sands, heavy clays and slightly alkaline, calcareous limestone soils—but does best in well-drained soils. Gliricidia abhors wet or waterlogged soils. Gliricidia tolerates fires well and trees quickly re-sprout with onset of the rains.

Edible Plant Parts and Uses

Gliricidia leaves and flowers are said to be eaten boiled or fried. In Mexico, the flowers are utilized as food (Delizo and Del Fierro 1974). Flowers are cooked in egg batter and fried or cooked as potherbs (Williams 1981; Facciola 1990). The flowers attract honeybees and are a good source of nectar.

Botany

A small unarmed, branched tree reaching heights of 10–12 m with smooth, weakly fissured, greyish-brown bark and a trunk diameter of 30 cm at breast height (dbh). Leaves alternate, imparipinnate, 15–30 cm long with 7–21 leaflets (Plate 1). Leaflets, pubescent when young, glabrous when mature, green, ovate-lanceolate to elliptic, 2–6 cm by 1–3 cm, acute to acuminate apex, rounded to acute bases and entire margin. Inflorescences borne on distal end of leafless branches, 5–15 cm long, with 20–40 flowers per raceme (Plates 2–3). Flowers bright pink to lilac, tinged with white, petals 5, standard petal usually with a diffuse pale yellow spot at the base, broad about 20 mm long, keel petals oblong, curved, 15–20 mm long, 4–7 mm wide, calyx—five toothed, glabrous, green, often tinged red, stamens 10 with whitish

Plate 1 Flowers and leaves (CT Ho)

Plate 2 Axillary inflorescences (CT Ho)

Plate 3 Flower buds (CT Ho)

Plate 4 Open flowers (CT Ho)

filaments, ovary reddish with a white style (Plates 1, 2, and 4). Pod oblanceolate, 10–18 cm long, 2 cm wide, green sometimes with reddish tinge when unripe, light yellow-brown w hen mature, valves twisting in dehiscence; seeds 4–10, yellow-brown to brown, nearly round.

Nutritive/Medicinal Properties

Phytochemical from Fruits/Seeds

Three saponins hederagenin-3-*O*-(4-*O*-acetyl-β-D-xylopyranosyl)-(1 → 3)-α-L-hamnopyranosyl-(1 → 2)-α-L-arabinopyranoside, hederagenin-3-*O*-(3,4-di-*O*-acetyl-β-D-xylopyranosyl)-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranoside and hederagenin-3-*O*-(3,4-di-*O*-acetyl-α-L-arabinopyranosyl)-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranoside were isolated from the fruits (Kojima et al. 1998).

Proximate nutrient composition of the seed was reported as crude fat 24.70 %, crude protein 18.7 %, crude fibre 3.01 %, ash 4.06 %, moisture 4.10 %, carbohydrate 45.41 %, Na 342.57 ppm, K506.55 ppm, Ca 293.10 ppm, Mg 83.65 ppm, Fe 128.11 ppm, Cu 1.10 ppm, Zn 21.78 ppm and Mn 32.30 ppm (Adewuyi et al. 2009). The lipid classes of the seed oil comprised polar lipids 7.50 %, sterols 2.70 %, diacylglycerols 5.30 %, monoacylglycerols 4.60 %, triacylglycerols 75.60 %, hydrocarbons 1.90 % and free fatty acids 2.40 %. The mineral content of the seed oil comprised Na 281.10 ppm, K 432.60 ppm, Ca 271.10 ppm, Mg 64.70 ppm, Fe 102 ppm, Cu 0.60 ppm, Zn 16.80 ppm and Mn 22.98 ppm. The physicochemical characteristics of the seed oil was reported as colour orange, acid value 1.40 mg KOH/g, free fatty acid 0.80 %, saponification value 94.4 mg KOH/g, iodine value 87.60 mg I/g, unsaponifiable matter 1.00 %, peroxide value 0.40 mg O_2/g oil, refractive index (25 °C) 1.4, specific gravity (25 °C) 0.876 and sate at room temperature liquid. The composition of the unsaponifiables of the seed oil comprised n-alkanes 21.20 %, triterpene alcohols 31 %, sterols 29.4 % and unknowns 18.40 % (Adewuyi et al. 2009).

Sotelo et al. (1986) have reported a thermostable non-protein amino acid toxin canavanine (2-amino-4-guanidooxy-butyric acid) in gliricidia seeds which killed mice within l week of feeding and may be associated with the toxicity of gliricidia in non-ruminants.

Phytochemical from Flowers

In the flower essential oil, the major compounds were coumarin (43.1 %), hydroquinone (21.6 %), myrtenol (12.73 %) and maltol (4.62 %) (Kaniampady et al. 2007). Other compounds included *p*-mentha-1,8-dien-9-ol 1.83 %, octanoic acid 1.53 %, 3-nonanol 1.5 %, 2-butyl-2-hexanol 1.46 %, γ-nonalactone 1.31 %, 2-octanoic acid 1.26 %, 2-butyl-3-hexenol 1.03 %, eucarvone 0.88 %, myrtenal 0.78 %, *p*-mentha-1,4-diene-2-ol 0.73 %, geraniol 0.72 %, *p*-mentha-1,4-diene-7-ol 0.71 %, dodecanoic acid 0.64 %, nonanol

0.62 %, tetradecanoic acid 0.46 %, allyl tiglate 0.44 %, 4-hydroxy-3-methylacetophenone 0.37 %, 3tetradecanoic acid 0.36 %, benzyl alcohol 0.35 %, decanoic acid 0.31 % and dihydrocarveol acetate 0.30 %.

Jose and Reddy (2010) reported the following chemical composition of the flower essential oil: coumarin 43.07 %, hydroquinone 21.64 %, myrtenol 12.73 %, maltol 4.42 %, *p*-mentha-*1*,8-dien-1-ol 1.83 %, γ-nonalactone 1.31 %, 2-butyl-2-hexanol 1.03 %,eucarvone 0.88 %, myrtenal 0.78 %, *p*-mentha-1,4-dien-2-ol 0.73 %, geraniol 0.72 %, *p*-mentha-1,4-dien-7-ol 0.71 %, dodecanoic acid 0.64 %, nonanol 0.62 %, nonanoic acid 0.55 %, tetradecanoic acid 0.46 %, benzyl alcohol 0.35 % and decanoic acid 0.31 %.

Phytochemicals from Leaves

G. sepium leaf meal was found to have the following amino acid composition: threonine 1.2 %, valine 1.60 %, cysteine 0.39 %, methionine 0.42 %, isoleucine 1.20 %, leucine 2.41 %, tyrosine 1.12 %, phenylalanine 1.54 %, lysine 1.12 %, histidine 0.51 % and arginine 1.59 % (Chadhokar 1982).

The leaves were found to contain coumarin, *O*-coumaric acid and melilotic acid (Griffiths 1962), cyanogenic glycoside, nitrate (Manidool 1985), pinitol (Calle et al. 1987), condensed tannins (Ahn et al. 1989) and lignans (pinoresinol and lariciresinol) (Ragasa et al. 2000). *G. sepium* leaves were found to contain condensed tannins (CT) which were all bound to proteins (Jackson et al. 1996). Two new triterpene saponins (1 and 2) possessing 3β,21β,24-trihydroxy-22-oxoolean-12-ene as an aglycon and oligosaccharide moiety linked to C-3 of the aglycon were isolated from leaves and roots (Rastrelli et al. 1999b). They contained two pyranoses (glucuronic acid and xylose) and the glucose residue of both 1 and 2 was also linked to C-21.

The major compounds of the leaf essential oil were propylene glycol (25.1 %), coumarin (18.2 %), (*Z*)-3-hexenol (17.7 %), β-farnesene (14.2 %) and (*E*)-2-hexenol (6.5 %) (Kaniampady et al. 2007). Other compounds included thymol (3.6 %), benzyl alcohol 3.5 %, caryophyllene (2.3 %), α-farnesene (2.0 %), 2-pentene-1-ol (<1 %), isovanillin (<1 %), isobutyl alcohol (<1 %), phenylethyl alcohol (<1 %), phenol (<1 %), crotonic aldehyde (<1 %) and 5,6-dihydro-4*H*-cyclopenta-(6)-furan (<1 %). Jose and Reddy (2010) reported the following chemical composition of the leaf essential oil: propylene glycol 25.1 %, coumarin 18.2 %, (*Z*)-2-hexenol 17.7 %, β-farnesene 14.2 %, (E)-2-hexenol 6.5 %, thymol 3.6 %, benzyl alcohol 3.5 %, caryophyllene 2.3 %, α-farnesene 2.0 %, 2-pentene-1-ol <1 %, isovanillin <1 % <isobutyl alcohol <1, phenylethyl alcohol <1 %, phenol <1 %, crotonic aldehyde <1 % and 5,6-dihydro-4H-cyclopenta-(6)-furan <1 %.

Phytochemicals from Bark, Heartwood, Root

Jurd and Manners (1977) isolated two new isoflavones, 2′,3′,7-trihydroxy-4′-methoxyisoflav-3-ene (sepiol) and 3′,7-dihydroxy-2′,4′-dimethoxyisoflav-3-ene (2′-*O*-methysepiol); a new phenolic isoflavan, robinetin; and 7,3′,4′-trihydroxyflavanone from gliricidia heartwood. Three additional flavonoid constituents (an isoflavone, a dihydroflavonol and a β-hydroxydihy drochalcone) were isolated from the wood (Manners and Jurd 1979). An isoflavan, 7,4′-dihydroxy-3′-methoxyisoflavan, along with three other isoflavonoids (isovestitol, formononetin and afrormosin), a pterocarpan, medicarpin, 4-hydroxy-3-methoxy-cinnamaldehyde (Herath et al. 1998), stigmasterol glucoside and 3′,4′-dihydroxy-*trans*-cinnamic acid octacosylester, along with three other known constituents (Herath and de Silva 2000), were isolated from the heartwood. From the methanol extract of *Gliricidia sepium* bark, Rastrelli et al. (1999a) isolated in addition to vestitol and 2′-*O*-methylvestitol, three new 12α-hydroxyrotenoids: gliricidol, 2-methoxy gliricidol and gliricidin. Hederagin was also isolated from the roots (Rastrelli et al. 1999b).

Nineteen compounds were identified and quantified from the bark volatile oil of *Gliricidia sepium* (Reddy and Jose 2010a). The major com-

ponents were methyl-3(*E*)-pentenyl ether (11.55 %), 3-methyl-2-butanol (10.65 %), 3-methoxy hexane (10.14 %), 1-(1-ethoxyethoxy)-2-hexene (9.72 %), 2-decanol (8.97 %), coumarin (8.07 %) and hexadecanoic acid (5.16 %). Other components included humulene epoxide (3.64 %), caryophyllene oxide (3.05 %), 2,4-dimethyl-3-hexanol (2.79 %), 2-ethyl hexanol (2.61 %), dodecanoic acid (2.37 %), methyl-3(*E*)-hexenyl ether (2.19 %), 4-ethoxy ethyl benzoate (2.1 %), 1-hexanol (1.92 %), *T*-muurolol (1.77 %), tetradecanoic acid (1.23 %), octadecanal (1.11 %) and methyl-3-butenyl ether (1.02 %).

Antioxidant Activity

G. sepium ethanol extract exhibited low DPPH radical scavenging activity but showed the highest ferric reducing antioxidant property of 88 % (Akharaiyi et al. 2012). *G. sepium* extract had the highest concentration of phenol with a value of 1.7 mg/ml and flavonoid content with a value of 0.46 mg/ml.

Antimicrobial Activity

Of 153 Panamanian plants tested, the crude plant extracts of *G. sepium* were one of three that showed most promising inhibitory activity in-vitro against *Candida albicans* and *Cladosporium cucumerinum* (Rahalison et al. 1993).

The methanol bark extracts of *G. sepium* exhibited antimicrobial effects against *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus pumilus* and *Vibrio cholerae* at doses of 200 µg (Pérez et al. 2001). *Gliricidia sepium* leaf alcohol extract was one of ten Guatemalan plants found to be most active in-vitro against five strains of *Neisseria gonorrhoeae* (Cáceres et al. 1995), and the bark and leaf extracts were found to be inhibitory to four pathogenic fungi, namely, *Aspergillus flavus*, *Epidermophyton floccosum*, *Microsporum gypseum* and *Trichophyton rubrum* (Cáceres et al. 1993). *G. sepium* bark oil exhibited pronounced activity against all tested microorganisms *Bacillus cereus*, *Enterobacter faecalis*, *Salmonella paratyphi*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus faecalis*, *Proteus vulgaris*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Serratia marcescens*, and its activity was quite comparable with the standard antibiotics screened under similar conditions (Reddy and Jose 2010a).

Lignans: pinoresinol and lariciresinol isolated from gliricidia leaves exhibited low antimicrobial activity against *Bacillus subtilis* and *Pseudomonas aeruginosa* and antifungal activity against *Trichophyton mentagrophytes* and *Aspergillus niger* (Ragasa et al. 2000). The ethanol leaf extract of *G. sepium* exhibited antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas* spp., *Salmonella typhi* and *Klebsiella* spp., with the best result against *E. coli* (Nazli et al. 2008).

The methanol, ethyl acetate and chloroform extracts of Gliricidia flowers exhibited significant activity against all the tested organisms, namely, *Bacillus cereus*, *Enterobacter faecalis*, *Salmonella paratyphi*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus faecalis*, *Proteus vulgaris*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Serratia marcescens* (Reddy and Jose 2010b). Flower aqueous extract was found to be effective on *Escherichia coli*, *Proteus vulgaris*, *Bacillus cereus*, *Enterobacter faecalis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Serratia marcescens* but elicited little effect on *Salmonella paratyphi*, *Klebsiella pneumoniae* and *Streptococcus faecalis*. The bark ethyl acetate extract exhibited marked activity against *Bacillus cereus*, *Enterobacter faecalis*, *Salmonella paratyphi*, *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Serratia marcescens* but was inactive against *Staphylococcus aureus*, *Streptococcus faecalis* and *Klebsiella pneumoniae*. The bark methanol extract was found to be active against *Bacillus cereus*, *Enterobacter faecalis*, *Salmonella paratyphi*, *Streptococcus faecalis*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Staphylococcus aureus* and *Proteus vulgaris* but was inactive against *Escherichia coli* and *Klebsiella pneu-*

moniae. Both chloroform and aqueous extracts of *Gliricidia sepium* bark inhibited the growth of *Bacillus cereus*. Chloroform extract inhibited *Bacillus cereus*, *Escherichia coli* and *Pseudomonas aeruginosa*. Bark aqueous extract exhibited appreciable activity against *Serratia marcescens*, *Bacillus cereus*, *Salmonella paratyphi* and *Streptococcus faecalis* but was less active against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Petroleum ether extracts of bark, leaf and flower had no antibacterial activity on the test microorganisms.

Leaf methanol extract showed appreciable inhibitory activity on all test bacteria except *Serratia marcescens*. The leaf aqueous extracts of *Gliricidia sepium* was found to be effective on *Escherichia coli* and *Serratia marcescens* but had little effect on *Salmonella paratyphi*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. *Gliricidia sepium* essential leaf exhibited potent antibacterial activity against *Salmonella paratyphi*, *Streptococcus faecalis*, *Proteus vulgaris*, *Serratia marcescens* and *Enterobacter faecalis*, and the activity was quite comparable with the standard antibiotics screened under similar conditions (Jose and Reddy 2010). The activity of leaf oil was found to be higher than flower oil. Ethanol leaf extract of *G. sepium* demonstrated antimicrobial activity against bacteria and fungi in-vitro (Nazali et al. 2011). The MIC value of 1 mg/ml was found for Gram-positive bacteria (*Staphylococcus aureus*, *Streptococcus intermedius*, *Bacillus pumilus*, *B. subtilis* and *B. cereus*) and 0.5 mg/ml for Gram-negative bacteria (*Salmonella typhi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Shigella flexneri*). The MIC value for fungi was higher 2 mg/ml for *Fusarium solani*, *Rhizomucor pusillus*, *Trichophyton rubrum*, *Macrophomina phaseolina* and *Rhizoctonia solani*; *Aspergillus effusus* was resistant to the extract.

The crude ethanol extract and fractions of *G. sepium* showed higher antibacterial activity than the methanol extract (Akharaiyi et al. 2012). Growth of the following bacteria was inhibited to varying degree: *Pseudomonas aeruginosa*, *Serratia marcescens*, *Escherichia coli*, *Enterococcus faecium*, *Salmonella typhi*, *Bacillus cereus*, *Proteus mirabilis*, *Staphylococcus aureus* and *Klebsiella pneumoniae*.

Studies showed that aqueous extracts from 22 Guatemalan plants including *Gliricidia sepium* tested inhibited one or more of the dermatophytes (Cáceres et al. 1991). The most commonly inhibited dermatophytes were *Epidermophyton floccosum* (43.2 %), *Trichophyton rubrum* (36.0 %) and *Trichophyton mentagrophytes* (31.8 %); the less inhibited were *Microsporum canis* (22.7 %) and *Microsporum gypseum* (24.0 %). In a study of scabies treatment among selected residents of Titay, Zamboanga, kakawati (*G. sepium*) preparation was found to be as effective as sulphur lotion in the treatment of scabies (Bañez et al. 1999). A significant difference was observed between pretreatment and posttreatment scores after 1 week. However, there was a noted increase of scabies lesions 2 and 4 weeks after. In a randomized, double-blind clinical trial, a 50 % *Gliricidia sepium* (kakwate/madre de cacao) ointment was found comparable with 2 % miconazole ointment in terms of mycologic cure and safety profile, but it was not as effective as 2 % miconazole in improving overall clinical response and reducing major signs and symptoms of *Tinea coporis* and *Tinea cruris* (Guillano and Alabado 2002). Coumarin isolated from the water leaf extract inhibited growth of *Trichophyton mentagrophytes* in-vitro an average antimicrobial index (AI) of 1.45, while the standard clotrimazole showed inhibition of AI at 2.0 (Rabena 2007).

Neuropharmacological Activity

At dosage of 1.25 g dried plant/kg weight aqueous extracts of bark and leaves of *Byrsonima crassifolia* and *Gliricidia sepium* demonstrated the most neuropharmacological activity: decrease in motor activity, back tonus, reversible palpebral ptosis, catalepsy and strong hypothermia (Morales et al. 2001). These extracts elicited very significant reductions in spontaneous locomotor activity, exploratory behaviour and rectal temperature, and they increased the sodium pentobarbital-induced sleeping time.

Cytotoxicity Activity

Gliricidol, 2-methoxygliricidol and gliricidin isolated from *Gliricidia* bark, exhibited activity against the brine shrimp *Artemia salina* larvae (Rastrelli et al. 1999a).

Antimalarial Activity

Significant in-vivo antimalarial activity against *Plasmodium berghei* was observed with the ethyl acetate and aqueous extracts of *Gliricidia sepium* leaves (Castro et al. 1996). Compounds identified include flavonoids, coumarins, melilotic acid and iridoids.

Mosquitocidal Activity

The ethanol leaf extract of *G. sepium* demonstrated 78 % repellency against *Aedes aegypti* compared with 74 % with citronella oil (Nazli et al. 2008). Results of studies revealed that ethanol extract of *G. sepium* showed significant larvicidal, ovicidal and pupicidal activity against malarial vector, *Anopheles stephensi* (Krishnappa et al. 2012). The ethanol extract elicited maximum mortality of larvae at 250 ppm concentration with LC_{50} value of 121.79 ppm and LC_{90} value of 231.98 ppm. Highest concentration of both solvent extracts exhibited 100 % ovicidal activity as assessed by egg hatchability. Similarly, pupae exposed to different concentrations of ethanol extract were found dead with 58.10 % adult emergence when it was treated with 25 ppm concentration. Similarly, 18.36 ($n=30$; 61.20 %), 21.28 (70.93 %,) and 27.33 (91.10 %) pupal mortality was recorded from the experimental pupae treated with 50, 75 and 100 ppm concentration of extracts.

Anthelmintic Activity

Of three forage legume, *Calliandra calothyrsus*, *Gliricidia sepium* and *Leucaena diversifolia*, *G. sepium* was found to be more active (2.9 and 0.0 % for embryonation and egg hatching of *Haemonchus contortus*, respectively) than *C. calothyrsus*, 16.5 and 33.5 %, and for *L. diversifolia* 33.7 and 33.3 %, respectively (Wabo Poné et al. 2011). Studies by von Son-de Fernex et al. (2012) found that the lyophilized leaf extract of *G. sepium* (1,200 µg of extract/ml) inhibited motility of *Haemonchus contortus* infective larvae.

Trypanocidal Activity

The ethanol extract of *G. sepium* bark showed some trypanocidal activity in-vitro against the protozoa, *Trypanosoma cruzi* (Berger et al. 1998).

Toxicity Studies

Studies by Gale et al. (1954) found that extracts of mature and young leaves, fruit, seeds and roots of *G. sepium* appeared to be devoid of any toxicity to mature albino rats. No mortality of rats was found that could be attributable to *Gliricidia* extracts administered.

Sotelo et al. (1986) have reported a thermostable toxin canavanine in gliricidia seeds which killed mice within 1 week of feeding and may be associated with the toxicity of gliricidia in non-ruminants. Ahn (1990) also found depressed intakes, weight loss and foetal deaths in rats offered a diet containing 20 % dried gliricidia leaf. Gliricidia bark and seeds were reported to be used as a rat poison in some countries (Sotelo et al. 1986), suggesting the presence of a toxic principle.

Traditional Medicinal Uses

In Mexico, the plant is used as an antihistaminic, antipyretic, expectorant and diuretic; crushed fresh leaves are applied as a poultice (Elevitch and Francis 2006). In Saint Lucia, the leaves are brewed as tea, sweeten and drank for cough and asthma; the leaves are also useful for skin infections (Slane 1987). Peasant in San Jacinto in

northern Columbia uses the flower liquid to clean eyes (Bonzani 1999). In Panama, decoction of leaves is used for urticaria, rash and also in burns and erysipelas (Jose and Reddy 2010). In Guatemala and Costa Rica, bark decoction is used against bacterial and protozoal infections (Berger et al. 1998). However, their study showed that no fraction of *G. sepium* bark showed marked trypanocidal activity against *Trypanosoma cruzi*. *G. sepium* extracts have been used to treat infections produced by *Microsporum canis*, *Trichophyton mentagrophytes* and *Neisseria gonorrhoeae* (Gupta 1995).

In the Philippines, leaf juice or decoctions of the leaf, root and bark are employed for scabies and dermatitis and as antipruritic on the skin; fresh leaves are applied to skin as insect repellent, and crushed leaves applied for rheumatic pains, sprains and closed fractures (Stuart 2012). Sap of bark, leaves and roots has also been used for wound healing. In Guatemala, the bark and leaves are used to treat skin diseases, and in other countries, the plant is used for headache, bruises, burns, colds, cough, fever, fatigue, gangrene, gonorrhoea, skin itches and sores and as antidote, insecticide and insect repellent (Stuart 2012).

Other Uses

Gliricidia is often planted as a living fence; the foliage is harvested and used as green manure and cut-and -carry fodder for large and small ruminants, and the branched are lopped for fuel wood. The leaves of *G. sepium* have a high feeding value with crude protein comprising 26.1 % of the dry matter, a crude fibre content of about 9.14 % and in-vitro dry matter digestibility of 62.8 % (Adejumo and Ademosun 1985). When feeding three browse plants to goats, the tannin and saponin in the leaves of *Gliricidia sepium*, *Manihot esculenta* and *Spondias mombin* were found significantly to influence dry matter intake, nitrogen intake and nitrogen balance but not body weight gain in West African dwarf goats (Onwuka 1992). Gliricidia leaf meal was found to be a useful additive in dietary supplements for laying hens (Montilla et al. 1974). *G. sepium* leaf meal was found to have the following amino acid composition: threonine 1.2 %, valine 1.60 %, cysteine 0.39 %, methionine 0.42 %, isoleucine 1.20 %, leucine 2.41 %, tyrosine 1.12 %, phenylalanine 1.54 %, lysine 1.12 %, histidine 0.51 % and arginine 1.59 % (Chadhokar 1982). *G. sepium* leaf meal was found to have the following amino acid composition: threonine 1.2 %, valine 1.60 %, cysteine 0.39 %, methionine 0.42 %, isoleucine 1.20 %, leucine 2.41 %, tyrosine 1.12 %, phenylalanine 1.54 %, lysine 1.12 %, histidine 0.51 % and arginine 1.59 % (Chadhokar 1982). *G. sepium* leaves were found to contain condensed tannins (CT) which were all bound to proteins (Jackson et al. 1996). *Gliricidia sepium*, *Acacia boliviana*, *Arachis pintoi*, *Centrosema latidens* and *Senna velutina* contained <55 g total CT/kg DM, suggesting that they could comprise a reasonable proportion of ruminant diets. All other species grown in South America contained 100–240 g CT/kg DM, suggesting that they should only be fed in small amounts as supplements to dilute the CT concentration.

Studies showed that gliricidia leaf mulch had immense potential as green manure to improve productivity in tropical soils (Bah and Rahman 2001). Surface-applied gliricidia leaves significantly increased N uptake by maize and supplied >30 % of the total N in the stover and >20 % of that in the corn grain, even in the presence of hedgerows. The leaves also provide useful mulch material. Leaves are placed on bananas in containers to hasten ripening. Gliricidia has been planted to reforest and ameliorate denuded areas and reduce soil erosion, as windbreaks and firebreaks. It is widely cultivated as shade trees for cocoa, coffee and tea, and yams and also as live support trees for pepper and vanilla and as an understory crop in coconut plantations and in alley farming. It yields timber which is hard, heavy, durable, strong, coarse structured, easily worked and polished and is resistant to termites and rots. The wood is widely used for railway ties, posts, heavy construction, furniture, farm implements, tool handles and small articles. The wood is a useful source of fuel-wood. Studies found that *G. sepium* wood ash could be formulated with cement for concrete ad mixture

as construction material for low-cost housing (Aman et al. 2009).

Various parts of the tree haven reported to have pesticidal properties. The toxic seeds, bark, leaves and roots are used as rodenticide to poison rodents (Uphof 1968). In the Philippines, branches are strewn in rice fields to help deter rice pest such as caseworm (*Nymphula* sp.) and whorl maggot (*Hydrellia* sp.) (Litsinger et al. 1978). Farmers in Latin America often bathe their livestock with a paste made of crushed *G. sepium* leaves to ward off tarsalos (American Warble fly). In the Philippines, the extract obtained from its leaves is used to remove external parasites such as fleas and ticks from cattle and dogs (Palacpac-Alo 1990). Water leaf extract of *Gliricidia sepium* was found to be toxic against *Microcerotermes losbanosensis* (Fernandez et al. 1989). The bioactive principle was identified as coumarin (Rabena 2007). Bioassay against termites (Macrocerotermes losbanosensis) manifested 95 % mortality (4 hours) and 100 % (8 hours) using 0.02 g/ml coumarin impregnated in filter paper in a Petri dish. However, the bioassay of crude water-soluble Gliricidia extract showed 75 % mortality (24 hours).

Gliricidia leaves were found to have acaricidal activity (Sivira et al. 2011; Alvarez et al. 2008). *Tetranychus cinnabarinus* oviposition decreased at a rate of 43.7 % or 57 % when 5 % oregano or gliricidia extracts were used, respectively. Also, 10 % oregano or gliricidia extracts caused 42.2 % or 72.5 % mortality of *T. cinnabarinus*, respectively. The presence of alkaloids, flavonoids, phenols and tannins, essential oils and saponins was verified in the plant material used. *Gliricidia sepium* was one of several plant species whose aqueous alcoholic extract exhibited marked inhibition on oviposition of the tick, *Boophilus microplus* (Alvarez et al. 2008). The ethanol leaf extract of *G. sepium* exhibited nematicidal activity against *Meloidogyne incognita* causing 60 % mortality (Nazli et al. 2008).

Comments

The tree is easily propagated by using stem cuttings.

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Hardenbergia violacea

Scientific Name

***Hardenbergia violacea* (Schneev.) Stearn**

Synonyms

Glycine violacea Schneev., *Hardenbergia monophylla* (Vent.) Benth., *Kennedia monphylla* Vent.

Family

Fabaceae.

Common/English Names

Climbing Morning Glory, False Sarsaparilla, Happy Wanderer, Native Lilac, Purple Coral, Purple Coral Pea, Native Sarsaparilla, Native Woodrose, Purple Twining Pea, Sarsaparilla.

Vernacular Names

Australia: Waraburra (Kattang Aborigines)
United States: Lilac Vine, Mexican Lilac Vine

Origin/Distribution

The species is native to Australia, growing in areas from Queensland to Tasmania. It has been introduced to the United States where it is grown as landscape plants.

Agroecology

In Australia the species is found in many habitats, growing widespread along the coast and adjacent ranges in the eastern and southern states on the mainland. It grows in coastal heath and forest and inland in drier eucalypt forests. In Tasmania, it is deemed as endangered, as it is only known from two small natural populations, on private land.

The species is moderately frost tolerant down to 0 to −5 °C and moderately drought tolerant. It thrives in areas with 400–2,400 m mean annual rainfall in summer or winter, mean annual temperature range of 10–21 °C, and tolerates a summer maximum of 33 °C. It grows best in full sun but tolerates light shade in well-drained acidic (<pH 6.5) clay loam, loam, sandy loam or sandy clay loam soils. It is intolerant of salinity.

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Edible Plant Parts and Uses

The leaves are boiled and used to prepare a sweet and pleasant beverage (Cribb and Cribb 1976; Kunkel 1984; Facciola 1990). The roots were also reportedly used in a similar way. The purple flowers are also eaten (Haslam 2011).

Botany

A hardy, evergreen, climbing or prostrate, glabrous subshrub with slender, woody stem growing to 2 m long. Leaf simple, ovate-narrow-lanceolate 3–10 cm by 1–5 cm wide, glabrous, dark green above, grey green beneath, leathery, margin entire, venation distinctly reticulate, tip mucronate, base rounded to indented (Plates 1 and 2), petiole 0.5–3 cm long, stipels 1–2 mm long, filiform. Inflorescence axillary, racemose panicle with 20–30 violet or reddish flowers, each axillary unit of 3 flowers with a subtending bract. Calyx 3–4 mm long with two dorsal sepals fully and the rest joined ¾ length; corolla 8 mm long, with violet purple (or red) standard with 2 yellowish white spots at the base, lateral wings on long yellow claw, violet purple and keel also violate purple or red (Plates 1, 2 and 3); stamens 9 joined into a tube and 1 free, diadelphous; ovary 3–3.5 mm long. Pod flattened oblong, 35–50 mm long, glabrous, dark brown to black. Seeds 4–8, reinform, 2.5–3 mm, olive green to brown, strophiolate.

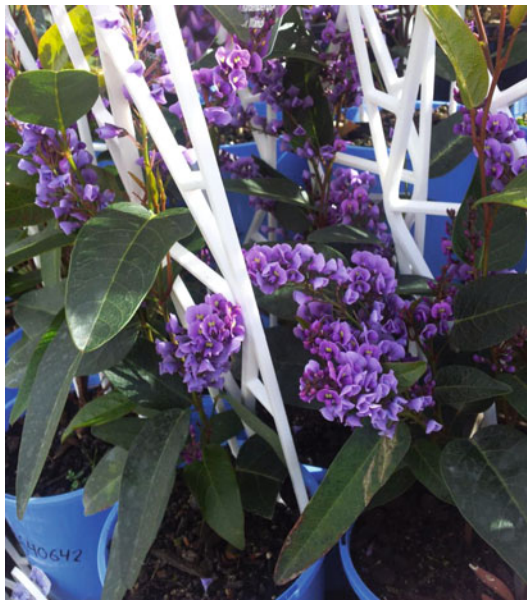

Plate 1 Flowers and foliage

Plate 2 Purple flowered variety

Plate 3 Red-flowered variety

Nutritive/Medicinal Properties

Percentage distribution in *H. violacea* pods and seeds of mineral nutrients respectively were as follows: Na, 57.5 %, 42.5 %; Fe, 56.2 %, 43.8 %; K, 50 %, 50 %; Ca, 49.7 %, 50.3 %; Mn, 46.9 %, 53.1 %; Cl, 37.7 %, 62.3 %; Zn, 39.7 %, 60.3 %; Cu, 37.6 %, 62.4 %; S, 28.9 %, 71.15; Mg, 26.1 %, 73.9 %; N, 10 %, 90 %; and P, 5.7 %, 94.3 % (Hocking and Kortt 1987).

Concentrations (per g dry weight) of minerals in the elaiosome, testa and embryo of the seed were reported, respectively, as dry matter, 2.6 mg, 32.5 mg, 20.6 mg; N, 31.55 mg, 2.14 mg, 86.90 mg; P, 0.72 mg, 0.74 mg, 4.36 mg; K, 5.91 mg, 8.84 mg, 16.15 mg; S, 1.14 mg, 0.91 mg, 4.27 mg; Ca, 0.84 mg, 2.53 mg, 1,61 mg; Mg, 0.50 mg, 1.41 mg, 2.08 mg; Cl, 0.50 mg, 0.38 mg, 0.46 mg; Na, 145.0 µg, 200 µg, 102 µg; Fe, 38.4 µg, 34 µg, 55.2 µg; Zn, 18.4 µg, 26.1 µg, 58.7 µg: Mn, 53.6 µg, 45.7 µg, 23 µg; and Cu, 2.76 µg, 2 µg, 18.85 µg. The fatty acid compositions of elaiosomes and mature seeds were, respectively: lauric, (12:0) 0.13 %, 0; myristic, (14:0) 0.46 %,): palmitic, (16:0) 21.93 %, 12.1 %; palmitoleic, (16:1) 2.55 %, 0; stearic, (18:0) 5.26 %, 5.1 %; oleic, (18:0) 60.62 %, 23.2 %; linoleic, (18:2) 7.54 % 55.9 %; g-linolenic, (18:3) and a-linoleic, (18:3) 1.22 %, 3.0 %; and elaidic acid, (20:0) 0.29 %, 0. The amino acid composition [nmol amino acid (per mg dry weight meal)] of elaiosomes and dehulled seeds were, respectively: lysine, 21, 28.8; histidine, 6.5,10.3; arginine, 37.7, 24.0; aspartic acid, 49.9,44.49; threonine, 15.3,21.9; serine, 18.4, 29.6, glutamic acid, 30.8, 74.0; proline, 18.8, 23; glycine, 33.1, 43.2; alanine, 23.1, 31.2; half-cystine, 3.8, 6.3;valine, 17.3, 22.4; methionine, 2.6, 5.0; isoleucine, 15.5, 15.5; leucine, 28.1, 34.1; tyrosine, 11.1, 13.1;phenylalanine, 15.9, 17.7; and canavanine 4.0, 47.

As seen from the above, the seeds accumulated about 50 % of the dry matter of a mature fruit; over 90 % of its N and P content; 50–75 % of its K, Ca, Mn, Cl, S, Zn, Cu and Mg, but less than 50 % of its Fe and Na (Hocking and Kortt 1987). Seeds contained higher levels of most nutrients than pods. The testa comprised 60 % of the dry matter content of a seed and contained the major proportion of its Ca, Mg, Cl, Na and Mn; the embryo contained most of the seed's contents of N, P, K, S, Zn and Cu. The elaiosomes had less than 5 % of the seed's dry matter and mineral nutrient content. The oil content of the elaiosome was 34 %, compared to 12 % for the embryo. Oleic acid made up over 60 % of the fatty acid content of elaiosome oil. Aspartic acid, arginine and glycine were the predominant amino acids in the elaiosome. The embryo contained 10 % of the non-protein antimetabolic amino acid, canavanine, the elaiosome only 1 %. The subunit protein compositions of the elaiosome and embryo were different. Earlier, Rivett et al. (1983) reported that *Hardenbergia violacea* had a chemical composition which may have the potential for human food. The fatty acid composition of the elaiosome was quite different from that of the dehulled seed (Rivett et al. 1983) in that the predominant fatty acid of the seed was linoleic acid versus oleic acid in the elaiosome.

Concentrations (per g dry weight) of minerals in the leaves at 94 days after flower anthesis were as follows: N, 27.95 mg; P, 0.87 mg; K, 12.10 mg; S, 1.64 mg; Ca, 9.40 mg; Mg, 1.93 mg; Na, 0.29 mg; Cl, 0.74 mg; Fe, 190 µg; Zn, 26.4 µg; Mn, 180.8 µg; and Cu, 7.8 µg (Hocking and Kortt 1987).

The plant has been reported to be used in bush medicine as a tonic drink (Cribb and Cribb 1976; Haslam 2011).

Other Uses

A grey-blue dye is obtained from the flowers (Cribb and Cribb 1982).

Comments

The plant is readily propagated from seeds.

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Mimosa pudica

Scientific Name

***Mimosa pudica* L.**

Synonyms

Mimosa hispidula Kunth

Family

Fabaceae, also placed in Mimosaceae

Common/English Names

Action Plant, Ant-Plant, Bashful Mimosa, Humble Plant, Live-and-Die, Modest Plant, Sensitive Plant, Sensitive Weed, Sleeping Grass, Shame Plant, Shameful Plant, Shrinking Plant, Shy Plant, Tickle-Me Plant, Touch-Me-Not, Touch-Shy Plant, Virgin Plant

Vernacular Names

Afrikaans: Kruidjie-Roer-My-Nie
Brazil: Dormideira, Juquiri, Malícia-Das-Mulhees, Não-Me-Toque, Sensitiva, Vergonha (Portuguese)
Brunei: Puteri Malu, Rumput Malu, Sopan Malu
Burmese: Hti Ka Yoan
Chamorro: Betguen Sosa
Chinese: Han Xiu Cao, He He Cao, Pa Chou Cho, Zhi Xiu Cao
Cook Islands: Paope ʻĀvare, Pikikaʻa, Pikikaʻa, Rākau ʻAvare, Rākau ʻAvarevare, Rākau Pikikaʻa, Rākau Pikikaʻa, Tiare Pikikaʻa, Titā ʻĀvarevare, Titā ʻĀvarevare, Titā Pikikaʻa (Maori)
Costa Rica: Dormilona
Cuba: Dormidera, Morivivi
Czech: Citlivka Stydlivá
German: Gemeine Mimose, Mimose, Schamhafte, Sinnpflanze, Sinnpflanze
Danish: Almindelig Mimose
Dutch: Kruidje-Roer-Me-Niet
Dominican Republic: Morí-Viví, Moriviví
Eastonian: Häbelik Mimoos
Finnish: Tuntokasvi
Fijian: Co Gadrogadro, Cogadrogadro, Cokadrokadro, Cokadrokadro, Ngandrongandro, Tho Kandrodandro, Tho Ngandrongandro
French: Mimeuse Commune, Mimeuse Pudique, Sensitive
Hawaiian: Pua Hilahila
India: Adoriban, Nilajban (Assamese), Laajak, Lajjavathi, Lajjaboti (Bengali), Reesamani (Gujarati), Chhui-Mui, Chuimui, Lajaalu, Lajalu, Lajawanti, Lajjavanthi, Lajouni, Lajvanti, Lajwanti, Najuk, Sharminda, Sharmpate (Hindi), Ganda Kaali, Hadergitte, Lajja, Lajjaavathi, Lajjavat, Lajjavathy, Lajje, Muchha Muri, Mudugudavara, Mudugudavare, Muduguthaavare, Mudurelegida, Muthamurike, Mutlamurike, Muttalu Muduru, Muttalu Muruka, Muttidare Muni, Muttidaremuniva,

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Naachike Gida, Naachike Mullu, Nachikay-Gida, Nacike, Nacikegida, Nacikimullu, Nasike, Thotuthe-Ramum, Thotutheramum (Kannada), Kambatsam-Thia, Sunteshuh (Khasi), Thendarmani, Thotavadi, Thottamvati, Thottavadi, Tindarmani, Tintarmani, Tottalvati, Tottamvati, Tottavati (Malayalam), Laajari, Lajaalu, Lajalu, Lajri, Lazalu (Marathi), Durum-Janum (Mundari), Lajakulilata (Orissa), Lajkuri (Oriya), Ajalikalika, Alambusa, Anjalikaraka, Anjalikarika, Asrarodhani, Gandamalika, Kandiri, Khadiraka, Khadirpatrika, Lajja, Lajjalu, Lajjaluh, Lajjika, Mahabhita, Mahaushadhi, Mamaskari, Namaskari, Prasarini, Raktamula, Raktapadi, Samanga, Samangga, Samipatra, Saptaparni, Shamipatra, Sparshalajja, Sprikha, Svagupta, Tamra, Tamramula, Varaha-Kranta, Varahakranta, Varakranta, Vashini (Sanskrit), Al, Alavananki, Alcunanki, Alcunankicceti, Arcalakacceti, Arcalakam, Camankai, Camanki, Caminnai, Cayanti, Cillam, Cinunki, Cunti, Cuntil, Cuntiyilai, Curukki, Cuvetamuli, Cuvetamulinicceti, Cuvetavati, Ilaccaki, Intiriyakkoti, Intu, Iracalakacceti, Iracalakam, Kacankukanni, Kacankukannicceti, Kaciro-rttam, Kasirottam, Laccaru, Milananceti, Namakkari, Nilaccurunki, Palakamoti, Palakamoticceti, Samangai, Tamiramulam, Tantakkari, Thotalpadi, Thotalvadi, Thottai-Surungi, Thottal Shurungi, Thottal-Surungi, Thottalsurungi, Thottalvadi, Thottar Chunnungi, Thottar-Chunungi, Thottasiningi, Total Vadie, Totalvadi, Tottachurungi, Tottakkalvati, Tottalcinunki, Tottalcurunki, Tottalvadi, Tottalvati, Tottalvaviricceti, Tottalvayiri, Tottar Cinunki, Tottar Cunanki, Tottar Curunki, Tottarcinunki, Tottarcunanki, Tottarcurunki, Urumarmulicceti, Urumarumuli, Vaku, Varakakkiranti, Vati (Tamil), Atthapatthi, Lajjavanthi, Manugumaramu, Mudatha Damara, Munuguda, Munuguda-Maramu, Muttavapulagamu-Chettu, Muttavapulagamucettu, Nidrakanti, Peda Nidrakanti, Pedda Nidrakanti, Peddanidrakanti, Siggaku, Thottalasingi (Telugu), Chhui-Mui (Urdu)

I-Kiribati: Te Kaimatu

Indonesia: Putri Malu (Malay), Kuchingan, Pis Kucing, Randelik, Ri Sirepan (Javanese), Bujang Kagit, Jukut Borang, Jukut Borangan, Jukut Gehgehran, Jukut Riyud, Rondo Kagit (Sundanese)

Italian: Sensitiva

Japanese: Nemurigusa

Khmer: Smau Bânla, Bânkrap

Korean: Mimosa

Laos: Fa:Z Langab, Thu'üb Nhub

Malaysia: Malu-Malu, Memalu, Puteri Malu, Keman, Kembang Gajah, Kemunchup, Rumput Rimau, Semalu (Malay), Todop-Todop (Dusun), Kommon (Kadazan)

Nicaragua: Sarka Dormilona

Niuean: Memege

Palauan: Mechiuaiu

Papua New Guinea: Matmat (Gunantuna, New Britain)

Philippines: Torog-Torog (Bikol), Huya-Huya, Kirom-Kirom (Bisaya), Babain, Dilgansusu (Iloko), Tuyag-Huyag (Panay Bisaya), Makahia (Pangasingan), Harupai, Kiromkirom (Samar Leyte Bisaya), Sipug-Sipug (Subanum), Damohia, Makahia (Tagalog)

Pohnpeian: Limemeirkelik, Limemeirpong, Limemeirpwong

Polish: Mimoza Wstydliwa

Portugal: Dormideira, Não-Me-Toque, Sensitiva

Rotuman: Aifeaefarmori

Russian: Mimoza Stydlivaja

Samoan: Vao Fefe, Vao Fefe

Spanish: Dormidera, Minosa, Sensitiva, Vergonzosa

Swahili: Kifyauwongo

Swedish: Sensitiva

Tahitian: Pohe Ha'Avare, Pope Ha'Avare

Thai: Ka-Ngap (Peninsular), Mai Yaraap, Ra Ngap (Central), Yaa Pan Yot (Northern)

Tibetan: Btsod Rigs Gcig Pa, Sa Mam Ga

Tonga: Mateloi

Vietnamese: Cỏ Trinh Nữ, Mắc Cỡ, Trinh Nữ, Xấu Hổ

West Indies: Mori Vivi

Wallisian: Malualoi, Malualoi

Origin/Distribution

The species is native to South America and Central America but is now a pantropical weed.

Agroecology

In the warm, wet tropics, the species has naturalized as a weed in cultivated areas, along roadsides, in plantations, in cropping areas, in orchards, in lawns, in pastures and on wasteland and forming mats on the dry mud of river banks, at elevations from near sea level up to about 2,000 m elevation. The plant is found on a wide range of soil types but thrives on well-drained soils, even scalped or eroded subsoils and soils with low nutrient concentrations and waterlogged soils. On coralline soils, iron chlorosis has been observed (Rachman 1999). The plant is tolerant to light shade but does not compete with tall vegetation or grow under forest canopies. This plant is spread mainly by seeds clinging to man and animals and the seeds can remain viable for many years.

Edible Plant Parts and Uses

Flowers are crystallized or used for the preparation of distilled flower water (Crowhurst 1972; Facciola 1990).

Botany

Mimosa pudica is a low sprawling, prickly, 15–40 cm, branched annual or perennial, that may grow into a 70–100 cm prickly sub-shrub. The leaves are very sensitive to touch, alternate, green, compound, digitately bipinnate with 1–2 pairs of pinna and 10–20 pairs of leaflets per pinna (Plate 1). Each leaflet is 0.6–1.2 cm long by 0.3–0.4 cm broad, sessile, narrowly oblong or linear oblong; obliquely rounded at base, acute tip, nearly glabrous and lack prickles. The flowers are produced in globose head borne on a bristly or prickly peduncle (Plate 1). Flowers pink or mauve, 4-merous, subtended by linear, marginally setose bracteoles; calyx minute; corolla glabrous or with puberulous, ovate-oblong lobes; stamens 4 exserted; ovary sessile. Fruit is a lomentum, simple, dry, flat, slightly curved, 1.5–1.8 cm by 0.4–0.5 cm, bristly along the margins, with 2–5 segments that break up at the sutures. Seeds subcircular to elliptic, pale-brown, flat, 2.5–3 mm across.

Plate 1 Globose flower head, foliage and prickly stems

Nutritive/Medicinal Properties

Plant (Aerial Parts) Phytochemicals

A non-protein amino acid leucine, mimosine, was isolated from *M. pudica* (Renz 1936) and its structure determined as 3-hydroxy-a-amino-4-oxo-1 (4H)-pyridinepropionic acid (Kleipool and Wibaut 1950). The same compound had been called leucenol. Serine and α-aminoadipic acid precursors of mimosine, pipecolic acid and 5-hydroxypipecolic acid, were found in *Mimosa pudica* (Tiwari et al. 1967). Norepinephrine was isolated from the plant (Applewhite 1973).

Two C-glycosylflavones, 2′-*O*-rhamnosylorientin and 2′-*O*-rhamnosylisoorietnin, were isolated from the aerial parts (Englert et al. 1994) Two C-glycosylflavones 4″-hydroxymaysin and cassiaoccidentalin B and myricetin were isolated from the aerial plant parts (Lobstein et al. 2002). Flavonoids found in *M. pudica* included orientin, kaempferol 7-rutinoside and kaempferol 3-glucoside-7-rhamnoside (Yusof et al. 2003).

Four compounds were isolated from *M. pudica* and identified as 7, 8, 3′, 4′-tetrahydroxyl-6-C-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranosyl flavone (I); 5, 7, 4′-trihydroxyl-8-C-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranosyl flavone (II); 5, 7, 3′, 4′-tetrahydroxyl-6-C-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranosyl flavone

(III); and catcher (IV) (Yuan et al. 2006). C-glycosylflavones were isolated from the whole plant of *Mimosa pudica*, and their structures elucidated as 5, 7, 3′, 4′-tetrahydroxy-6-C-[β-D-apiose-(1 → 4)]-β-D-glucopyranosyl flavone and 5, 7, 4′-trihydroxyl-8-C-β-D-glucopyranosyl flavones (Yuan et al. 2007a) and 6, 7, 3′, 4′-tetrahydroxyl-8-C-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranosyl flavones and, 5, 7, 3′,4′-tetrahydroxy-8-C-[β-D-apiose-(1 → 4)]-β-D-glycopyranosyl flavone (Yuan et al. 2007b). Crocetin dimethyl ester and tannin have been isolated from the plant. The mucilage from seed was composed of D-xylose and D-glucuronic acid 4-*O*-(3,5-dihydroxybenzoic acid)-β-D-glucuronide. Mimosine, α-spinasterol and phenyl ethylamine derivatives were isolated from the plant (Muthumani et al. 2012).

Leaf Phytochemicals

M. pudica pulvinus was found to contain adenosine triphosphatase; the molecular weight of purified Ca, Mg-ATPase, was determined to be 139,000, and it played a role in the seismonastic movements of the leaf (Liubimova-Engel'gardt et al. 1978). Actin-like protein was found in the leaves (Ghosh et al. 1987). From *Mimosa pudica* fresh leaves and pulvinar callus cells, tubulin protein was isolated and purified (Pal et al. 1990). The purified protein consisted of alpha and beta subunits and trace quantities of other proteins. This protein constituted 5–6 % of the total extractable protein in the leaves. They postulated that movement of the leaves of this plant may be regulated by the presence of a high amount of this protein. Turgorin, the periodic leaf movement factor 1 (PLMF-1) (gallic acid β-D-glucopyranosyl-6′-sulphate), and sulphotransferase, the enzyme involved in sulphation of the turgorin, were found to be localized in the pulvinus of *M. pudica* plant (Varin et al. 1997). The pulvinus was also found to have annexin which may also have contributed to the nyctinastic movement in the pulvinus (Hoshino et al. 2004). The amount of annexin in the pulvinus increased at night and was sensitive to abscisic acid. Two tonoplast proteins, a putative water-channel protein (aquaporin belonging to the [gamma]-TIPs [tonoplast intrinsic proteins]) and the catalytic A-subunit of H+-ATPase, were found in the mature motor cell in the leaves (Fleurat-Lessard et al. 1997). [Gamma]-TIP aquaporin was detected almost exclusively in the tonoplast of the colloidal vacuole, and the H+-ATPase was also mainly localized in the membrane of the same vacuole. *M. indica* was found to contain a gelsolin/fragmin family actin-modulating protein that severed actin filament in a Ca^{2+}-dependent manner (Yamashiro et al. 2001). Kanzawa et al. (2006) found that changes in actin isoforms, fragmentation of actin filaments and the leaf bending movement were all inhibited after injection of a tyrosine phosphatase inhibitor. On this basis they propose that the phosphorylation status of actin at tyrosine residues affected the dynamic reorganization of actin filaments and caused seismonastic movement.

The cerebroside fraction of lipids of both the leaves and chloroplasts of *M. pudica* was found to contain a polyunsaturated fatty acid (20:4ω3) and a long-chain sphingosine base (Choudhury and Chakrabarti 1980). A phenolic ketone, 4-(24′-methoxy-24′-methyl-1′ -oxo-5′-*n*-propyl-tetracosanyl)-phenol, was isolated from the leaves (Josewin et al. 1999).

A 5-deoxyflavonol derivative identified as 7,3,4-trihydroxy-3,8-dimethoxy flavone and *p*-coumaric acid were isolated from the leaves (Kirk et al. 2003).

Flower Phytochemicals

Flavonoids identified in pollens: isoquercetin, quercetin and isorhamnetin were most commonly found; other less commonly found in decreasing frequency were kaempferol, myricetin, tricetin and luteolin (Freire et al. 2012).

Seed Phytochemicals

A saponin (Jiang et al. 1990) and a novel bufadienolide, hellebrigenin-3-*O*-α-L-rhamno-

pyranosyl-(1 → 4)-*O*-β-D-galactopyranoside, from the seeds *of Mimosa pudica* (Yadava and Yadav 2001). The mucilage from seed was reported to compose of D-xylose and D-glucuronic acid 4-*O*-(3,5-dihydroxybenzoic acid)-β-D-glucuronide (Chatterjee and Pakrashi 2006). *Mimosa* mucilage was found to contain yellowish-brown and odourless flakes, which hydrate rapidly on contact with water to swell but is sparingly soluble in water (Singh et al. 2009). The pH of 1 % (wt/vol) aqueous dispersion of the mucilage was found to be 6.0–6.5. The swelling index of mucilage was found to be 81.77 % (vol/vol). The mucilage showed a loss on drying of 6.8 % (wt/wt) and yielded 0.106 % (wt/wt) of water-soluble extractive; the total ash contents were found to be 86.75 % (wt/wt); water-soluble ash and acid-insoluble ash were 61 and 7.5 % (wt/wt), respectively.

M. pudica seed oil extract was found to contain amino acids and derivatives: D-alanine, N-DL-alanylglycine, DL-alanine ethyl ester, DL-alanyl-DL-valine, 1-alanine ethyl amide; fatty acid derivatives: 9, 12-octadecadienoic acid (Z, Z), methyl ester; 9, 12-octadecadienoic acid, methyl ester; 11, 13-eicosadienoic acid, methyl ester, carbohydrate derivatives: meglumine; 1, 3-dioxolane-4-methanol; other compounds: methylamino-N- phenyl-acetamide; 1-butanamine, N-methyl; 2-methylamino-N-phenyl acetamide; 1-alanine ethylamide (S); 1-octamine, N-methyl; and 2, 5-dimethoxy-4-(methylsulphonyl) amphetamine (Saraswat and Pokharkar 2012).

Root Phytochemicals

One new sterolglucoside characterized as 4-a,24-dimethylcholest-7-en-3β-ol-3β-D-glucoside along with stigmasterol, β-sitosterol and betulinic acid isolated from the roots (Dinda et al. 2006). The proximate analysis of *M. pudica* roots revealed values for total ash 17.365 %, water-soluble ash 9.65 %, alcohol-soluble ash 4.55 %, loss on drying 2.55 %, moisture content 0.58–5 %, foreign organic matter 0.5 % and sulphated ash 3.78 % (Pande and Pathak 2010). The petroleum ether fraction was found to contain flavonoids, phytosterol, alkaloids, amino acids. Flavonoids were found in the acetone fraction and alkaloids in the chloroform fraction.

According to the Herbal Medicine Research Center, Malaysia (2002), the plant is believed to have diuretic, antiviral, antibacterial, anti-inflammatory, antispasmodic and hypoglycaemic properties. These and other pharmacological properties of the plant have been reported in in-vitro and some in-vivo animal studies.

Antioxidant Activity

The dichloromethane and methanol extracts of both *M. pudica* and *M. rubicaulis* showed prominent antioxidant property, with the RC_{50} values ranging from 4.70×10^{-1} to 2.10×10^{-2} mg/ml (Genest et al. 2008). The dichloromethane and methanol extracts of both *M. pudica* and *M. rubicaulis* showed prominent antioxidant property, with the RC_{50} values ranging from 4.70×10^{-1} to 2.10×10^{-2} mg/ml (Genest et al. 2008). The sequence of antioxidant activity of the ethanol extracts of *M. pudica* was as follows: leaf > the whole plant > seed > stem (Zhang et al. 2011). Leaf extracts of *M. pudica* contained the highest amount of total flavonoid and total phenolic, significantly higher than in other parts of the plant. The antioxidant sequence of the 5 flavonoid monomers was 5, 7, 3′, 4′-tetrahydroxy-6-C-[β-D-apiose-(1 → 4)]-β-D-glycopyranosyl flavone (1) > isorientin (2) > orientin (3) > isovitexin (4) > vitexin (5), and the antioxidant activity of compound 1 was equivalent to the synthetic antioxidant trolox or a bit stronger than trolox, and significant correlations were found among the active ingredient contents and the results of antioxidant activity.

Antiinflammatory Activity

The ethanol and aqueous leaf extracts of *M. pudica* exhibited significant dose-dependent antiinflammatory activity in the carrageenan-induced paw oedema and cotton pellet tests in

rats while the petroleum ether extract exhibited minimum effect (Goli et al. 2011). The ethanol extract of dried, powdered *M. pudica* plant significantly inhibited the HMC-1 cell migration induced by stem cell factor and blocked the release of monocyte chemotactic protein-1 (MCP-1) and interleukin-6 (IL-6) in EoL-1 cells in BALB/c mice with asthma induced by ovalbumin (Yang et al. 2011). Leukocytosis, eosinophilia and mucus hypersecretion in asthmatic lung were significantly suppressed by mimosa extract. The release of ovalbumin-specific IgE in bronchoalveolar lavage fluid and serum was also decreased. The extract treatment resulted in no liver cytotoxicity. The results suggested that *M. pudica* extract had inhibitory properties on asthma and may be used as a potent therapeutic agent for allergic lung inflammation.

Anticonvulsant Activity

The decoction of *Mimosa pudica* leaf decoction administered intraperitoneally at dose of 1,000–4,000 mg/kg protected mice against pentylenetetrazol- and strychnine-induced seizures (Bum et al. 2004). It also antagonized N-methyl-D-aspartate-induced turning behaviour. These properties could explain its use in African traditional medicine.

Antiulcerogenic Activity

The methanolic leaf extract of *M. pudica* was found to possess remarkable ulcer-protective properties at 100 and 200 mg/kg in the aspirin-induced ulcer model in rats when compared to the other chloroform and diethyl ether extracts (Vinothapooshan and Sundar 2010). Pretreatment of rats with *Mimosa pudica* leaf extracts produced a dose-dependent protection in the ethanol-induced ulceration model as compared to control group. The methanolic, chloroform and diethyl ether extracts in doses of 100 and 200 mg/kg produced a reduction in the ulcer index, gastric volume, free acidity, total acidity and raised gastric pH significantly in comparison with control rats. The control animals had ulcers and haemorrhagic streaks, whereas in animals administered with the extracts of *Mimosa pudica*, there was significant reduction in the ulcer index.

Hepatoprotective Activity

Methanolic leaf extract of *M. pudica* showed significant hepatoprotective effect against carbon tetrachloride-induced toxicity Wistar albino rats by lowering the serum levels of various biochemical parameters such as serum glutamic oxaloacetate transaminase (SGOT), serum glutamic pyruvates transaminase (SGPT), alkaline phospatase (ALP), total bilirubin (TBL) and total cholesterol and by increasing the levels of total protein and albumin (Rajendran et al. 2009). These biochemical observations were in turn confirmed by histopathological examinations of liver sections and were comparable with the standard hepatoprotective drug silymarin (100 mg/kg body weight i.p.) which served as a positive control. Simultaneous administration of the aqueous leaf extract of *Mimosa pudica* along with the toxin ethanol in rats showed a considerable protection against the toxin-induced oxidative stress and liver damage as evidence by a significant increase in superoxide dismutase (SOD) catalase (CAT), glutathione peroxidase and glutathione levels (Nazeema and Brindha 2009). The study revealed that the co-administration of *Mimosa pudica* aqueous extract significantly lowered the level of lipid peroxidation in alcohol-fed mice.

Anticancer Activity

Mimosine, an iron chelator, was found to have potent cytotoxic and antiproliferative effects on human (CaOV-3 & OvCAR) and rat (NuTu 19) ovarian cancer cells in-vitro (Restivo et al. 2005). Iron challenge studies indicated that the antiproliferative effect of mimosine was mediated by iron chelation. Further, mimosine-induced apoptosis was confirmed by DNA fragmentation analysis.

The alkaloid fractions of the ethanol extracts of *Ervatamia coronaria* and *M. pudica* showed significant cytotoxicity with LC_{50} values of 65.83

and 85.10 µg/ml in the brine shrimp lethality bioassay, respectively (Hullatti et al. 2013).

Antiophidic Activity

The aqueous root extract of *M. pudica*, particularly the normal water extract, displayed a significant inhibitory effect on the lethality, myotoxicity and tested enzyme activities of *Naja kaouthia* venom compared with alcoholic root extracts (Mahanta and Mukherjee 2001). The aqueous root extract of *Mimosa pudica* dose dependently inhibited the hyaluronidase and protease activities of Indian snakes (*Naja naja, Vipera russelli* and *Echis carinatus*) venom (Girish et al. 2004). The water extract of *Mimosa pudica* showed 100 % ability in neutralizing the $2LD_{50}$ lethality of *Naja naja kaouthia* venom (Vejayan et al. 2007). *M. pudica* also exhibited >50 % ability in neutralizing the $2LD_{50}$ toxicity of venoms of other snakes, namely, *Ophiophagus hannah, Bungarus candidus, B. fasciatus* and *Calloselasma rhodostoma*. Aqueous extract of *Mimosa pudica* dried roots displayed significant inhibitory effect on the lethality, phospholipase activity, oedema-forming activity, fibrinolytic activity and haemorrhagic activity of venoms of *Naja naja* and *Bungarus caeruleus* (Meenatchisundaram et al. 2009). About 0.14 and 0.16 mg of *M. pudica* extracts were able to completely neutralize the lethal activity of $2LD_{50}$ of *Naja naja* and *Bungarus caeruleus* venoms, respectively.

Mimosa pudica tannin isolate (MPT) obtained from the root exhibited promising in-vitro activity in neutralizing *Naja kaouthia* venom, but MPT injected into mice preincubated with the *Naja kaouthia* venom showed no in-vivo protection against the venom (0.875 mg/kg) in four different rescue modes (Ambikabothy et al. 2011). In contrast in another study, preincubation of $2LD_{50}$ (1.84 mg/kg) of *Naja kaouthia* venom with *M. pudica* tannins was able to completely neutralize the snake venom since the survival rate of mice was 100 % after 24 hours of observation (Sia et al. 2011). In the mouse group in which there was no preincubation, no protection against the effects of the venom was observed. Preincubation of the venom with commercial tannic acid showed only a mouse survival rate of 12.5 %. Tannins obtained from *M. pudica* were eight times more effective in neutralizing the lethal effects of *N. kaouthia* venom compared to the tannic acid.

Antimicrobial Activity

The dichloromethane and methanol extracts of *M. pudica* displayed considerable bacteriostatic activity against all six bacterial strains (MIC range = 0.625–2.50 mg/ml) including *Bacillus cereus, B. subtilis, Escherichia coli*, ampicillin-resistant *Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa* (Genest et al. 2008).

Organic extracts (ethanol, petroleum ether and chloroform) of *Mimosa pudica* exhibited antibacterial properties against Gram-positive (*Staphylococcus aureus*, *Bacillus cereus*, *Bacillus subtilis*, *Bacillus megaterium*) and Gram-negative (*Shigella shiga*, *Shigella dysenteriae*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Pseudomonas aeruginosa*), human pathogenic bacteria (Akter et al. 2010). *M. pudica* extract was found to have antimicrobial activity against *Aspergillus fumigatus*, *Citrobacter divergens* and *Klebsiella pneumonia* (Gandhiraja et al. 2009). Ethanolic leaf extract showed antimicrobial activity against *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Aspergillus flavus* and *Trichophyton rubrum* (Tamilarsi and Ananthi 2012).

Anxiolytic Activity

Aqueous leaf extract of *M. pudica* was found to have antidepressant-like profile similar to two tricyclic antidepressants, clomipramine and desipramine (Molina et al. 1999). *M. pudica* (6.0 and 8.0 mg/kg, I.R) reduced immobility in the forced swimming test and increased the rate of reinforcers received in the differential reinforcement of low rates of response at 72 second test; the data suggested that *M. pudica* exerted antidepressant effects in the rat.

Wound Healing Activity

Treatment of wounds with ointment containing 2 % (w/w) methanolic and 2 % (w/w) aqueous extract of *M. pudica* roots exhibited significant wound healing activity in three types of model in rats, namely, excision, incision and estimation of biochemical parameter (Kokane et al. 2009). The methanolic extracts of *M. pudica* shoot and roots showed marked wound healing activity when compared to the standard drug gentamicin, but the chloroform root extract exhibited negative result (Kannan et al. 2009). In the incision, excision and burn wound models in rats, chloroform and methanolic extracts of *Mimosa pudica* roots at high as well as low doses demonstrated significant reduction in wound contraction and period of epithelialization compared to control (Paul et al. 2010). In the incision wound model, a significant rise in breaking strength was observed in all treated group animals. Both extracts produced a significant increase in the breaking strength, dry weight and hydroxyproline content of the granulation tissue in dead space wound model. The results suggested that both extracts applied topically or administered orally possess wound healing activity.

Antiobesity/Hypolipidaemic Activity

In hyperlipidaemic rats, chloroform leaf extract of *M. pudica* showed significant hypolipidaemic effect by significantly lowering the serum levels of biochemical parameters such as serum cholesterol, triglyceride, LDL and VLDL and increasing in HDL level which was similar to the standard drug Atorvastatin (Rajendran and Krishnakumar 2010). These biochemical observations were in turn confirmed by histopathological examinations of aorta, liver and kidney sections.

Quercetin [-2-(3, 4-dihydroxyphenyl)-3, 5, 7-trihydroxychromen-4-one], a flavonol present in *Mimosa pudica*, was found to antagonize peripheral hypothalamic cannabinoid-1 (CB1) receptor involved in the regulation of appetite, lipogenesis and insulin resistance (Shrinivasan et al. 2012). The docking of quercetin with CB1 receptor showed a binding energy of −6.56 Kcal/mol with four hydrogen bonds in comparison to the known drug Rimonabant. The blocking of CB1 receptor could reduce body weight and improve cardiometabolic abnormalities in experimental and human obesity.

Hypoglycaemic Activity

The alcoholic, petroleum-water extracts of dried whole plants and the isolated quaternary alkaloids were found to lower blood glucose level in diabetic rats, beginning 2 hours following oral administration and peaking after 6 hours (Dechatiwong et al. 1988). The ethanolic *M. indica* leaf extract significantly decreases blood glucose level in alloxan-induced diabetic rats (Sutar et al. 2009). Another study found that significant reduction in fasting blood glucose (FBG) levels of the normoglycaemic mice was observed at 4 and 3 hours with plant extracts of *Mimosa pudica* (200 mg/kg bw) and *Rauwolfia serpentina* (100 mg/kg bw) (Manosroi et al. 2011). In alloxan-induced diabetic mice, all extracts showed significant hypoglycaemic activity.

'Ilogen-Excel', an Ayurvedic herbal formulation composed of eight medicinal plants (*Curcuma longa, Strychnos potatorum, Salacia oblonga, Tinospora cordifolia, Vetiveria zizanioides, Coscinium fenestratum, Andrographis paniculata* and *Mimosa pudica*) exhibited antihyperglycaemic effect in streptozotocin-induced diabetic rats (Umamaheswari and Mainzen Prince 2007). It significantly lowered levels of blood glucose glycosylated haemoglobin, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and vitamin E in diabetic rats and significantly increased levels of plasma insulin, hepatic glycogen and total haemoglobin.

Hyperglycaemic Activity

Ethanolic extract of *Mimosa pudica* leaves given by oral route to mice at a dose of 250 mg/kg

exerted a significant hyperglycaemic effect (Amalraj and Ignacimuthu 2002).

Antinociceptive Activity

In the acetic acid-induced writhing animal model, the aqueous extract of *Mimosa pudica* at a dose of 200 and 400 mg/kg body weight showed significant inhibition of writhing response of 46.24 and 56.0 %, respectively. In the hot plate test, the extract produced a significant increase in the latency in a dose-related manner. This study confirmed the analgesic properties of *Mimosa pudica*.

Antispasmodic Activity

The total alkaloidal extract of *M. pudica* roots antagonized the contractions of the isolated guinea pig ileum induced by histamine hydrochloride and acetylcholine (Quashem et al. 1977).

Anxiolytic and Antipyretic Activities

In stress-induced hyperthermia test, *M. pudic*a at the dose of 180 mg/kg exhibited antipyretic activity; it significantly prevented the increase of temperature in mice (Bum et al. 2011). In the elevated plus maze test, *M. pudica* also reduced the percentage of mice entries and time in closed arms, indicating its anxiolytic-like property. Acute treatment with *M. pudica* extract had an anxiolytic effect on mouse behaviour in the elevated T maze, specifically on inhibitory avoidance behaviour (Mbomo et al. 2012). The extract alone had no effect on the activity of DRN 5-HT neurons. However, when co-applied with the GABA(A) receptor agonist THIP (4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol), the extract enhanced the inhibitory effect of the THIP on DRN 5-HT neurons. The study suggested that the aqueous extract of *M. pudica* contained a positive modulator of GABA(A) receptor function.

Treatment for Uterine Prolapse

Shivanandaiah and Indudhar (2010) found *Mimosa pudica* to be useful in cases of uterine prolapse with bleeding, based on their experience of working with the condition for more than 45 years and treating hundreds of such cases of uterine prolapse. Hysterectomy had been avoided thus far.

Hair Growth Inhibition Activity

Mimosine was found to be responsible for hair loss in animals following ingestion of seeds and foliage of *Leucaena glauca* and in women after consumption *of Leucaena glauca* seeds (Crounse et al. 1962). The toxic principle contained in the plant was found to be a water-soluble amino acid termed leucenol, which was identical with mimosine obtained from *Mimosa pudica*. Mimosine appeared to be the preferred name for the compound, both by historical precedent, and to avoid confusion with leucinol, an alcoholic derivative of leucine.

Antifertility Activity

Mimosa pudica leaf extract exhibited antioestrogenic activity and anti-implantation effect in female albino rats (Devi et al. 2001). *Mimosa pudica* root powder (150 mg/kg bw), when administered intragastrically, altered the oestrous cycle pattern in female *Rattus norvegicus*. Nucleated and cornified cells were absent in all rats (Valsala and Karpagaganapathy 2002). There was a significant reduction in the number of normal ova in rats treated with the root powder compared with the control rats and a significant increase in the number of degenerated ova. Studies found that *M. pudica* root powder did not possess oestrogenic activity, as it did not cause an increase in uterine weight of immature female rats (Valsala and Karpagaganapathy 2002). It showed antioestrogenic activity by blocking the increase in uterine weight caused by administration of estradiol monobenzoate.

M. pudica root extract exhibited antifertility effect (Ganguly et al. 2007). It prolonged the estrous cycle and disturbed the secretion of gonadotropin hormones in albino mice. The decrease in follicle-stimulating hormone level in the proestrus and estrus stages in the extract-administered group compared with those of control animals indicated the disturbance of estrous cycle and ovulation through suppression of follicle-stimulating hormone.

Anthelmintic Activity

The methanol leaf extract of *M. pudica* was found to inactivate 50 % the roundworm *Strongyloides stercoralis* filariform larvae (causal agent of strongyloidiasis) in-vitro within an hour (Robinson et al. 1990). Studies indicated that the crude alcoholic extract and aqueous extracts of *M. pudica* significantly demonstrated paralysis and also caused death of test worms (*Pheretima posthuma*) in dose-dependent manner as compared to standard reference albendazole (Bendgude et al. 2012), while petroleum ether extracts showed weak anthelmintic effect.

Enzyme Inhibitory Activity

One of the phenyl ethylamine derivatives isolated from the plant exhibited amylase and urease inhibitory activity in-vitro (Muthumani et al. 2012).

Absence of Antiurolithiatic Activity

Studies in albino rats showed that *M. pudica* was not effective in either preventing stone deposition or dissolving preformed stones (Joymma et al. 1990).

Tablet Formulation Studies

Studies by Singh et al. (2009) found that *Mimosa* seed mucilage can be used as matrix-forming agent for sustained drug delivery in tablet formulations. Studies by Ahuja et al. (2010) found that *Mimosa pudica* seed mucilage had potential as bucoadhesive polymer in the formulation of buccal discs. *Mimosa pudica* seed mucilage was found to be a potential tablet disintegrant and binder (Ahuja et al. 2013). The disintegration time of mucilage containing tablets was found to be in the order of 3 % > 1 % > 5 % > 7.5 % > 10 %. On comparative evaluation with standard disintegrants, it was observed that the order of disintegration of tablets was Ac-Di-Sol < mucilage (3 %, w/w) < corn starch. *Mimosa* mucilage at 10 % (w/w) concentration provided tablets with adequate hardness and friability.

Chromoblastomycosis Source

Robinson et al. (1990) reported a case of chromoblastomycosis in a patient. Clinical diagnosis of chromoblastomycosis was established by direct microscopic examination and cultures from the patient's lesion. The causal fungus, *Fonsecaea pedrosoi,* was isolated from the patient and from the thorns of *Mimosa pudica* plant. The data indicated that *M. pudica* could be a natural source of infection for the fungus *F. pedrosoi.*

Traditional Medicinal Uses

Mimosa pudica has been used traditionally for the treatment of insomnia, diarrhoea and inflammatory diseases (Yang et al. 2011). According to the Herbal Medicine Research Center, Malaysia (2002), the plant has been used to treat bronchitis, herpes, hernia, dysentery, menstrual problems, asthma and swellings and to purify blood. A decoction of the roots is believed to be useful for treating urinary infections. The roots mixed with other plant ingredients to make a tonic are taken for good health and vitality. In Malaysia, bits of the plant are placed under the sleeping mats of fretful child, which is believed to induce sleep, and twigs are sold for this purpose in Java (Burkill 1966). The Malays would bathe a fretful child in a plant decoction to cure insomnia and

apply pounded leaves as poultice for swellings. *Mimosa pudica* var. *hispida* has been traditionally used for the treatment of diabetes mellitus and other diseases for several generations by the Thai-Lanna people in the Northern part of Thailand (Manosroi et al. 2011); the plant is also used for insomnia in Thailand (Rachman 1999).

In Fiji, the plant is used to treat fever, syphilis, venereal disease, leprosy, insomnia, insect bites, nervousness and haemorrhoids and as a vermifuge (WHO 1998); the leaves are mixed with other plants and are used to treat urinary infections and haemorrhoids. In the Philippines, the leaves are soaked in coconut oil and placed on wounds and ulcers; the plant decoction is considered antiasthmatic, and the roots are used to treat dysentery and dysmenorrhoea and also used as a diuretic (de Padua et al. 1977). In Vietnam, the leaves are considered to be sedative, hynoptic in folkloric medicine and beneficial for people suffering from insomnia; a leaf infusion is used to treat febrile stiffness, and the roots are used to treat arthritis (Nguyen 1993). The seeds are used as emetic in Indo-China. In New Britain, Papua New Guinea, the roots and leaves have been used to treat swollen testicles, and in South America, the roots have been used to treat diarrhoea and dysentery and used as an emetic (Rachman 1999). Stuart (2012) reported that in Mexico and China, the plant is used for treatment of anxiety and depression, and the roots are used as vomitive in the Antilles, Guiana and La Reunion. *Mimosa pudica* has been reported to be used for childbirth and infertility in folkloric medicine in Trinidad and Tobago (Lans 2007).

In La Reunion, its stem, leaves and roots are mentioned as a calming remedy against sleepiness, spasms and convulsions of children (Lavergne and Vera (1989). *Mimosa pudica* is used in traditional medicine in Cameroon to treat insomnia, epilepsy, anxiety and agitation (Bum et al. 2011). In the Republic of the Congo (Congo-Brazzaville), the entire plant is pounded and rubbed onto people suffering pains in their body sides and kidneys (Burkill 1995). In Senegal, the leaves are employed for lumbago and nephritis. All parts of the plant have been utilized to treat glandular tumours and uterine cancer.

The herb has been used traditionally for ages in India in the treatment of urogenital disorders, piles, dysentery and sinus and also applied on wounds (Ahmad et al. 2012). The leaves are used for increasing the sexual potency in men in Kurukshetra District (Haryana), India; the leaves and roots are used for gravel and other kidney diseases, also for piles and fistula in the Sagar District, Madhya Pradesh, India, and the roots are used in an oral snakebite remedy (Ahmad et al. 2012). Remote communities in India use the plant for inflammation, diabetes, fever, pile and various diseases (Goli et al. 2011). The plant is useful in vitiated conditions of 'pitta', leucoderma, vaginopathy, metropathy, ulcers, dysentery, inflammations, burning sensation, haemorrhoids, jaundice, asthma, fistula, small pox, strangury, spasmodic, affections and fever. The leaves are bitter, sudorific and tonic and are useful in hydrocele, haemorrhoids, fistula, scrofula, conjunctivitis, cuts and wounds and haemorrhage. The whole plant is used internally for vesicle calculi and externally for oedema, myalgia rheumatism and tumours of the uterus (Sharma et al. 2001). The plant is also used in the treatment of sore gum and is used as a blood purifier (Ghani 2003). In Ayurvedic and Unani system of medicine, this plant has been used in diseases arising from corrupted blood and bile, bilious fever, piles, jaundice, leprosy, ulcers and small pox. *Mimosa pudica* is one of the folk medicinal plants commonly used as antifertility agent in some places in India (Ganguly et al. 2007). The roots of *M. pudica* have been used in folkloric medicine for temporary birth control in Assam (Tiwari et al. 1982). The Irula tribe of the Chittoor district of Andhra Pradesh uses the leaves for diabetes and filariasis and the roots for whooping cough (Vedavathy et al. 1997).

In Orissa (Kandhamal District) the warmed root paste is plastered with the help of a cloth on boils to get relief (Behera et al. 2006). The paste of root fried in castor oil is applied on deep cut wounds to stop bleeding and for healing. The paste of root fried in ghee is applied on caries teeth for relief from toothache. The warmed leaf paste is applied around furuncle, abscess and boils to the burst and release of pus and applied

on the burst boils and itches for quick healing. The leaf paste is applied on forehead to get relief from headache and migraine. The leaf paste with honey is prescribed twice a day in empty stomach for 3–4 days for stomachache and intestinal worms.

Other Uses

Young stems with soft prickles and leaves are useful as forage. It is also used as green manure and cover crop as in Thailand where it is used as ground cover on road verges. The plant contains tannin which can be used for the production of leather. In some countries, this plant is grown as an indoor ornamental annual or curiosity plant.

The plant has nematicidal activity. *M. pudica* seeds showed nematicidal activity against the second stage juvenile larvae of *Meloidogyne incognita* (Vijayalakshmi et al. 1979). The root extract at a dose of 300 ppm completely inhibited egg hatch *of M. incognita* and also significantly affected the infectivity and development of the larvae (Le and Davide 1979).

Comments

The plant has become an invasive species in many countries around the world in Asia, North and South America, Africa, Australia and the Pacific Islands. In Australia, the species has been declared a weed in the Northern Territory and Western Australia and a controlled weed in Queensland. The plant can also be a pest in tropical pastures where high plant populations and the sharp prickles restrict grazing.

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Pterocarpus indicus

Scientific Name

***Pterocarpus indicus* Willd.**

Synonyms

Lingoum echinatum (Pers.) Kuntze, *Lingoum indicum* (Willd.) Kuntze, *Lingoum rubrum* Rumph., *Lingoum saxatile* Rumph., *Lingoum wallichii* Pierre, *Pterocarpus blancoi* Merr., *Pterocarpus carolinensis* Kaneh., *Pterocarpus casteelsi* var. *ealaensis* Hauman, *Pterocarpus draco* sensu auct. Misapplied, *Pterocarpus indica* Willd., [spelling variant] *Pterocarpus klemmei* Merr., *Pterocarpus obtusatus* Miq., *Pterocarpus pallidus* Blanco, *Pterocarpus papuanus* F. Muell., *Pterocarpus pubescens* Merr., *Pterocarpus santalinus* Blanco, *Pterocarpus vidalianus* Rolfe, *Pterocarpus wallichii* Wight & Arn., *Pterocarpus zollingeri* Miq.

Family

Fabaceae

Common/English Names

Amboyna Wood, Andaman Redwood, Angsana, Beeswing Narra, Blanco's Narra, Burmese Rosewood, Malay Paduak, Narra, New Guinea Rosewood, Pashu Padauk, Philippine Mahogany, Prickly Narra, Red Sandalwood, Redwood, Tenasserim Mahogany

Vernacular Names

Chinese: Zi Tan
Fijian: Padouk
French: Amboine, Santal Rouge Amboine
India: Bethonne, Hanemara (Kannada), Pitsala (Sanskrit), Narra, Vengai, Vangai Maram (Tamil), Peddagi, Yerravegisa (Telugu)
Indonesia: Angsana, Angsena, Chendan Merah, Lingod, Sena, Sonokembang
Japanese: Yaeyama-Shitan
Kampuchea: Tnug
Laos: Chan Deng;
Malaysia: Angsana, Paduak, Pokok Sena, Sena
Myanmar: Ansanah, Pashu-Paduak
Palauan: Las
Papau New Guinea: New Guinea Rosewood
Philippines: Kamarag, Tagga, Tagka (Ibanag), Sagat (Iloko), Vitali (Lanao), Balauning (Mangyan), Sagat (Negrito), Daitanag, Naga (Pampangan), Odiau (Pangasingan), Bital (Sulu), Agaña, Asana, Nara, Narra (Tagalog)
Samoa: Pinati
Solomon Islands: Liki (Kwara'Ae, To'Oabaita), Ligi (Ngini, Kwaio, Bugotu) Nyia Neli (Ayiwo), Na (Vaiakau), Noi'Eni (Graciosa Bay), Ringi (Roviana), Rigi (Morovo), Dandara (Kusage), Nakumu (Varisi), Grigi (Maringa), Riki (Santa Ana)
Swedish: Amboinaträd

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Thailand: Praduu Baan, Pradoo, Duu Baan
Vanuatu: Bluwota (Bislama) Neniera (Torres Island), Nar, Narara (Banks Group), Nanara (Maewo), Navilae, Navulae, Nula, Philae, Philai, Vulae (Santo), Vuvilae (Malo), Nakambis, Nusmar Weiwuli (Malekula), Burmeia, Purmeia (Epi), Vohovati (Erromango), Nakautufe, Kautufa (Tanna), Kautora (Aniwa), Kautofa, Nakautefa (Aneityum)
Vietnam: Giáng Hương ấn; Giáng Hương Mắt Chim; Gióc; Huỳnh Bá Rừng
Yapese: Arau

Origin/Distribution

Pterocarpus indicus is native to Southeast Asia, northern Australasia and the western Pacific Ocean islands. According to Rojo (1972) its western limit is southern Myanmar, extending eastward to peninsular Thailand, Malaysia, Laos, Kampuchea to Vietnam and Taiwan, farther eastward reaching the Solomons in the Pacific via Sumatra, West Java, Borneo, Philippines, Sunda Islands, the Moluccas, New Guinea and the Pacific (Ryukyu, Carolines and Vanuatu).

Agroecology

A widespread tree found in lowland evergreen primary and some secondary forest from near sea level to 1,300 m elevation, mainly along tidal creeks and rocky shores (Corner 1988; Rojo and Alonzo 1994; Thomson 2006). It thrives in areas with mean annual temperatures of 22–32 °C and mean annual precipitation of 1,300–4,000 mm. It tolerates low temperatures down to 5–8 °C but is frost sensitive, and it is drought resistant. It grows best in full sun but will tolerate light shade (25 %). Angsana is adaptable to a wide range of soil types including infertile, alkaline, stony soils to deep, fertile, loamy, alluvial soils. It is most commonly found growing in well-drained, sandy to clay loams of slightly acid to slightly alkaline pH from pH of 4.0–7.5. According to Thomson (2006) narra is expected to be damaged (including some leaf scald and drop) by salt-laden winds and is not recommended for planting in the most exposed seaside locations. However, it often occurs near to the sea and presumably has a moderate level of tolerance of foliar salt spray.

Edible Plant Parts and Uses

Both fragrant flowers and young leaves are eaten in Thailand (Burkill 1966).

Botany

A large, tall deciduous tree, 15–30 m high with high buttresses, greyish bark and a trunk diameter up to 2 m. Stipules caducous, linear and pubescent. Leaves imparipinnate, 12–22 cm long, with 5–11 leaflets, rachis and petiolule glabrescent (Plate 1). Leaflet ovate-elliptic, 4–5 by 6–10 cm, chartaceous to subcoriaceous; surfaces concolorous and glabrous, lateral veins 6–8 pairs, margin entire, base rounded, obtuse to acute, apex acuminate. Inflorescence laxly branched panicle (Plates 1 and 2), 10–18 cm long mostly axillary rarely terminal. Flowers few to numerous. Bracteoles 2, linear-oblong, at base of calyx. Calyx campanulate, 5–6 mm long, deltoid lobes hairy inside towards the top. Corolla yellow, petals long clawed; standard ovate-orbicular to oblong, 16–18 mm; wings oblong, as long as standard; keel narrowly oblong, smaller than wings. Stamens 10, diadelphous (9 + 1). Ovary shortly

Plate 1 Flowers and imparipinnate leaves

Plate 2 Laxly branched panicle with yellow flowers

stipitate, oblong, 7–8 mm, densely pubescent with two ovules. Style curved with minute stigma. Fruit orbicular or semiorbicular legume, brown to blackish, densely hairy, 4–6.6 cm across, shortly stalked and broadly winged around margin, wing to 2 cm wide. Seeds reniform, narrow and oblique 2–5 by 8–10 mm, smooth and brownish.

Nutritive/Medicinal Properties

Leaf Phytochemicals

A mixture of terpenoids, loliolide (>85 %) and paniculatadiol (<15 %) was obtained from the ethyl acetate leaf extract of *Pterocarpus indicus* (Ragasa et al. 2005).

Wood/Bark Phytochemicals

Pterocarpin and homopterocarpin were isolated from the red dye found in the hardwood of *P. indicus* and *P. santalinus* (Ryan and Fitzgerald 1912/1913). The following isoflavonoids were isolated from the heart wood: formononetin, isoliquiritigenin, (−)-*p*-hydroxyhydratropic acid, 2-arylbenzofuran, angolensin and pterocarpin (Cooke and Rae 1964). Pterocarpol and β-eudesmol were isolated from the heartwood (Parthasarathy and Seshadri 1965). Hager's Handbook (List and Horhammer 1969–1979) reported the presence of pterocarpin and pterostilben homopterocarpin, prunetin (prunusetin), formononetin, isoliquiritigenin, *p*-hydroxyhydratropic acid, pterofuran, pterocarpol and β-eudesmol in the wood.

The bark had been reported to contain kino which exude out as sap when an incision is made on the bark (Burkill 1966). Its chief constituent is kinotannic (coccotannic) acid (Kress 1995–2013). The red sap exuding from incision of the bark afforded a kind of red crystal which was found to be a macromolecular compound of tannic condensation and glucoside (Wang et al. 1997). The wood also contains the red-colouring matters, narrin and santalin, and angolensin (Duke 1983). Narrin is a dark red amorphous powder which yields phloroglucinol and resorcinol on fusion with alkali. A nondialyzable polyphenolic substance, PI, molecular weight 20,400, with antiplasmin activity, was isolated from *Pterocarpus indicus* bark (Takeuchi et al. 1986a). An antifungal compound, β-eudesmol, a sesquiterpene alcohol, was isolated from the *n*-hexane solubles in methanolic extracts of amboyna wood by bioassay-guided fractionation using *Pleurotus pulmonarius*, a wood-rotting fungus (Kusuma et al. 2004). Fluorescence from the aqueous extract of the tropical hardwood *Pterocarpus indicus*, erstwhile known as *Lignum nephriticum*, was demonstrated (Muyskens and Vitz 2006).

Anticancer Activity

Studies showed that injection of an aqueous extract of *P. indicus* leaves significantly inhibited the growth of Ehrlich ascites carcinoma cells in mice (Endo and Miyazaki 1972). Of the extract treated group, 40/50 survived more than 84 days, whereas all mice in the control died within 21 days. The nuclei and cytoplasm of tumour cells became soft and larger and then disintegrated. The active principle was found to be an acidic polypepticide, consisting of 17 amino acids. The LD_{50} in mice was 122 mg/kg i.p.

A polyphenolic substance, PI, from *P. indicus* bark, inhibited plasmin esterolytic activity at $ED_{50} = 2.5$ μg/mL and also showed carcinostatica effect on mice bearing ascites Ehrlich carcinoma

at a dose of 2 mg/kg (Takeuchi et al. 1986a). Further, examination of PI effects on alteration of native and TPA (12-*O*-tetradecanoyl-phorbol-13-acetate)-induced in-vitro phenotypes revealed that PI suppressed both the plasmin and ODC (ornithine decarboxylase) activities of the cells that increased with spontaneous malignancy, and also the TPA-induced ODC activity increase (Takeuchi et al. 1986b). TPA-induced decrease of ^{125}I-mEGF (epidermal growth factor)-binding ability was reversed by PI, to larger extent in the HeLa cells than in the untransformed RME-5-3-1 cells.

Antimicrobial Activity

The petrol, dichloromethane, ethyl acetate, butanol and methanol fractions of *P. indicus* leaf, root and stem bark exhibited a wide spectrum of antibacterial activity (Khan and Omoloso 2003). The activity was more pronounced in the butanol and methanol fractions. None were active against moulds. β-Eudesmol, isolated from wood, inhibited growth of *Pleurotus pulmonarius*, a wood-rotting fungus in-vitro, in a concentration-dependent manner (Kusuma et al. 2004).

A mixture of terpenoids, loliolide and paniculatadiol from the leaves exhibited in-vitro antimicrobial activity against *Candida albicans* and low activity against *Pseudomonas aeruginosa*, *Escherichia coli* and *Aspergillus niger* but was inactive against *Staphylococcus aureus*, *Bacillus subtilis* and *Trichophyton mentagrophytes* (Ragasa et al. 2005).

Wood contains the red-colouring matters, narrin and santalin, and angolensin (Duke. Narrin is a dark red amorphous powder which yields phloroglucinol and resorcinol on fusion with alkali. Hager's Handbook (List and Horhammer 1969–1979) reported the presence of pterocarpin and pterostilben homopterocarpin, prunetin (prunusetin), formononetin, isoliquiritigenin, *p*-hydroxyhydratropic acid, pterofuran, pterocarpol and β-eudesmol in the wood. Distilled wood gives a moderately heavy tar. Cups made from the wood and chips of wood impart to water a beautiful blue and yellow colour, which changes in light and shadow (Little and Wadsworth 1964) fluorescent, and this odd response to light may have been associated with remedies.

Traditional Medicinal Uses

Kino is a well-known Malay medicine; it is used commonly for treating sores especially oral sores (Burkill 1966). In Java, Kino or a bark decoction is employed for thrush and to arrest diarrhoea. The young leaves are applied to ripening boils, ulcers and prickly heat. A leaf infusion is used as hair wash. Juice from the roots is used for syphilitic sores. Angsana wood is used as a folk remedy for stomach pains, sprue, palpitations of the heart, rheumatism, leucorrhoea, gravel and yaws. Burkill also reported that in Kampuchea, the wood is used for fevers and is considered as diuretic and antidysenteric. The red sap from its incision of the bark becomes a kind of red crystal after some hours of exposure to air, which is used as an astringent and against other diseases (Wang et al. 1997). According to Hartwell (1967–1971), the red latex is used in folk remedies for tumours, the plant for cancers, especially of the mouth. In the Carolyn Islands, finely powdered leaves are applied to a ruptured vagina.

Other Uses

P. indicus is widely planted as an avenue/roadside tree and as shade trees in car parks, gardens and parks in Southeast Asia. The flowers are a honey source. The reddish hard wood is an excellent timber and is listed among the most valuable timbers in the Philippines. The beautiful, termite-resistant, rose-scented reddish timber is marketed as Amboyna, Blanco's Narra, Burmese Rosewood, Malay Padauk, Narra, Philippine Mahogany, Prickly Narra and Tenasserim Mahogany. It is used for cabinetry, cart wheels, carvings, construction, floorings and musical instruments, and when finely sliced,

it produces an extremely decorative veneer, used for decoration and furniture. The tree also provides kino, a reddish dye narrin, resin and gum used for tanning. The *n*-hexane extract from *P. indicus* heartwood exhibited active inhibition on the activities of the subterranean termite, *Coptotermes curvignathus* with MIC of 2 % (Brata et al. 1999).

Comments

P. indicus is the national tree of the Philippines as well as the provincial tree of Chonburi and Phuket in Thailand. It is very easily propagated from seed or large stem cuttings.

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Senna alata

Scientific Name

***Senna alata* (L.) Roxb.**

Synonyms

Cassia alata L. basionym, *Cassia alata* var. *perennis* Pamp., *Cassia alata* var. *rumphiana* DC., *Cassia bracteata* L. f., *Cassia herpetica* Jacq. (nom. illeg.), *Cassia rumphiana* (DC.) Bojer, *Herpetica alata* Cook & Collins, *Herpetica alata* (L.) Raf.

Family

Fabaceae also placed in Caesalpiniaceae

Common/English Names

Candelabra Bush, Candelabra Plant, Candle Bush, Candlestick Senna, Empress-Candle-plant, Emperor's Candlesticks, Christmas-Candle, Emperor's Candle Plant, Emperor's Candlesticks, Golden-Candle Senna, Golden Candelabra Tree, King-of-the-Forest, Ringworm Bush, Ringworm Plant, Ringworm Senna, Ringworm Bush, Ringworm Shrub, Roman Candle Tree, Seven Golden Candles, Seven-Golden-Candlesticks, Stick Senna, Winged Senna, Yellowtop

Vernacular Names

Antilles: Taratana
Argentina: Taperibá Guazú
Bangladesh: Dadmardan, Dadmari
Brazil: Café-Beirão, Fedegoso-Gigante, Fedegoso-Grande, Mangerioba-Do-Pará, Mangerioba-Grande, Mata-Pasto (Portuguese)
Brunei: Raun Suluk (Dusun), Paaul-Ul, Tarump (Malay)
Burmese: Pway-Mezali, Pwé: Hsé:Mè:Za.Li, Thinbaw-Mezali
Chamorro: Acapulco, Akapuku, Andadose, Candalaria, Take-Biha
Chinese: Chi Jia Jue Ming, Yi Bing Jue Ming
Chuukese: Arakak, Arekak, Yarakaak
Creole: Kas Ailé, Zèb À Dartres
Czech: Kasie Křídlatá
Fijian: Mbai Ni Thangi
French: Bois Dartre, Catépen, Dartrier, Epis D'or, Quatre Épingle; Dartrier, Casse Ailée, Plante Des Cros-Cros, Buisson De La Gale, Quatre Épingles
Cuba: Guacamayón, Palo Santo
German: Kerzenstrauch
India: Kharpat (Assamese), Dadmari, Dadmardan (Bengali), Dadmari, Dadmurdan, Dat-Ka-Pat, Datkapat, Vilayati-Agati, Deo-Mardon (Hindi), Doddasagate, Sheemigida, Shime-Agase, Simyagase, Dhavala Gida, Dodda Thagache, Seeme Agase, Seeme Thangadi, Dodda Thangadi, Daddumardu, Dahvala, Doddacagate, Doddachagate, Puritappu, Simeagase,

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Simeyagase, Dhawala Gida, Dodda Chagache (Kannada), Elakajam, Shima-Akatti, Simayakatti, Shimayakatti, Simaagati (Malayalam), Daopata (Manipuri), Dadamardana (Marathi), Tuihlo (Mizoram), Jadumari (Oriya), Dadrughna, Dvipagasti (Sanskrit), Anjali, Shimai-Agatti, Vandukolli, Simaiyagatti, Vandugolli, Peyakatti, Vantukkolli, Vandu-Rolli, Alata, Malai Tagarai, Seemai Agathi, Vandu Kolli, Pei Agathi, Seemai Agathy, Seemaiagatti, Semmai Agatti, Sheemai-Agatti, Vendukolli, Vendu-Kolli, Vandu Kollu, Seemie Aghatee, Calavakatti, Calavakatticceti, Cimaiakatti, Cimaiyakatti, Cimaiyavutti, Cintuki, Cintukiyakatti, Cirikai, Kacampakatti, Karccakkinam2, Pairavam, Pairavamaram, Ponnakatti, Puliyacikacceti, Puliyacikam, Pulukkolli 2, Tatturukkinam, Tiruttakatti-maram, Tiruttavutti, Vantukatiyilai, Vantunelli 2 (Tamil), Mettatamara, Sheemaavisi, Shima-Avishi-Chettu, Sima Avisl, Simayavisa, Mitta Tamara, Seemaavasie, Seemaavise, Simaavishi, Simaavisi, Simayavise, Mettataamara, Seema Avise, Seemayavisa (Telugu)

Indonesia: Ketepeng, Daun Kupang (Malay, Manado), Ketepeng, Ketepeng Kebo, Ketepeng China (Java), Ketepeng Badak, Ketepeng Manila (Sundanese)

Japanese: Kasshia Arata, Kyandorubusshu

Kapingamarangi: Rakau Honuki, Tirakahonuki, Tuhkehn Kilin Wai

Khmer: Dang Het

Kwara'Ae: Bakua

Laotian: Khi Let Ban

Malaysia: Gelenggang, Gelenggang Besar, Ludangan, Daun Kurap (Peninsular), Daun Sulok, Gelingok, Rugan, Serugan (Iban—Sarawak), Daun Ingram, Tarum (Melanau—Sarawak), Solok (Malay—Sarawak)

Mexico: Flor Del Secreto

Nicaragua: Soroncontil

Niuean: Mulamula

Palauan: Kerula Besokel, Yult

Papua New Guinea: Kabaiuara (Harigen, Sepik), Levoanna (Gaire and Tubusereia, Central Province), Orere (Awala, Northern Province)

Philippines: Buni-Buni (Bagobo), Kasitas (Bikol), Kasitas, Palo-China (Bisaya), Sunting (Cebu Bisaya), Ancharasi (Igorot), Andadasi, Andadasi-A-Dadakell, Andadasi-Ng-Bugbugtong (Iloko), Pakayomkom-Kastila (Pampangan), Kapis (Subanum), Akapulko, Andalan (Sulu), Akapulko, Bayabasin, Bikas-Bikas, Gamotsa-Buni, Kapurko, Katanda, Pakagonkon, Sonting (Tagalog), Adadisi (Tinggian)

Pohnpeian: Truk-En-Kili-N-Wai

Portuguese: Alcapulco, Dartial, Cortalinde, Café Beirão, Fedegoso, Fedegosão, Fedegoso-Gigante, Mangerioba-Do-Pará, Mangerioba-Grande, Mata-Pasto-Grande

Samoan: Fa'I Lafa, Fa'I Lafa, La'Au Fa'I Lafa, La'Au Fa'I Lafa

Spanish: Bajagua, Flor Del Secreto, Guacamaya Francesa, Guajavo, Hierba De Playa, Majaguilla, Majaguillo, Mocuteno, Mocoté, Soroncontil

Sri Lanka: Eth Thora (Sinhala)

Swahili: Upupu Wa Mwitu

Tanzania: Muambangoma

Thai: Khi-Kak (Northern), Chumhet-Yai, Chum Het Thet (Central), Chum Het Tet (Peninsular)

Tongan: Fa'I Lafa, La'Au Fa'I Lafa, Te'Elango

Venezuela: Mocote

Vietnamese: Muồng Trâu

Yapese: Flay-N-Sabouw

Origin/Distribution

Senna alata is indigenous to tropical South America (French Guiana, Guyana, Surinam, Venezuela, Brazil and Colombia). It has been distributed globally and has naturalized in Central America, southeastern United States (Florida), tropical Africa, tropical Asia, the Caribbean and on several Pacific Islands (the Cook Islands, Fiji, Guam, Palau, Tonga, Western Samoa and Hawaii), Papua New Guinea and throughout northern and eastern Australia.

Agroecology

S. alata is found in diverse habitats: alongside waterways, rivers and drainage channels, margins tof ponds and ditches, in open forest, coastal

plains, floodplains, wetlands, native bushland, disturbed sites, waste areas, roadsides, overgrazed pastures, orchards and around villages. However, it prefers open areas and sunny locations at low to medium altitude but can also be found up to 1,400 m altitude. It often forms thickets and is aggressive in areas where there is a high water table. It is reported to tolerate an annual rainfall of 600–4,300 mm and average annual temperatures of 15–30 °C and is frost sensitive. It grows on both heavy and sandy, acid to slightly alkaline, well-drained soils but thrives best in deep, well-drained soil rich in organic matter with a pH range of 5.5–6.5.

Edible Plant Parts and Uses

Flowers or leaves are edible after cooking and may be used as a laxative (Burkill 1966). The inflorescence are boiled with chilli and consumed for constipation (Monkheang et al. 2011). In Myanmar, fresh leaves and flowers are used as vegetables and in curries (Myanmar Department of Traditional Medicine 2008). In Sabah and Peninsular Malaysia, the young shoots are cooked and eaten as vegetable. Toasted leaves along with *Glycine* beans are sometimes made into a drink similar to coffee (Burkill 1966). Young immature pods are eaten in small quantities, raw or steamed in the Philippines (Pardo de Tavara 1901).

Botany

Coarse, erect, branched shrub growing from 1.5 to 4 m tall; leaves to about 50–80 cm long, alternate, pinnate, with 8–14 pairs of large leaflets (the distal ones largest), up to 17 cm long, ovate-oblong, obtuse, truncate or even slightly notched at apex, margin entire, subsessile (Plates 1 and 2). The inflorescence is a long-pedunculate, erect, dense, oblong spike, terminal or axillary, 10–15 cm long, with overlapping and crowded yellow flowers, 4 cm in diameter. Flowers are enclosed within dark-yellow or orangey bracts which shed off during flower opening (Plate 1). Flower bisexual, zygomorphic and pentamerous, with 5 oblong sepals, 5 bright yellow ovate-orbicular petals (20 mm long by 12 wide), 10 stamens, 2 fertile with elongated anthers and 8 with rudimentary anthers; elongated recurved, pubescent ovary with short slender style and stigma. Pod is green, ripening brown to black, straight, papery in texture, winged, up to 15–20 cm long and slightly over 1 cm wide; seeds numerous (to 50), shiny, flat and triangular.

Plate 1 Terminal inflorescences and yellow flowers

Plate 2 Slender upright branches and pinnate leaves

Nutritive/Medicinal Properties

Nutrient and Phytochemicals in the Leaves

Nutrient composition of the edible leaves per 100 g based on analyses carried out in Nigeria was reported as moisture 58.4 g, energy 159 kcal, protein 6.8 g, fat 0.6 g, carbohydrate 31.5 g, fibre

0.1 g, ash 1.8 g, vitamin A 52 μg RE, vitamin A 26 RAE μg, β-carotene 310 μg, thiamine 0.45 mg, riboflavin 0.58 mg, niacin 0.54 mg, folic acid 15 μg, vitamin C 7.74 mg, calcium 755 mg, phosphorus 739 mg, iron 14.8 mg and zinc 3.7 mg (CINE 2007).

Hauptmann and Nazario (1950) isolated rhein (1,8-dihydroxyanthraquinone-3-carboxylic acid) along with hydroxymethyl anthraquinones and chrysophanic acid from the alcoholic leaf extract. Physcione, kaempferol, rhein methyl ester diacetate and β-sitosterol (Rao et al. 1975); 1,3,8-trihydroxy-2-methylanthraquinone (aloe-emodin), chrysophanol, deoxycoelulatin, sennoside A, sennoside B, sennoside C and sennoside D (Mulchandani and Hassrajani 1975; Villaroya and Bernal-Santos 1976); aloe-emodin, rhein glycoside and aloe-emodin glycoside (Rai 1978); anthraquinones and anthracene derivatives of rhein, emodol, aloe-emodin, sennosides A and B, 4,5-dihydroxy-1-hydroxymethylanthrone and 4,5-dihydroxy-2-hydroxymethylanthrone (Fuzellier et al. 1982); aloe-emodin and chrysophanol (Harrison and Garro 1997), isochrysophanol and physcion-L-glucoside (Smith and Sadaquat 1979); rhein (cassic acid) (Palanichamy et al. 1991); and aloe-emodin (1,8-dihydroxy-3-(hydroxymethyl) anthraquinone), sitosterol and stigmasterol (Hofileña et al. 2000), 3,5,7,4′-tetrahydroxy flavone and 2,5,7,4′-tetrahydroxyisoflavone (Rahaman et al. 2006, 2008) were isolated from the leaves. Kaempferol-3-*O*-gentiobioside was the major flavonoid glycoside in *Senna alata* (Moriyama et al. 2003c) The mature leaf was found to contain the highest content of this metabolite. The contents ranged from 2.0 to 5.0 % and 1.0 to 4.0 % in mature and juvenile leaves, respectively. Kaempferol-3-*O*-gentiobioside was not detected in the seed. Earlier, Moriyama et al. (2001) reported the disappearance of kaempferol 3-gentiobioside in the sun-dried leaves, while there was little or no change in the kaempferol 3-gentiobioside concentration in the heat-treated leaves when incubated in an aqueous solution, suggesting a possible presence of enzymatic activities in the sun-dried leaves. They concluded that heat treatment may be a good method to stabilize kaempferol 3-gentiobioside in *Cassia alata* leaves.

Hazni et al. (2008) isolated kaempferol, kaempferol 3-*O*-β-glucopyranoside, kaempferol 3-*O*-gentiobioside and aloe-emodin from the leaves. Cassiaindoline, a dimeric indole alkaloid (Villaseñor and Sanchez 2009) and kaempferol-3-*O*-β-D-glucoside (astragalin) (Saito et al. 2012) were isolated from *Cassia alata* leaves. Four anthraquinones (rhein (cassic acid), aloe-emodin, emodin and chrysophanol) were isolated from *Senna alata* leaves (Panichayupakaranant et al. 2009). Twelve compounds were isolated from *C. alata* leaves and identified as chrysoeriol (1), kaempferol (2), quercetin (3), 5,7,4′-trihydroflavanone (4), kaempferol-3-*O*-β-D-glucopyranoside (5), kaempferol-3-*O*-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (6), 17-hydrotetratriacontane (7), *n*-dotriacontanol (8), *n*-triacontanol (9), palmitic acid ceryl ester (10), stearic acid (11) and palmitic acid (12) (Liu et al. 2009). Six compounds (kaempferol, kaempferol-*O*-diglucoside, kaempferol-*O*-glucoside, quercetin-*O*-glucoside, rhein and danthron) were isolated from the aqueous leaf extract (Saito et al. 2010). Leaves were also found to contain saponins (1.22 %), flavonoids (1.06 %), cardiac glycosides (0.20 %), cardenolides and dienolides (0.18 %), phenolics (0.44 %) and alkaloids (0.52 %) (Yakubu and Musa 2012).

The essential oil obtained by hydrodistillation of leaves of *C. alata* collected in Gabon afforded 44 compounds representing 92.5 % of the oil; the major constituents were linalool (23.0 %), borneol (8.6 %) and pentadecanal (9.3 %) (Agnaniet et al. 2005). The antioxidant activity of the oil was found to be low compared to that of butylated hydroxytoluene (BHT). Fifteen out of twenty-five constituents of *C. alata* leaf essential oil were identified in trace amount (i.e. <0.1 %) (Ogunwande et al. 2010). The oil was dominated by mono- and sesquiterpene compounds (48.7 and 47.9 %, respectively). The essential oil constituents were 1,8-cineole 39.8 %, β-caryophyllene 19.1 %, caryophyllene oxide 12.7 %, germacrene D 5.5 %, α-selinene 5.4 %, bicyclogermacrene 5.4 %, limonene 5.2 %, α-cadinol 4.2 %, α-phellandrene 3.7 %,

(*E*)-2-hexenal 3.3 %, α-bulnesene 1.0 %, tricyclene trace, (*E*)-β-ionone trace, benzaldehyde trace, α-terpinene trace, *n*-pentadecane trace, *p*-cymene trace, δ-cadinene trace, β-elemene trace, *n*-hexadecane trace, humulene epoxide II trace, (*E*)-geranyl acetone trace, tetradecanal trace, α-humulene trace and (*E*)-β-farnesene trace.

Phytochemicals in the Stem

Stems of *Cassia alata* were found to contain 1,5,7-trihydroxy-3-methylanthraquinone (alatinone) and dalbergin, 2,6-dimethoxybenzoquinone, santal, luteolin, β-sitosterol and β-sitosteryl-β-D-glucoside (Hemlata and Kalidhar 1993) and alatonal (Hemlata and Kalidhar 1994).

Phytochemicals in the Flower, Pod and Seed

Two glycosides, chrysoeriol-7-*O*-(2″-*O*-β-D-mannopyranosyl)-β-D-allopyranoside and rhamnetin-3-*O*-(2″-*O*-β-D-mannopyranosyl)-β-D-allopyranoside, were isolated from the *Cassia alata* seeds (Gupta and Singh 1991). Two polyalcohols, glycerol and erythritol, were found in the seeds (Singh 1998). Hydroxyanthracene derivatives were found in the leaves, flowers and pods of *Cassia alata* (Panichayupakaranant and Intaraksa (2003). A water-soluble galactomannan with molecular weight 26,400 was isolated from the seeds (Gupta et al. 1987). The polysaccharide comprised of heptasaccharide units joined by β-(1→4) linkages.

Phytochemicals in the Roots

Two new anthraquinone pigments 1,3,8-trihydroxy-2-methyl anthraquinone (A) and 1,5-dihydroxy-8-methoxy-2-methyl-anthraquinone-3-*O*-β-D-(+)-glucopyranoside (B) and β-sitosterol were isolated from the roots (Tiwari and Yadav 1971). Alquinone, an anthraquinone (Yadav and Kalidhar 1994); stigmasterol; and emodin (1,6,8-trihydroxy-3-methylanthraquinone) (Husain et al. 2005) were isolated from the roots. Chatsiriwej et al. (2006) found that root cultures established from the high-anthraquinone-producing plants accumulated higher amounts of emodin and chrysophanol than those established from the low-anthraquinone-producing plants and leaves and roots of the intact plants.

Six phenolic compounds, five anthraquinones (rhein, aloe-emodin, emodin, chrysophanol and physcion) and a flavonoid (kaempferol) were isolated from *C. alata* roots (Fernand et al. 2008).

Various plant parts of *Senna alata* have multifarious pharmacological activities that include laxative, antimicrobial, antiinflammatory, antimutagenic, analgesic, choleretic, hypoglycaemic and hepatoprotective.

Antioxidant Activity

Methanol extracts of ten selected Nigerian medicinal plants including *C. alata* were found to contain steroids, terpenoids and cardiac glycosides, alkaloids, saponins, tannins and flavonoids (Akinmoladun et al. 2010). The highest amounts of total flavonoids were found in the leaf extracts of *C. alata* (275.16 μg/mL quercetin equivalent). The extract demonstrated significant antioxidant and radical scavenging activities, namely, 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging and hydroxyl radical scavenging activities, high lipid peroxidation inhibitory activity but low nitric oxide radical scavenging activity. The ethyl acetate extract of *S. alata* aerial parts was found to possess antioxidant properties as expressed by increase in antioxidant enzymes and the presence of phenolic compounds flavonoids naringin and apigenin (Okpuzor et al. 2009).

A refined *C. alata* leaf extract exhibited strong DPPH free radical scavenging activity with an IC_{50} value of 2.27 μg/mL and showed no prooxidant activity in yeast, *Saccharomyces cerevisiae* (Saito et al. 2012). Three of its major components were shown to bind to DNA in vitro. One major component, identified as kaempferol-3-*O*-β-D-glucoside (astragalin), showed high affinity to DNA. The astragalin-DNA binding

was found to occur through interaction with G–C base pairs, possibly by intercalation stabilized by H-bond formation.

Laxative Activity

Cassia alata and *Cassia podocarpa* have identical laxative potency and were the most likely candidates for laxative drug development in Nigeria (Elujoba et al. 1989). *Senna alata* leaves were found to have laxative effect and presumed to be due to active ingredient anthraquinones. In a multicentre randomized controlled clinical trial involving 80 adult patients with constipation, 28 patients were given at bedtime 120 mL of fluid with caramel colour, 28 administered mist. alba and 24 given *Cassia alata* infusion (Thamlikitkul et al. 1990). Eighteen per cent of patients in the placebo group passed stools within 24 hours, whereas 86 and 83 % of patients in mist. alba and *Cassia alata* groups, respectively, passed stools. The differences observed between placebo and mist. alba and placebo and *Cassia alata* were statistically highly significant. Minimal self-limited side effects, that is, nausea, dyspepsia, abdominal pain and diarrhoea, were noted in 16–25 % of the patients. Studies found *Cassia alata* fresh leaves showed significant purgative efficacy on volume and frequency in healthy subjects compared to placebo (Than et al. 2002).

In Thailand, *Senna alata* has been approved as a laxative drug in the Thai Herbal Pharmacopoeia 1998 and the Thai National List of Essential Drug 1999 (Panichayupakaranant and Intaraksa 2003). Hydroxyanthracene derivatives were demonstrated as the active constituents in this plant for the laxative property. The efficiency of herbal medicines depended on the plant raw material quality, which was usually related to the content of the active compounds. Recently, poor quality of *S. alata* leaves due to lower content of hydroxyanthracene derivatives relative to the standard value (i.e. not less than 1.0 % w/w of hydroxyanthracene derivatives, calculated as rhein-8-glucoside on a dried basis) had been a major problem in the production of the herbal medicines from *S. alata.* Studies found that the method and temperature of drying markedly affected the hydroxyanthracene derivative content. Drying of the leaves in a hot air oven at 50 °C gave a higher hydroxyanthracene derivative content (1.43 % w/w) than drying in a hot air oven at 80 °C (0.44 % w/w) or drying in the sun (0.95 % w/w). Study on the stability of hydroxyanthracene derivatives in *C. alata* leaf powder, which was kept in tight container at room temperature, found that the hydroxyanthracene derivative content did not decrease within 9 months.

Antimicrobial Activity

In-Vitro Studies Leaf Extracts

Aqueous leaf extract of *C. alata* exhibited significant antifungal activity in-vitro against dermatophytes (Pankajalakshmi et al. 1993). *C. alata* leaf extract exerted no significant in-vitro activity against *Candida albicans, Penicillium* sp., *Aspergillus fumigatus, A. flavus, Mucor* sp. or *Rhizopus* sp., but at a dose of 2.5 % w/v, it completely inhibited the growth of *Trichophyton mentagrophytes, Trichophyton rubrum* and *Microsporum gypseum* (Palanichamy and Nagarajan 1990b). A combination of ethanol extracts of leaves of *Senna alata* and *Ocimum sanctum* exhibited anti-*Cryptococcus* activity. The activity of combination of the extracts was heat stable and worked at acidic pH. A 10-year human study indicated that the leaf extract could be reliably used as an herbal medicine to treat *Pityriasis versicolor,* a yeast fungus that causes skin disease (Damodaran and Venkataraman 1994). The leaf extract had no side effects.

Fuzellier et al. (1982) also found that rhein, emodol and some anthrones in *S. alata* leaves possessed antifungal activity against some fungal dermatophytes and yeast. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for the water extract of *S. alata* against *Escherichia coli* were 1.6 and 60 mg/mL, respectively; corresponding data for chloramphenicol were 2 and 10 μg/mL (Crockett et al. 1992). Similarly, the MIC and minimum fungicidal concentration (MFC) for the extract against *Candida albicans* were 0.39 and 60 mg/mL in

contrast to 0.58 and 0.98 µg/mL for amphotericin B. From the dose–response curve plots, the extract had an IC_{50} of 31 mg/mL for *E. coli* and 28 mg/mL for *C. albicans*. The scientists suggested that *S. alata* extracts contained agent(s) with therapeutic potential and might be useful if isolated and developed for the treatment of opportunistic infections of AIDS patients. Ethanol leaf extract exhibited high in vitro activity against various species of dermatophytic fungi but low activity against non-dermatophytic fungi (Ibrahim and Osman 1995). However, bacterial and yeast species showed resistance. The minimum inhibitory concentration (MIC) values of the extract revealed that *Trichophyton mentagrophytes* var. *interdigitale, Trichophyton mentagrophytes* var. *mentagrophytes, Trichophyton rubrum* and *Microsporum gypseum* had an MIC of 125 mg/mL, whereas *Microsporum canis* had MIC of 62.5 mg/mL. The inhibition observed on the macroconidia of *Microsporum gypseum* was structural degeneration related to cell leakage as observed by irregular, wrinkle shape and loss in rigidity of the macroconidia. Both aqueous and ethanol bark extracts of *Cassia alata* inhibited growth of *Candida albicans* in vitro (Reezal et al. 2002). The inhibitory activity was comparable to miconazole.

Aloe-emodin from *C. alata* leaves was found to be active against *Bacillus subtilis, Pseudomonas aeruginosa, Candida albicans, Trichophyton mentagrophytes* and *Aspergillus niger* with inhibitory activity indices of 1.8, 0.5, 0.5, 0.5 and 0.2, respectively (Hofilena et al. 2000). *Candida albicans* showed concentration-dependent susceptibility towards both the ethanol and water extracts from the barks but was resistant towards the extracts of leaves (Somchit et al. 2003). The growth of *Aspergillus fumigatus* and *Microsporum canis* was not affected by all types of the plant extracts. The antibacterial activity of *S. alata* extracts on *Staphylococcus aureus* was detected with only the leaf extracts using water and ethanol. The water extract exhibited higher antibacterial activity than the ethanol leaf extract.

The chloroform leaf extract was the most active against *Trichophyton mentagrophytes*, at a concentration of 50 mg/mL but it had no activity against *Candida albicans* (Villaseñor et al. 2002). The hexane and ethyl acetate extracts showed some activity against both organisms, with the ethyl acetate extract being more active against *C. albicans*. Crude leaf extract of *Senna alata* showed significant inhibitory effect on *Streptococcus mutans,* a prominent bacterium that causes teeth decay (Limsong et al. 2004). In-vitro study showed that ethanol extract of *Senna alata* at 0.5 % inhibited adherence of *S. mutans* on glass surface significantly. The extract inhibited adherence of *S. mutans* ATCC 25175 and TPF-1 onto hydroxyapatite coated with saliva with IC_{50} 0.5 and 0.4 %, respectively, as well as reduction of activities of glucosyltransferase and glucan-binding lectin by *Streptococcus mutans* strains. The findings showed that *Senna alata* could be a promising herb for toothpaste formulation with anti-teeth decay property. Among the methanol leaf extract of *Cassia alata, Cassia fistula* and *Cassia tora, C. alata* was the most effective leaf extract against *Trichophyton rubrum* and *Microsporum gypseum* with the 50 % inhibition concentration (IC_{50}) of hyphal growth at 0.5 and 0.8 mg/mL, respectively, whereas the extract of *C. fistula* was the most potent against *Penicillium marneffei* with the IC_{50} of 0.9 mg/mL (Phongpaichit et al. 2004). Furthermore, all three *Cassia* leaf extracts also affected *M. gypseum* conidial germination where treated hyphae and macroconidia were shrunken and collapsed, which might be due to cell fluid leakage.

Of three crude leaf extracts, the methanol extract showed the highest activity followed by the ethanol extract and petroleum ether extract (Owoyale et al. 2005). The leaf extract exhibited higher activity against *Mucor* sp., *Rhizopus* sp. and *Aspergillus niger* with MIC of 70 µg/mL and lower activity against *Escherichia coli, Bacillus subtilis, Salmonella typhi, Pseudomonas aeruginosa, Staphylococcus aureus* and *Candida albicans* with MIC of at 860 µg/mL. Both aqueous and methanol leaf extracts of *C. alata* exhibited more antifungal than antibacterial activity (Makinde et al. 2007). The in vitro growth of the following fungi was inhibited (*Microsporum canis, Blastomyces dermatitidis, Trichophyton mentagrophytes, Candida albicans*

and *Aspergillus* flavus), while only two bacteria species were inhibited (*Dermatophilus congolensis* and *Actinomyces bovis*). Both aqueous and ethanol *S. alata* leaf inhibited the growth of *Candida albicans, Microsporum canis* and *Trichophyton mentagrophytes* better than the ketoconazole 200 mg used as a positive control (Timothy et al. 2012b). The minimum inhibitory concentration (MIC) of the water leaf extract for *Candida albicans, Aspergillus niger, Penicillium notatum, Microsporum canis* and *Trichophyton mentagrophytes* were 26.90, 32.40, 29.50, 30.30 and 27.80 mg, respectively, while the MIC of ethanol leaf extract for *Candida albicans, Aspergillus niger, Penicillium notatum, Microsporum canis* and *Trichophyton mentagrophytes* were 5.60, 3.50, 4.90, 12.60 and 9.80 mg, respectively. In another study, Timothy et al. (2012a) found that the aqueous leaf extract showed higher activity on *Escherichia coli* than ethanol leaf extract at 160 mg, whereas ethanol leaf extract had higher activity than aqueous leaf extract on *Salmonella typhi* at the same dose. The MIC for aqueous leaf extract ranged between 3.50 and 25.15 mg, while that of ethanol leaf extract was from 1.41 to 3.55 mg on the organisms tested. The presence of saponins, anthraquinones, cardiac glycosides, flavonoids, reducing sugars and terpenes were detected in both extracts.

The butanol and chloroform leaf extracts of *S. alata* both exhibited inhibition against methicillin-resistant *Staphylococcus aureus* (MRSA) with inhibition indexes of 1.03 and 0.78 at the concentration of 50 mg/mL (Hazni et al. 2008). The butanol leaf extracts afforded kaempferol (1), kaempferol 3-*O*-β-glucopyranoside (2), kaempferol 3-*O*-gentiobioside (3) and aloe-emodin (4) on purification. The four constituents showed varying degrees of inhibition against MRSA. Both 1 and 4 exhibited MIC_{50} values of 13.0 and 12.0 μg/mL, respectively. The kaempferol glycosides 2 and 3 were less active with MIC_{50} values of 83.0 and 560.0 μg/mL, respectively.

The acetone and ethanol (95 %) extract of *Senna alata* showed high antimicrobial activity against nearly all test microorganisms: *Staphylococcus aureus*, *Staphylococcus aureus* coagulase positive, *Bacillus subtilis*, *Bacillus cereus, Bacillus stearothermophilus*, *Escherichia coli*, *Vibrio cholerae*, *Salmonella typhi*, *Shigella dysenteriae* and *Klebsiella pneumoniae* (Sakharkar and Patil 1998) The inhibitory effects of extracts were very close and identical in magnitude and were comparable with that of standard antibiotics used.

Cassia alata aqueous leaf extract exhibited antimicrobial activity against *Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus aureus* and *Bacillus subtilis* (Saito et al. 2010). The extract also inhibited biofilm formation of *S. epidermidis* and *P. aeruginosa*. Six compounds from four bioactive fractions were identified as kaempferol, kaempferol-*O*-diglucoside, kaempferol-*O*-glucoside, quercetin-*O*-glucoside, rhein and danthron. In the *Salmonella*/microsome assay, the leaf extract showed weak mutagenicity (MI <3) only in strain TA98. *Cassia alata* leaf extract was found to have antibacterial activity in vitro against *Staphylococcus aureus* and *Bacillus subtilis* (Alalor et al. 2012).

Both flavonoid compounds 3,5,7,4′-tetrahydroxy flavone and 2,5,7,4′-tetrahydroxy isoflavone (100 μg/disc) from *C. alata* leaves exhibited antifungal activity against most of the fungi, namely, human pathogens (*Trichophyton schoenleinii, Trichophyton longifurus, Pseudallescheria boydii, Candida albicans, Aspergillus niger*), animal pathogens (*Microsporum canis, Trichophyton mentagrophytes*) and plant pathogens (*Fusarium oxysporum* var. *lycopersici, Fusarium solani var. lycopersici, Macrophomina phaseolina, Rhizoctonia solani*) except for the human pathogen *Epidermophyton floccosum* (Rahaman et al. 2008). Compound 2,5,7,4′-tetrahydroxyisoflavone was highly active against *Trichophyton longifurus* and *Pseudallescheria boydii*, while compound 3,5,7,4′-tetrahydroxy flavones were moderately active against *Trichophyton longifurus* and *Pseudallescheria boydii.* Both compounds were moderately active against *Microsporum canis* and *Trichophyton mentagrophytes.* Both compounds were active against the plant pathogen *Fusarium solani var. lycopersici* but showed no activity against the other three plant pathogens.

S. alata leaf extract containing 16.7 % w/w anthraquinone exhibited antifungal activity against

Trichophyton rubrum, T. mentagrophytes and *Microsporum gypseum* with MIC values of 15.6, 62.5 and 250 µg/mL, respectively (Sakunpak et al. 2009). Five extracts of *Senna alata* leaf powder, namely, anthraquinone aglycone extract, anthraquinone glycoside extract, anthraquinone aglycones from glycosidic fraction, crude ethanol extract and anthraquinone aglycone from crude ethanol extract, were tested against clinical strain of dermatophytes: *Trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum* and *Microsporum gypseum* (Wuthiudomlert et al. 2010). The anthraquinone aglycones from glycosidic fraction qualitatively and quantitatively gave the best antifungal activity compared to the other extracts.

In-Vitro Studies Other Plant Part Extracts

The methanol extracts of *C. alata* leaves, flowers, stem and root barks exhibited a broad spectrum of antibacterial activity (Khan et al. 2001). The activity was increased on fractionation (petrol, dichloromethane, ethyl acetate), the dichloromethane fraction of the flower extract being the most effective. No activity was shown against tested fungi.

The crude *S. alata* flower extracts, containing steroids, anthraquinone glycosides, volatile oils and tannins, exhibited a high MIC of 500 µg/mL against *Staphylococcus aureus, Streptococcus faecalis, Micrococcus luteus, Bacillus subtilis* and *Pseudomonas putida* but was generally inactive against *Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens* and *Pseudomonas fluorescens* (MIC >1,000 µg/mL) (Adedayo et al. 2001). However, the partially purified flower extract was bacteriostatic at a low concentration of 100 µg/mL, with a minimum bactericidal concentration of 500 µg/mL, primarily against the Gram-positive organisms. At a concentration slightly above the MIC, the purified extract was nearly as potent as standard antibiotics, even against multiple antibiotic-resistant local isolates that were resistant to methicillin, penicillin and streptomycin. The partially purified extract of *Senna alata* flower exhibited appreciable antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Micrococcus luteus* and *Pseudomonas putida* (Adedayo et al. 2002). The mechanism of antibacterial activity of the *Senna alata* plant extract involved potassium ion and protein leakage. While maximum potassium leakage occurred within 30 minutes, protein efflux was at a peak after 75 minutes. Microscopic examination suggested that *Bacillus subtilis* cells were mummified while *Staphylococcus aureus* cells were lysed.

Extracts of water, methanol, chloroform and petroleum ether of *Senna alata* flowers also exhibited antimicrobial properties (Idu et al. 2007). Extracts tested at a final concentration of 500 µg/mL produced in vitro antimicrobial activities in assays against clinical isolates of *Staphylococcus aureus, Candida albicans, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa* and *Bacillus subtilis*. Preliminary phytochemical analysis of the plant extracts showed the presence of phenols, tannins, anthraquinones, saponins and flavonoids. In another study, aqueous flower extract of *Senna alata* elicited 100 growth inhibition of aflatoxin-producing fungi *Aspergillus flavus* and *A. parasiticus* at 10 and 15 mg/mL concentrations (Abubacker et al. 2008). For the pathogenic fungi *Candida albicans* and *Microsporum audouinii* and plant pathogenic fungi *Fusarium oxysporum* and *Helminthosporium oryzae*, total inhibition occurred at 15 mg/mL concentration. The MIC values of the extract varied from 5.75 to 8.00 mg/mL for these fungi. *Senna alata* crude stem exhibited marked in vitro antifungal effects against *Microsporum canslaslomyces, Trichophyton verrucosum and Trichophyton mentagrophytes* at concentrations of 10.00 and 5.00 mg/mL and *Epidermophyton floccosum* at concentration of 10.00 mg/mL (Sule et al. 2011). Phytochemical analysis revealed the presence of important secondary metabolites (tannins, steroids, alkaloids, anthraquinones, terpenes, carbohydrates and saponins) in the plant.

An herbal soap formulated with ethanol extract of *Cassia alata* exhibited excellent antimicrobial effect against Gram-positive bacteria and opportunistic yeast in the in vitro studies as well as in the palm-washing studies on volunteers

(Esimone et al. 2008). At a reduction time of 5 minutes, the herbal soap recorded a significantly lower mean viable microbial count of 2.12×10^4 cfu/mL (a reduction in microbial load of 94.78 %) as against the 4.07×10^5 cfu/mL recorded before the application of the soap. The herbal soap formulated with *Cassia alata* may have potential as an excipient in the production of antiseptic soaps.

Clinical Studies

Oladele et al. (2010) conducted a clinical trial involving 33 prison inmates; 19 were treated with *S. alata* soap and 14 untreated control (placebo). The *S. alata* soap consisted of *S. alata* leaf powder incorporated with caustic soda and palm kernel oil to make 1.5 % w/w. *Tinea versicolor* and *Tinea corporis* were the major fungal infections found on the skin lesions prior to study commencement, while *Epidermophyton floccosum* and *Cryptococcus* sp. were microscopically observed to be responsible for the lesions. After 4 weeks, *S. alata* soap significantly cleared the lesions on 16 subjects (94.1 %), comprising (11) *T. versicolor* and (5) *T. corporis*. None of the controls was cleared significantly. The study clearly confirmed the folkloric claims on *S. alata* as an antimicrobial agent for treating skin infections.

Hypoglycaemic Activity

Senna alata leaf extract administered orally had no effect on glucose levels in normoglycaemic animals, but it reduced the blood sugar value in streptozotocin-induced hyperglycaemic animals (Palanichamy et al. 1988). The ethyl acetate leaf extract was found to be hypoglycaemic (Villaseñor et al. 2002). At a dosage of 5 mg/20 g mouse, it decreased the blood sugar level of mice by 58.3 %.

Antiplatelet Activity

Adenine was isolated as a platelet-aggregating inhibitor from the leaves of *Senna alata* (Moriyama et al. 2003a). The inhibitory effect of adenine was observed in the platelet aggregation induced by collagen (1.0 μg/mL as the final concentration), but little inhibitory effect was noted in the aggregation induced by ADP (adenosine 5′-diphosphate), whereas adenosine exhibited potent inhibitory effects on platelet aggregation induced both by collagen and ADP under the same experimental conditions.

Antiinflammatory Activity

Both the hexane and ethyl acetate leaf extracts exhibited antiinflammatory activity at a dosage of 5 mg/20 g mouse with a 65.5 and 68.2 % decrease in carrageenan-induced inflammation, respectively (Villaseñor et al. 2002). Antiinflammatory activities of heat-treated *Senna alata* leaf extract and kaempferol 3-*O*-gentiobioside (K3G) isolated from *C. alata*, a flavonoid glycoside, were demonstrated (Moriyama et al. 2003b). Strong inhibitory effects on concanavalin A-induced histamine release from rat peritoneal exudate cells both in the extracts of heat-treated and sun-dried *S. alata* leaves were observed. The heat-treated leaf extract was observed to exhibit stronger inhibitory effects than the effects of the sun-dried leaf extract at low concentrations in the studies of concanavalin A-induced histamine release, 5-lipoxygenase inhibition and also inhibition of cyclooxygenases (COX-1 and COX-2). In contrast, K3G showed weak inhibitory effects on concanavalin A-induced histamine release, 5-lipoxygenase and COX-1. No anti-hyaluronidase effect was detected in any of the materials tested.

Cassia alata hexane leaf extract significantly reduced knee circumference swelling in complete Freund's adjuvant (CFA) arthritic rats (Lewis and Levy 2011). Total and differential leukocyte counts in both blood and synovial fluid from *Cassia alata*-treated animals were significantly lower than in control animals. Protective effects against cartilage degradation on the femoral head of the knee joint were observed in *Cassia alata*-treated animals, as normal cartilage structure and chondrocyte arrangement were maintained. The results indicated that *Cassia alata* exerted

antiinflammatory activities that could potentially be exploited for antiarthritic therapies.

Hepatoprotective Activity

Crude extracts of flower petals in 0.5 % ethanol administered into the rats by intubation for 14 days prior to injection of 0.5 mL carbon tetrachloride (CCl_4)/kg elicited hepatoprotective activity (Wegwu et al. 2005). Serum aspartate aminotransferase and alanine aminotransferase levels decreased significantly in rats treated with the flower extract than in CCl_4-treated rats. In another study, pretreatment of *Cassia alata* leaf extract reduced the biochemical markers of hepatic injury-like elevated levels of serum glutamate pyruvate transaminase (SGPT), serum oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total bilirubin and gamma glutamate transpeptidase (GGTP) induced by paracetamol in albino rats (Jayakar et al. 2009). Histopathological observations also revealed that pretreatment with the extract protected the animals from paracetamol-induced liver damage.

Anticancer Activity

Cassia alata was one of 29 Malaysian plants screened that exhibited in-vitro photocytotoxic activity by means of a cell viability test using a human leukaemia cell line HL60 (Ong et al. 2009). These 29 plants were able to reduce e in vitro cell viability by more than 50 % when exposed to 9.6 J/cm^2 of a broad spectrum light when tested at a concentration of 20 μg/mL.

Cassia alata leaf extract was cytotoxic in parental A549 lung cancer cells and caspase-9 negative but not caspase-3 and -8 negative A549 cells (Levy and Lewis 2011). The IC_{50} values were 143 and 145 μg/mL in parental and caspase-9 negative A549 cells, respectively. The flavonoid kaempferol was identified as a constituent of *Cassia alata* leaf extract and may be responsible for the effect. Rhein (4,5-dihydroxyanthraquinone-2-carboxylic acid), the primary anthraquinone in the roots of *Cassia alata,* inhibited vascular endothelial growth factor (VEGF(165))-stimulated human umbilical vein endothelial cell (HUVEC) tube formation, proliferation and migration under normoxic and hypoxic conditions (Fernand et al. 2011). Further, rhein suppressed in vitro angiogenesis by inhibiting the activation of phosphatidylinositol 3-kinase (PI3K), phosphorylated-AKT (p-AKT) and phosphorylated extracellular signal-regulated kinase (p-ERK) but showed no inhibitory effects on total AKT or ERK. Rhein dose-dependently inhibited the viability of MCF-7 and MDA-MB-435s breast cancer cells under normoxic or hypoxic conditions and inhibited cell cycle in both cell lines. Additionally, rhein inhibited heat shock protein 90alpha (Hsp90α) activity to induce degradation of Hsp90 client proteins including nuclear factor-kappa B (NF-κB), COX-2 and HER-2. Rhein also inhibited the expression of hypoxia-inducible factor-1 alpha (HIF-1α), vascular endothelial growth factor (VEGF(165)), epidermal growth factor (EGF) and the phosphorylation of inhibitor of NF-κB (I-κB) under normoxic or hypoxic conditions. The findings indicated rhein to be a promising antiangiogenic compound for breast cancer cell viability and growth.

Antimutagenic Activity

Aloe-emodin from *C. alata* leaves was found to have antimutagenic activity (Hofilena et al. 2000). Micronucleus test indicated a 71 % reduction in the number of micronucleated polychromatic erythrocytes induced by mitomycin C. The chloroform leaf extract was antimutagenic, at a dosage of 2 mg/20 g mouse, with a 65.8 % inhibition in the mutagenicity of tetracycline (Villaseñor et al. 2002).

Anthelmintic Activity

C. alata leaves are used as anthelmintic for dogs in Trinidad and Tobago (Lans et al. 2000). *C. alata* leaf extracts inhibited egg hatchability and killed infective larvae of *Haemonchus*

contortus in a concentration-dependent manner (Ademola and Eloff 2011). The best-fit values were 0.562, 0.243, 0.490, 0.314 and 0.119 mg/mL for the acetone extract, chloroform, hexane, butanol and 35 % water in methanol fractions, respectively, when tested against nematode eggs. The best-fit LC_{50} values were 0.191, 0.505, 1.444, 0.306 and 0.040 mg/mL for acetone extract, chloroform, hexane, butanol and 35 % water in methanol fractions, respectively, when tested against larvae. The 35 % water in methanol fraction was the most active against the larvae and eggs of *H. contortus* demonstrating the lowest LC_{50} values.

Cestode parasites *Hymenolepis diminuta* treated with *C. alata* leaf extract showed a decrease in motility with an increase in concentrations and complete immobilization took lesser time compared to control (Kundu et al. 2012). Ultrastructural micrographs of paralyzed worms revealed swelling of the tegument and blebbing on the tegumental surface throughout the body accompanied with destruction of microtriches and changes such as shrinkage in the scolex region. Depletion of parenchyma cells and destruction in the connective tissues along with sparsely cytoplasmic cytons were also observed, and these observations were similar with worms treated with a known drug praziquantel.

Antiallergic Activity

The hydroalcoholic extract of *Cassia alata* leaves significantly inhibited mast cell degranulation at 200 mg/kg dose in rats (Singh et al. 2012). Both its chemical constituents rhein and kaempferol also showed potent (>76 %) inhibition of mast cell degranulation at 5 mg/kg. The extract and rhein inhibited lipoxygenase enzyme with IC_{50} values of 90.2 and 3.9 μg/mL, respectively, whereas kaempferol was inactive. The results suggested that *Cassia alata* exhibited antiallergic activity through mast cell stabilization and lipoxygenase have inhibition and may have potential as alternative treatment for allergic diseases.

Antimalarial Activity

Saye, a combination remedy prepared from N'Dribala, *Cochlospermum planchonii* root, *Cassia alata* leaf, *Phyllanthus amarus* whole plant and *Azadirachta indica* fruits, is a plant remedy commonly used by traditional healers for the treatment of malaria in Burkina Faso (Traoré et al. 2008; Yerbanga et al. 2012). 'Saye' showed a significant effect against *Plasmodium falciparum* and *Plasmodium berghei* parasites grown in vivo (IC_{50} = 80.11 μg/mL; ED_{50}) = 112.78 mg/kg). In vitro the activity was lower. Aqueous extracts of Saye, N'Dribala and *Azadirachta indica* preparations orally administered to mice elicited prophylactic activity and reduced *Plasmodium berghei* parasitaemia in treated mice, with respect to controls, by 52.0, 45.5 and 45.0 %, respectively (Yerbanga et al. 2012). No evidence of transmission blocking effects was detected with any of the tested remedies.

Choleretic Activity

Studies in rats showed that choleretic activity of *Senna alata* at 15 mg/kg was better than 15 mg/kg of hydroxycyclohexenyl-butyrate (Hebecol ND), a synthetic choleretic, but at elevated doses, the plant extract inhibited bile secretion (Assane et al. 1993).

Analgesic Activity

The extract of the leaves of *Senna alata* and kaempferol 3-*O*-sophoroside exhibited analgesic activity (Palanichamy and Nagarajan 1990a). Maximum analgesic activity of the extract was apparent 120 minutes after intraperitoneal injection using the tail clip, tail-flick, tail immersion and acetic acid-induced writhing methods. Fifty milligrams of kaempferol 3-*O*-sophoroside appeared equivalent to 100 mg of the extract. Cassiaindoline, a dimeric indole alkaloid isolated from *Cassia alata* leaves, exhibited analgesic activity at a dosage of 125.0 mg/kg mouse and decreased the number of writhings induced by acetic acid by 49.4 % (Villaseñor and Sanchez

2009). It also showed a 57.1 % antiinflammatory activity at a dosage of 75 mg/kg mouse.

Acaricidal Activity

The ethanol leaf extract of *C. alata* produced a concentration-dependant increase in the adult tick *Rhipicephalus (Boophilus) annulatus* mortality (Ravindran et al. 2012). The highest mortality (45.8 %) and inhibition of fecundity (10.9 %) were observed at the highest concentration tested (100 mg/mL). The leaf extract did not affect egg hatchability.

Hypolipidaemic/Anti-obesity Activity

Studies demonstrated that *Cassia fistula* and *S. alata* methanol leaf extracts could significantly lower body weight of diet-induced lipidaemic mice (Chichioco-Hernandez and Leonido 2011). Furthermore, parametrial fat weight of mice was also decreased in a dose-dependent manner, thus confirming the weight-lowering potential of both plants.

Immunological Activity

Among the eight pollen types sample extract tested, *Ricinus communis* was found to contain the highest amount of soluble protein, free amino acid and total carbohydrate, per gram of dry weight followed by *Imperata cylindrica* and *Cassia alata* (Sharma et al. 2009). Maximum numbers of protein polypeptide bands were detected in the sample extract of *Cassia alata* followed by *Acacia auriculiformis, Imperata cylindrica* and *Cocos nucifera*. IgE binding protein fractions were maximum in *Cassia alata* and minimum in *Trewia nudiflora*.

Abortifacient Activity

Senna alata leaf extract (250, 500, 100 mg/kg bw) administered to pregnant Wistar rats significantly reduced the number of live foetus, weight and survival ratio of the foetus, numbers of implantations and corpora lutea, implantation index, progesterone, prolactin, estradiol, follicle stimulating and luteinizing hormones whereas the number of dead foetus, number and percentage of rats that aborted, percentage vaginal opening, resorption index and pre- and post-implantation losses increased significantly (Yakubu et al. 2010). The abortifacient effects were most pronounced at 500 and 1,000 mg/kg body weight of the extract and were similar to the animals treated with 2.85 mg/kg body weight of mifepristone, the reference drug. All cases of abortion were accompanied with vaginal bleeding. Although, the final weight of the rats increased significantly, the feed and water intake were not significantly altered in all the treatment groups. The weight of the uterus, uterine-body weight ratio, length of the right uterus horn and uterine cholesterol decreased significantly in all the treatment groups. The uterine alkaline phosphatase activity and glucose concentration increased in only the extract-treated animals, whereas mifepristone decreased the uterine alkaline phosphatase activity and glucose content of the animals. Hormonal influence, changes in implantation site, estrogenicity and uterogenicity were suggested as possible mechanism of abortifacient activity of aqueous extract of *S. alata* leaves. Phytochemical screening of the leaf extract showed positive results for saponins (1.22 %), flavonoids (1.06 %), cardiac glycosides (0.20 %), cardenolides and dienolides (0.18 %), phenolics (0.44 %) and alkaloids (0.52 %). Overall, the extract may be used as an abortifacient especially at 500 and 1,000 mg/kg body weight and therefore not safe for consumption as oral remedy during pregnancy. The results provided evidence to the age-long claim of *S. alata* leaves in 'washing the uterus'. In subsequent studies, they found that administration of the crude alkaloids from *Senna alata* leaves elicited decreases in the activities of alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), aspartate (AST) and alanine transaminases in the liver and kidney of the animals by the alkaloids and were accompanied by corresponding increases in the serum enzymes (Yakubu and

Musa 2012). The alkaloids reduced liver- and kidney-body weight ratios, serum globulin, urea, uric acid and phosphate ions, while the serum concentrations of albumin, bilirubin, creatinine, potassium ions, AST/ALT ratio and blood urea nitrogen to creatinine ratio increased. They concluded that the alkaloid at doses of 250–1,000 mg/kg body weight produced permeability changes in the plasma membrane of the organs and adversely affected the normal secretory, synthetic and excretory functions of these organs.

Miscellaneous Pharmacological Activities

Pharmacological studies showed that the hexane, chloroform and ethyl acetate leaf extracts caused an immediate decrease in motor activity, enophthalmos, hyperaemia, micturition and diarrhoea (Villaseñor et al. 2002). At a dosage of 150 mg/20 g mouse, the ethyl acetate leaf extract caused paralysis, screen grip loss and enophthalmos accompanied by drooping and closure of the eyelids.

Toxicity Studies

The aqueous leaf extract of *Senna alata* induced an adverse effect on haematological indices in albino rats (Sodipo et al. 1998). Increasing doses (10, 50, 100 and 150 mg/kg bw) of the extract administered orally to different groups of rats daily for a period of 14 days produced significant dose-dependent decreases in the levels of haemoglobin (Hb) and erythrocyte count. However, mean corpuscular haemoglobin (MCH) did not show any change. Clinical symptoms of loss of appetite, emaciation and loss of weight in the treated rats indicated toxicity. The observed symptoms of toxicity were attributed to the saponin content of the plant extract. Contradictory results were found in another study. Acute and subacute toxicity study of aqueous ethanol leaf extracts of *S. alata* in Swiss mice and Wistar albino rats found no observable toxicity symptoms or animal death during or at the end of the experimental period (Pieme et al. 2006). The results indicated that the medium lethal dose (LD_{50}) was about 18.50 g/kg of body weight. Rats treated with various doses of hydroethanolic leaf extract had a progressive weight gained, and this increase in weight was significantly different from that of the control. The effect of *S. alata* appeared to have a protective effect, after 26 days dosage of hydroalcoholic extract of *S. alata*; there were no significant changes in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (APL) activities in the serum of both sexes and the 20 % homogenate liver samples. The extract had a protective effect on hepatocytes and appeared to improve liver architecture. The study presented strong evidence of the nontoxic effect of the hydroethanolic leaf extract of *S. alata*.

The TRAMIL research group in the Caribbean validated the recommendation of the use of the leaves to cure eczema and 'ringworm', by rubbing on the skin or using an infusion of 15–20 leaflets per litre of water to wash affected areas of the skin (Robineau 1995). TRAMIL researchers have shown that following peritoneal dosing in rats at 2 g/kg, the ethanol extract from the leaf showed no significant toxicity. In all cases extemporaneous preparation should not be kept for more than 1 day. They also found the bark to be rich in tannins and seeds to be a good source of gums for use in ointments and herbal soaps. They found that sennosides are contraindicated in cases of obstruction, acute intestinal inflammation, ulcerative colitis, appendicitis and abdominal pain of unknown origin and for children under the age of 12. With chronic use, hypokalaemia may occur. During the first trimester of pregnancy, senna pod preparations should be used only if a therapeutic effect cannot be obtained with a change in diet or through the use of bulk laxatives.

Traditional Medicinal Uses

The leaves, flowers, fruits, seeds and root bark are used for medicinal purposes in folkloric medicine. In the Indian system of medicines, namely,

Ayurveda, Siddha and Unani, decoctions of the leaves, flowers, bark and wood are used in skin diseases like eczema, pruritus, itching and constipation (Kirtikar and Basu 1975). In the Philippines, the leaves are employed for ringworm and other skin diseases, like itches (BPI 2005). According to Philippines Bureau of Plant Industry (BPI 2005), the leaves are official in the Pharmacopoeia of India. The Pharmacopoeia of India mentions an effective ointment made of the leaves. In India, the plant is regarded as a cure for poisonous bites and for venereal eruptions. The sap of the leaves is an efficient antiherpetic. The leaves are taken internally as an aperient. A decoction of the leaves and flowers is used as an expectorant in bronchitis, asthma and dyspnoea; as an astringent; and also as a mouthwash in stomatitis. A strong decoction of the leaves and flowers is a good wash for eczema. A strong decoction of the leaves is abortifacient. The seeds are used as a vermifuge. A decoction of the roots is used against tympanitis. The wood is used as an alternative. Decoctions of the wood are used to treat liver problems, urticaria, rhinitis and loss of appetite caused by gastrointestinal problems. In the Antilles, Reunion and Indo-China, it is reported that the plant is reputed as hydragogue, sudorific and diuretic. Decoctions of the leaves, flowers, bark and wood are used in skin diseases such as eczema, pruritus and itching and in constipation (Palanichamy and Nagarajan 1990b). The flowers are also used in bronchitis and asthma. The leaves are traditionally used for the treatment of skin diseases such as ringworm and pityriasis versicolor (Husain et al. 2005). An infusion of the roots is used to treat rheumatism and also used as a strong laxative (Reezal et al. 2002). The seeds and leaves are used as fungicide, vermifuge and for skin problems in Mangalore, India (Shiddamallayya et al. 2010).

For laxative purposes usually a decoction of the leaves is drunk, and less often the flowers, roots or the stem are used. Skin problems treated with *Senna alata* include ringworm, favus and other mycoses, impetigo, syphilis sores, psoriasis, herpes, chronic lichen planus, scabies, rash and itching (Bosch 2007). Other ailments treated in tropical Africa with *Senna alata* include stomach pain during pregnancy, dysentery, haemorrhoids, blood in the urine (schistosomiasis, gonorrhoea), convulsions, heart failure, oedema, jaundice, headache, hernia and one-sided weakness or paralysis. A strong decoction made of dried leaves is used as an abortifacient. In veterinary medicine too, a range of skin problems in livestock is treated with leaf decoctions. Such decoctions are also used against external parasites such as mites and ticks. *Cassia alata* extract is used in traditional medicine practice for the treatment of some external skin infections in Nigeria, the juice expressed from the young leaves being applied topically to the skin (Benjamin and Lamikanra 1981; Alalor et al. 2012). *Senna alata* is widely used in ethnomedicine practice for the treatment of hypertension, sickle cell anaemia and diabetes in southwestern Nigeria (Okpuzor et al. 2009). Saye, a combination remedy prepared from *Cochlospermum planchonii, Cassia alata* and *Phyllanthus amarus*; N'Dribala, a *Cochlospermum planchonii* root decoction; and a fruit preparation of *Azadirachta indica* are plant remedies of the folk medicine in Burkina Faso and are commonly used by traditional healers for the treatment of malaria (Yerbanga et al. 2012) Leaves are commonly employed for constipation in Nigeria and other African countries. Leaves are used as tea for intestinal worm infestation and a leaf decoction drunk for gonorrhoea in Ghana (Irvine 1961) and in Senegal (Kerharo and Adam 1974), while a root decoction is drunk for gonorrhoea in Congo (Bouquet 1969). In Togo and Gabo, pounded leaves are used directly on the skin or mixed with palm oil for dermatitis (Adjanohoun et al. 1986; Akendengue and Louis 1994).

In Thailand, *S. alata* has been approved as a laxative drug in the Thai Herbal Pharmacopoeia 1998 and the Thai National List of Essential Drug 1999. In Thailand, aqueous extracts of the leaves of *Cassia alata* and Lawsonia alba are used in native medicine for ringworm infections (Pankajalakshmi et al. 1993). In Thailand, the leaves are used as laxative for treating constipation; fresh leaves are pounded with water, garlic and red lime and smear on ringworm-infected skin; shoots and leaves are boiled and used and

the preparation used for cleaning abscesses and wounds as antiinflammatory (Monkheang et al. 2011). In Vietnam, *C. alata* is employed to treat constipation, oedema, hepatalgia and jaundice (Le and Nguyen 1999). It is used externally for ringworm, tinea imbricata (tokelau) and herpes circinatus. In Peninsular Malaysia, the juice of the leaves is used or sometimes mixed with lime for ringworm infestations (Burkill 1966). Roots are also used externally for ringworm and also prescribed for constipation. The pods and seeds are eaten as vermifuge. A decoction of the cooked leaves or flowers was taken as purgative in Indonesia. In Sarawak, pounded fresh leaves are rubbed on ringworm infestations and for dhobi itch, and a drink is prepared from young leaves and roots for diarrhoea (Chai 2006).

Other Uses

The tree is planted as shade tree, for soil covering, as protection against driver ants and as medicinal plant. It is often grown as an ornamental, and in the Pacific Islands, it is sometimes planted to improve taro patches. The seeds are a source of gum.

The leaf extract can be used in veterinary medicine. The use of ointments made with ethanol leaf extracts of leaves of *Senna alata*, as topical treatments on chronic crusty or acute lesions of bovine dermatophilosis, induced healing of the disease in infected animals treated without recurrence for more than 3 years (Ali-Emmanuel et al. 2003).

Comments

S. alata has been introduced and naturalized in many countries, and in some countries, it has become a weed. For instance, *Senna alata* is regarded as a significant environmental weed in the Northern Territory and as an environmental weed in Queensland and Western Australia. It is also regarded as a potential environmental weed or 'sleeper weed' in northern New South Wales.

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Senna auriculata

Scientific Name

***Senna auriculata* (L.) Roxb.**

Synonyms

Cassia auriculata L., *Cassia densistipulata* Taub.

Family

Fabaceae also placed in Caesalpiniaceae

Common/English Names

Avaram Senna, Matara Tea, Styptic Weed, Tanner's Cassia, Tarwar

Vernacular Names

Burmese: Peikthingat
Chinese: Er Ye Jue Ming
French: Avaram
India: Tangedu (Andra Pradesh), Awala (Gujarati), Anwal, Aval, Awai, Tarawar, Taroda, Tarval, Tarvar, Tarwan, Tarwar (Hindi), Aavarike, Athi, Avara, Avara-Gida, Avarakka, Avarike, Avarikke, Bobbade, Cakusina, Chaknsiva, Chakoosina Gida, Charma Hada Aavarike, Chookusina Gida, Honnaavare, Honnaavarike, Honnarike, Honnavari Gida, Honnavarike, Olaniyaro, Olle Thangadi, Olletangadi, Olletangedi, Olletangedu, Sakusina, Tangadi, Tangadi-Gida, Tangedi, Taravada, Taravada-Gida, Thangadi (Kannada), Avara, Avarakka, Avaram, Aveeram, Aviram, Jimute, Ponnaviram (Malayalam), Arsuai, Avul, Taravada, Taroda, Tarvad, Tarwad, Tarwar, Tharoda (Marathi), Timirihari (Oriya), Adarisimbi, Ahula, Ahulya, Ahulyam, Avartaki, Avarttaki, Awarteki, Bhumyahulya, Carmaranga, Charamranga, Charmaranga, Mandari, Mayahari, Mayharie, Pitakalika, Pitakilaka, Pitapuspa, Talopota, Timirihari, Visanika (Sanskrit), Aavaarai, Aavarai, Akuli, Anakavarai, Anakavaraicceti, Avarai, Avarai, Avarai, Avaraicceti, Avaram, Avary, Avavirai, Avaviraicceti, Avirae, Avirai, Avirai Arici, Aviraittol, Aviraiyilai, Avirantol, Aviri, Aviricceti, Cakacaka, Cakuli, Canakkirampul, Caruvantirakam, Catilaka, Catilakacceti, Catinakam, Catinam, Catirakuli, Caturkkalicceti, Caturkkuli, Caturkuli, Cemmai, Cemmala, Cemmalai, Cemmalaviraicceti, Ceppalai, Cicuravikam, Cittiraippal, Corikkattai, Cularai, Cummai, Cutcumapattiram, Cuvarnaputpatam, Emaputpi, Ilanci, Kapalacanti, Kapalatti, Kapalatticceti, Kari, Karikacceti, Katavukacikacceti, Katavukacikam, Kotaikkuvatan, Kotakacalai, Mancalavarai, Mekacatturu, Mekamaki, Mekari, Mikupattam, Mikupattavarai, Muntakaveni, Muntakavenicceti, Nattavarai, Nattunilavarai, Patarai, Pataraicceti, Periyaavirai, Periyatakarai, Peyaviram, Pitantavarai, Pitaputpi, Pitattavarai, Rukkumam, Sadurguli, Sadurgulu,

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Semmalai, Summai, Talapattiram, Talapetam, Talapotakam, Talapotam, Talapotam, Talapotavirai, Tamirakari, Tankamavarai, Tavapotakam, Turonikai, Turonikaivirai, Tuvakai, Vanamakiyamuli, Vanamakumuli, Vanamikumuli, Vanamikuntamulicceti, Vanamulikai, Vanatteri, Vanattericceti, Varnaputpakam (Tamil), Avaray, Merakatangedu, Merakathangedu, Merikatangaru, Merka Tangedu, Tangar, Tangedu, Tangera, Tanghedu, Tangheroo, Thangedu, Thangera (Telugu)

Portuguese: Avúl

Sri Lanka: Ranawara (Sinhalese)

Origin/Distribution

Senna auriculata is a native of India, Myanmar and Sri Lanka and has been successfully introduced into several African countries. It has been suggested that it is indigenous in Tanzania, but an early introduction and naturalization seem more likely. It is cultivated in India and Sri Lanka and occasionally elsewhere.

Agroecology

Under natural or naturalized conditions, *Senna auriculata* is found in woodlands and wooded grasslands up to 600 m altitude. It usually grows wild in dry regions with a minimum annual precipitation of 400 mm, but it also tolerates wet climates with an annual precipitation of up to 4,300 mm. It grows well in areas with mean annual temperature range of 16–27 °C. *Senna auriculata* needs full sun. It tolerates many soil types, including saline soils but prefers fairly rich, well-drained, friable soils.

Edible Plant Parts and Uses

The flowers, young leaves and young tender pods are edible (Watt 1908; Burkill 1966; Facciola 1990; Rahmansyah 1991; Reddy et al. 2007). Flowers are eaten as vegetables in Andhra Pradesh, India (Reddy et al. 2007). The leaves are made into a refreshing cooling drink in India. The leaves are sometimes used to make tea, dried flowers serve as a coffee substitute, and in times of food scarcity, the young tender pods, young leaves and flowers are eaten as a vegetable (Rahmansyah 1991). A fermented mixture of pounded bark and dissolved molasses serves as an alcoholic beverage in some parts of India.

Botany

A branched shrub or small tree 1.5–5 m high (Plate 1), with a trunk diameter up to 20 cm and with thin, brown, lenticellate bark. Leaves alternate, paripinnately compound with 6–13 pairs leaflets (Plates 1 and 2); stipules large and leafy, broadly reniform, 7–22 mm wide, persistent; petiole 10–14 cm long; rachis provided with a gland between each pair of leaflets. Leaflet oblong-elliptical to obovate-elliptical, 10–35 × 5–12 mm, rounded and mucronate at apex, glabrous to pubescent. Inflorescence an axillary raceme, 2–8 flowered (Plates 1 and 3). Flower (Plate 4) bisexual, zygomorphic, pentamerous, 4–5 cm across; sepals rounded at apex, imbricate, glabrous; petals free, imbricate, unequal, 1.5–3 cm long, yellow; stamens 10, the 3 lower ones largest and fertile, others usually sterile; ovary superior, falcate, with 1.5 cm long, stalked, style (fruit a flattened cylindrical pod 5–18 × 1–2 cm, transversely undulate between the 10–20 seeds, indehiscent, green turning to brown when mature.

Plate 1 Flowers and foliage (GF Chung)

Plate 2 *Upper* and *lower* surface of pinnate leaves (GF Chung)

Plate 3 Inflorescence with yellow flowers (GF Chung)

Plate 4 Close up of flower (GF Chung)

Plate 5 Ripe and mature pods (GF Chung)

Seeds compressed ovoid-cylindrical, 7–9×4–5 mm, with a distinct areole on each surface (Plate 5).

Nutritive/Medicinal Properties

Leaf Phytochemicals

Five compounds were isolated from the leaves (Varshney et al. 1973). Compounds A, B and C were found to be saturated higher aliphatic fatty alcohols and formed 2:4-dinitrophenylhydrazone derivatives, compound D gave all characteristics of a sterol, and compound E was identified as an anthraquinonepigment,emodin(1,6,8-trihydroxy-3-methylanthraquinone). Di-(2-ethyl) hexyl phthalate was isolated from *Cassia auriculata* leaves (Nageswara Rao et al. 2000). Leaves were reported to contain carbohydrates, phenols, lipids, proteins, saponins, flavonoids, tannin, terpenoids and cardiac glycosides (Senthilkumar and Vijayakumari 2012). Thirteen bioactive compounds were identified in the ethanol leaf extract, and the major constituents were phytol, octadecane 1-(ethenyloxy)- and *E-10*-pentadecenol. Other components included resorcinol; 3-*O*-methyl-D-glucose; 1,14-tetradecanediol; 3,7,11,15-tetramethyl-2-hexadecen-1-ol; 2*H*-cyclopropa[a] naphthalen-2-one,1,1a,4,5,6,7,7a,7b-octahydro-, 1,7,7-tetramethyl-(1aa,7a,7aa,7ba)-; azulene, 1,2, 3,5,6,7,8,8a-octahydro-1,4-dimethyl-7-(1-

methylethenyl)-, [1*S*-(1a,7a,8aa)]-; 1,2-benzene dicarboxylic acid, diisooctyl ester; squalene; 1-cyclohexylnonene; and 1-4-[(2-diethylamino] ethylamino[-6-methyl-2-pyrimidinyl]-3-[3,4,5-trimethoxyphenyl] guanidine.

Twenty-nine compounds were found in *C. auriculata* leaves (Anandan et al. 2011). The main constituents were 3-*O*-methyl-D-glucose (48.50 %), α-tocopherol-β-D-mannoside (14.22 %), resorcinol (11.80 %), *n*-hexadecanoic acid (3.21 %), 13-octadecenal, (*Z*)- (2.18 %), 1,2,3,4-tetrahydroisoquinolin-6-ol-1-carboxylic acid (1.98 %), unknown (3.29 %), unknown (2.61 %) and unknown (1.14 %). Other minor constituents were glycerine (0.16 %), thymine (0.11 %), 1-butanol, 3methyl-, formate (0.17 %), 4*H*-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl (0.46 %), benzaldehyde,4 methyl- (0.83 %), 2-propenoic acid, 4-methylpentyl ester (0.125), sucrose (1.2 %), 1,6,anhydro-β-D-glucopyranose (levoglucosan) (0.3 %), β-D-glucopyranoside, methyl (0.36 %), 1,2-benzenedicarboxylic acid, bis(2-methylpropyl) ester (1 %), benzenamine,2,3,4,5,6-pentamethyl (0.87), unknown (0.57 %), hexadecanoic acid, ethyl ester (0.1 %), 1-tridecyne (0.3 %), 13-oxabicyclo[10.1.0] tridecane (0.42 %), phytol (0.61 %), 1-*E*,11,*Z*-13-octadecatriene (0.56 %), 1 octadecanoic acid (0.46 %), *a*-tocopherol (1.16 %) and *N*-acetyl tyramine (1.24 %).

Seed/Pod Phytochemicals

Sterols, anthracene derivatives, triterpenoid and tannins were isolated from the ethanol extract of the pods (Suresh et al. 2007).

The following chemicals were identified in the seed extract: *n*-hexadecanoic acid (21.31 %), grapeseed oil (linoleic and oleic acids) (31.02 %), *E*,*Z*-1,3,12-nonadecatriene (12.27 %), stearic acid (9.39 %), benzoic acid, 2-hydroxy-methyl ester (0.07 %), β-ethoxypropionaldehyde diethyl acetal (0.86 %), ethyl caprylate (0.14 %), 2-methoxy-4-vinylphenol (0.36 %), glycine, *N*-(trifluoroacetyl)-, 1-methylbutyl ester (0.10 %), 2,3-dihydro-3,5-dihydroxy-6-methyl-4*H*-pyran-4-one (0.12 %), capric acid ethyl ester (0.16 %), resorcinol (0.21 %) dodecanoic acid (0.48 %), 3′5′-dimethoxyacetophenone (0.58 %), 9-octadecenoic acid, (*E*)-(12.60 %), palmitic acid β-monoglyceride (2.95 %), dl-α-tocopherol (1.22 %) and stigmasta-5,23-dien-3-ol,(3β)-(1.21 %) (Raj et al. 2012).

Polyphenols quantified in the hydroalcoholic seed extract of *C. auriculata* were epicatechin (14 %), catechin (4.5 %) and procyanidin B1 (1 %), while the supercritical fluid extract contained catechin (6 %) and epicatechin gallate (20 %) (Puranik et al. 2011).

Flower Phytochemicals

The flower of *C. auriculata* was found to contain a flavonol glycoside 5-*O*-methylquercetin 7-*O*-glucoside (Manogaran and Sulochana 2004). The hydromethanolic extract and its ethyl acetate and *n*-butanol fractions of the flowers were found to contain phenolic compounds, carbohydrates, tannins, steroids and amino acids (Surana et al. 2009).

Root Phytochemicals

Phytochemical analysis of the crude root extracts revealed the presence of an array of active chemical constituents such as tannins, flavonoids, glycosides, carbohydrates, steroids and triterpenoids (Wadekar et al. 2011).

Plant Phytochemicals

C. auriculata was reported to contain leucopelargonidins, flavan-3,4-diols of the 'phloroglucinol series' (Paris and Cubukcu 1962). From the aerial plant parts, the following compounds were isolated: kaempferol-3-*O*-rutinoside, rutin, kaempferol, quercetin and luteolin (Juan-Badaturuge et al. 2011; Habtemariam 2013), and oleanolic acid (Senthilkumar and Reetha 2011).

Some of the reported pharmacological properties of the various plant parts of *Cassia auriculata* are elaborated below.

Antioxidant Activity

The ethanol and methanol extracts of *C. auriculata* flowers showed antioxidant activity in both 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assays (Kumaran and Karunakaran 2007). The flower powder of *Cassia auriculata* significantly decreased the thiobarbituric acid reactive substances (TBARS), hydroperoxide and conjugated dienes and increased the antioxidant enzymes (catalase, superoxide dismutase and glutathione peroxidase) and non-enzymatic antioxidants (ascorbic acid, vitamin E and reduced glutathione) in streptozotocin-induced diabetic rats (Jeyashanthi and Ashok 2010). The antioxidative effect of 200 mg/kg body weight (bw) of the extract was significantly better than 100 mg/kg body weight extract and the reference drugs (tolbutamide and metformin). Antioxidative effect was not observed in normoglycemic rats in the experiment. In another study, oral administration of *C. auriculata* aqueous leaf extract to streptozotocin-induced mild diabetic (MD) and severe diabetic (SD) rats (100, 200 and 400 mg/kg bw per day for a period of 21 days) produced significant fall in fasting blood glucose (FBG) in a dose-dependent manner (Gupta et al. 2009c). Treatment with the extract (400 mg/kg) showed significant reduction in serum levels of thiobarbituric acid reactive substances (TBARS) and oxidized low-density lipoprotein (OxLDL) in both MD and SD rats. The antioxidant defence system was also found to be improved in extract-treated (400 mg/kg) MD and SD rats, as revealed by significant increase in activities of erythrocyte's antioxidant enzymes, that is, superoxide dismutase (SOD) and catalase (CAT) with a concomitant elevation in erythrocyte's reduced glutathione (GSH) content. Moreover, there were no toxic signs in rats treated with high doses of the extract (1,000 and 2,000 mg/kg bw per day for 21 days). Blood glucose, hepatic and renal function parameters in these rats were found within normal limits.

The alcoholic extract of the aerial part of *C. auriculata* exhibited potent antioxidant activity when assessed by DPPH radical scavenging, lipid peroxidation and reducing power analysis (Juan-Badaturuge et al. 2011). Fractionation of the crude extract showed that the ethyl acetate fraction was the most active followed by the chloroform fraction, while the petroleum ether, *n*-butanol and water fractions were less active than the crude extract.

Anticancer Activity

Cassia auriculata leaf ethanol extract dose-dependently inhibited the growth of human breast adenocarcinoma MCF-7 and human larynx carcinoma Hep-2 cell lines in vitro with IC50 values of 400 and 500 µg through induction of apoptosis (Prasanna et al. 2009). The MCF-7 and Hep-2 cells showed decreased expression of antiapoptotic Bcl-2 protein and increased expression of Bax/Bcl-2 ratio upon treatment. When *Cassia auriculata* extract and curcumin were combined, a synergistic effect of anticancer activity at a much lower concentration of both was noted (Prasanna et al. 2011).

Antimicrobial Activity

Cassia auriculata leaf extract exhibited significant broad spectrum activity in-vitro against *Bacillus subtilis* and *S. aureus* (Samy and Ignacimuthu 2000). Studies conducted in birds with *Escherichia coli* infection showed that *C. auriculata* herbal extract had more potent microbicidal activity compared to *Piper betle* (Prakash 2006). The methanol leaf extract (5 mg/disc) and methanol flower extract (2.5 mg/disc) showed in-vitro growth inhibitory activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Enterococcus faecalis* (Duraipandiyan et al. 2006). The methanol flower extract (5 mg/disc) showed antibacterial activity against all four bacteria and *Escherichia coli.*

The ethanol, methanol and aqueous extracts of dry flowers and ethanol, methanol and acetone extracts of fresh flowers of *Cassia auriculata* exhibited in-vitro antibacterial activity against *Staphylococcus aureus, Enterococcus faecalis,*

Bacillus subtilis, Salmonella typhi, Salmonella paratyphi A, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Vibrio cholerae and *Shigella dysenteriae* (Maneemegalai and Naveen 2010). The maximum activity was observed against all organisms except *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. The minimum inhibitory concentration ranged between 12.5 and 75 mg/mL depending on microorganism and various extract. Presence of phytochemicals such as terpenoids, tannins, flavonoids, saponin, cardiac glycosides and steroids was observed. Of several plant species, *Cassia auriculata* was selected as the efficient plant, which showed antibacterial activity against *Escherichia coli, Salmonella typhi, Proteus mirabilis* and *Klebsiella pneumoniae* at different concentrations Senthilkumar and Reetha 2011).

Antiinflammatory Activity

The 50 % acetone flower extract of *C. auriculata* showed marked antiinflammatory activity (56 %) in carrageenan-induced oedema in rats (Manogaran and Sulochana 2004).

Antidiabetic Activity

Administration of aqueous *Cassia auriculata* flower extract at 0.45 g/kg significantly decreased blood glucose, glycosylated haemoglobin and gluconeogenic enzymes and increased plasma insulin, haemoglobin and hexokinase activity in streptozotocin diabetic rats (Latha and Pari 2003a). The elevated gluconeogenesis during diabetes was reverted to normal by the extract in enhancing the utilization of glucose through increased glycolysis. The effect of the extract was more prominent than that of glibenclamide. The methanol flower extract of *C. auriculata* was found to have potential alpha-glucosidase inhibitory activity in vitro, preferably on maltase with a low IC_{50} value of 0.023 mg/mL and inhibited the maltase activity competitively (Abesundara et al. 2004). Oral administration of *C. auriculata* methanol extract in Sprague–Dawley rats significantly and potently lowered blood glycemic response towards maltose ingestion which was observed at 30 minutes after dosing of 5 mg/kg, thus concurrently suppressed insulin activity. The ED_{50} of the extract (4.9 mg/kg) clearly indicated that the antihyperglycemic effect was as potent as that of therapeutic drug, acarbose (ED_{50} 3.1 mg/kg). In another study, oral administration of water-soluble fraction of the ethanol extract of *C. auriculata* flowers to alloxan diabetic rats significantly reduced blood glucose level and elevated plasma insulin level compared to the aqueous extract-treated rats and diabetic control (Hakkim et al. 2007). Treatment with water-soluble fraction of ethanol extract and aqueous extract of *C. auriculata* flowers restored altered hyperlipidaemic parameters and enzymatic markers in diabetic animals. The water-soluble fraction of the ethanol extract exerted a more efficient antihyperglycemic effect compared to the aqueous extract. Surana et al. (2009) reported that the n-butanol fraction of the hydromethanol flower extract exhibited significant reduction in blood glucose levels and was also found effective in restoring the blood lipids and proteins to normal level. The activity was found comparable with standard drug phenformin. The flower and leaf extracts of *Cassia auriculata* exerted a significant reduction in the serum glucose and triglycerides and cholesterol levels and increase in the plasma insulin levels in alloxan-induced diabetic rats when compared to root and stem extracts (Umadevi et al. 2006).

An aqueous leaf extract of *Cassia auriculata* was found to lower the serum glucose level in normal rats and alloxan-induced diabetic rats (Sabu and Subburaju 2002). The extract was also found to inhibit the body weight reduction induced by alloxan administration. Glucose uptake and glycogen deposition studies suggested that *C. auriculata* leaf extract probably had no direct insulin-like effect which can enhance the peripheral utilization of glucose. In separate studies, oral administration of aqueous leaf extract of *Cassia auriculata* (100, 200, 400 and 600 mg/kg bw daily for 21 days) to alloxan-induced mild diabetic (MD) and severe diabetic (SD) rabbits produced dose-dependent fall in

fasting blood glucose up to 400 mg/kg dose from day 3 to day 21 (Gupta et al. 2009b). Further, a significant increase in insulin levels and fall in glycosylated haemoglobin (HbA1c) was observed in both MD and SD rabbits when treated with 400 mg/kg dose of the extract. The extract also caused a significant decrease in serum levels of triglycerides (TG), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) with a concomitant increase in high-density lipoprotein cholesterol (HDL-C) in MD and SD rabbits. Atherogenic indices (TG/HDL-C, TC/HDL-C and LDL-C/HDL-C) were also significantly reduced in both diabetic models of rabbits fed with the extract. Effect of the extract at 400 mg/kg dose was comparable to that of glibenclamide (600 μg/kg), a reference antidiabetic drug. Similar results were obtained with the leaf extract in streptozotocin (STZ)-induced mild diabetic (MD) and severe diabetic (SD) rats (Gupta et al. 2009a). In another study, Gupta et al. (2010) found that aqueous leaf extract of *C. auriculata-treated* mildly diabetic (MD) and severely diabetic (SD) rats showed significant reduction in fasting blood glucose. Assessment of plasma insulin and C-peptide following treatment with the leaf extract revealed significant elevation in their levels. Administration of the leaf extract enhanced the activity of hepatic hexokinase and phosphofructokinase and suppressed glucose-6-phosphatase and fructose-1,6-bisphosphatase in both MD and SD rats. A significant rise in glycogen content was also observed in both liver and muscles of leaf extract-fed MD and SD rats. Histopathological examination of pancreatic sections revealed increased number of islets and β-cells in leaf extract-treated MD as well as SD rats. The results of the study suggested that the antidiabetic effect of the leaf extract could be due to its insulinogenic action as well as through pancreatic as well as extrapancreatic action. In another recent study, supplementation of *C. auriculata* aqueous leaf extract to the streptozotocin-induced diabetic rats produced significant reduction in fasting blood glucose along with significant reversal in altered serum lipid profile and apolipoprotein B (Gupta et al. 2011). Lipid peroxidation was found to be significantly suppressed in extract-fed diabetic rats. Significant reduction in serum levels of oxidized low-density lipoprotein, soluble vascular cell adhesion molecule and plasma fibrinogen with a concomitant elevation in serum nitric oxide was observed in diabetic rats following treatment with extract. Histopathological examination of heart myocardium of extract-treated diabetic rats revealed reversal of fatty change towards normal. The results suggested that *C. auriculata* aqueous leaf extract exhibited anti-atherosclerotic role in the diabetic state and may help to prevent the progression of cardiovascular diseases.

Gold nanoparticles (AuNPs) using *Cassia auriculata* aqueous leaf extract were synthesized, and the stabilizing and reducing molecules of nanoparticles may promote antihyperglycemic effect but required further testing (Kumar et al. 2011). Green leafy *Cassia auriculata* porridge should not be recommended as breakfast meals for diabetics because of its high GI (77) compared to other green leafy porridges (Anuruddhika and Ekanayake 2013).

Oral administration of ethanol (400 mg/kg) and aqueous extract (250, 500 mg/kg) of whole plant of *C. auriculata* to streptozotocin-induced neonatal model of non-insulin-dependent diabetes mellitus (NIDDM) rats led to suppression in elevated glucose, cholesterol and triglycerides levels (Juvekar and Halade 2006).

Diamed an herbal formulation composed of the aqueous extracts of three medicinal plants (*Azadirachta indica, Cassia auriculata* and *Momordica charantia*) was found to have antihyperglycaemic action in alloxan-induced experimental diabetes in rats (Pari et al. 2001). Oral administration of Diamed resulted in a significant reduction in blood glucose, glycosylated haemoglobin, and an increase in plasma insulin and total haemoglobin. Diamed also prevented a decrease in body weight.

Antihyperlipidaemic Activity

The crude extract of *C. auriculata* aerial parts displayed in-vitro inhibitory activity against pancreatic lipase with IC_{50} of 6.0 μg/mL

(Habtemariam 2013). The most active antilipase compound in the extract was kaempferol-3-*O*-rutinoside with IC_{50} value (2.9 μM) only about twice weaker than the standard antilipase drug, orlistat (IC_{50} = 1.45 μM). Luteolin, quercetin and rutin were found to be weak pancreatic lipase inhibitors (IC_{50} > 100 μM), whereas kaempferol showed no activity up to 250 μM.

Cassia auriculata flowers were found to possess antihyperlipidaemic effect in addition to antidiabetic activity (Pari and Latha 2002). Oral administration of aqueous flower extract of *C. auriculata* suppressed the elevated blood glucose and lipid levels in streptozotocin-induced diabetic rats. The effect was found to be comparable to glibenclamide. Administration of the ethanol extract of *C. auriculata* flowers to triton WR 1339 induced hyperlipidaemic rats to revert the parameters of hyperlipidaemia to normal (Vijayaraj et al. 2011, 2013). Treatment with the extract significantly reduced the total cholesterol (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL) levels and significantly increased the high-density lipoprotein (HDL) level associated with reduction of atherogenic index in hyperlipidaemic rats. Lipid peroxidation decreased whereas the activities of superoxide dismutase, glutathione peroxidase and catalase increased in extract treated rats. Pronounced changes were comparable to the standard drug lovastatin.

Hepatoprotective Activity

The study of Kumar et al. (2002) showed that treatment with *C. auriculata* leaf extract had a lipid-lowering effect in rats with experimentally induced, alcohol-related liver damage. This was associated with a reversal of steatosis in the liver and of spongiosis in the brain. They reported that administration of *C. auriculata* leaf extract to rats with alcohol-induced hepatotoxicity significantly lowered the levels of thiobarbituric acid reactive substances (TBARS) and hydroperoxides and elevated the activities of superoxide dismutase (SOD) and catalase (CAT) and the levels of reduced glutathione (GSH) in the liver, brain, kidney and intestine compared to unsupplemented alcohol-treated rats (Kumar et al. 2003). The leaf extract restored the serum vitamin E and vitamin C levels also to near those of the experimental control animals. Histopathological studies of the liver and brain confirmed the beneficial role of *Cassia auriculata* leaf extract.

Nephroprotective Activity

The ethanol root extract of *Cassia auriculata* at doses of 300 and 600 mg/kg body weight reduced elevated blood urea and serum creatinine and normalized the histopathological changes in the curative regimen in cisplatin-induced renal injury in male albino rats (Annie et al. 2005). In the gentamicin-induced renal injury model, the ethanol extract at a dose of 600 mg/kg body weight reduced blood urea and serum creatinine effectively in both the curative and the preventive regimen. The probable mechanism of nephroprotection by *C. auriculata* against cisplatin- and gentamicin-induced renal injury could be due to its antioxidant and free radical scavenging property.

Immunomodulatory Activity

Polyphenols derived from *Cassia auriculata* were found to boost T-cell immunity by increasing the number of T cells and B cells percentage along with enhanced proliferation of splenocytes in both resting and LPS-stimulated cells in aged rats (John et al. 2011). *Cassia* polyphenol supplementation reduced the oxidative burst activity of neutrophils in response to PMA (phorbol myristate acetate) and *Escherichia coli* activation that could potentially harm multiple biological systems in aged rats.

Neuroprotective Activity

Streptozotocin diabetic rats treated with aqueous flower extract of *Cassia auriculata* or glibenclamide

showed significant decrease in thiobarbituric reactive substances (TBARS) and hydroperoxide formation in the brain, suggesting the role of the extract in protection against lipid peroxidation-induced membrane damage by antiperoxidative efficacy (Latha and Pari 2003b).

Laxative Activity

Studies showed that the ethanol pod extract of *C. auriculata* (200 mg/kg p.o.) exhibited laxative activity in rats (Suresh et al. 2007). The ethanol extract induced an increase in gastrointestinal transit as compared to control. It was also concluded that the anthracene derivatives present could be attributed for the laxative activity.

Antipyretic Activity

The flower and leaf extracts of *C. auriculata* were reported to have antipyretic activity (Vedavathy and Rao 1991).

Herbal Drug–Drug Interaction

Studies demonstrate that a significant increase (32.5 %) in the steady state levels of theophylline occurred when this drug was administered concurrently with herbal tea-prepared dried flowers of *Cassia auriculata* (Thabrew et al. 2004b). They cautioned that herbal teas prepared from *C. auriculata* should therefore be avoided by patients treated with theophylline as these herbal teas had the potential to influence the bioavailability of the prescription drug. They also found that *C. auriculata* tea had the potential to influence the bioavailability of carbamazepine and hence its therapeutic actions. They demonstrated that in rats receiving the *Cassia auriculata* tea and carbamazepine, the blood levels of the prescription drug were significantly enhanced by 47.1 %, when compared with the levels in animals receiving only carbamazepine for the same time period, with no apparent changes in toxicity. Concurrent ingestion of carbamazepine with herbal teas containing *Cassia auriculata* was therefore best avoided by patients under treatment for epilepsy.

Antiplasmodial Activity

The methanol leaf extract of *C. auriculata* showed promising antiplasmodial activity against blood stage CQ-sensitive (3D7) and CQ-resistant (INDO) strains of *Plasmodium falciparum* in culture with IC_{50} value of 14 μg/mL. The high TC_{50} in mammalian cell cytotoxicity assay and the low IC_{50} in antimalarial *P. falciparum* assay indicated selectivity and good resistance indices for the leaf extract.

Insecticidal Activity

Benzene root extract was found to be most potent among all extract showing comparable paralysis of *Pheretima posthuma* and death time comparable to the standard anthelmintic drug albendazole (Wadekar et al. 2011). Phytochemical analysis of the crude root extracts revealed the presence of an array of active chemical constituents such as tannins, flavonoids, glycosides, carbohydrates, steroids and triterpenoids. The petroleum ether, ethyl acetate, ethanol and aqueous extracts of *Cassia auriculata* leaves exhibited dose-dependent anthelmintic activity against the earthworm, *Eisenia foetida* (Kainsa et al. 2012). The decreasing order of activity of extracts was ethyl acetate, ethanol, petroleum ether and aqueous extracts.

Insecticidal Activity

The acetone, chloroform, ethyl acetate, hexane, methanol and petroleum ether extracts of leaf, flower and seed of *Cassia auriculata* showed moderate larvicidal effects; however, the highest

mortality was found in leaf petroleum ether, flower methanol extracts of *C. auriculata*, against the larvae of *Anopheles subpictus* (LC_{50} = 44.21, 44.69 ppm; LC_{90} = 187.31, 188.29 ppm, respectively) and against the larvae of *Culex tritaeniorhynchus* (LC_{50} = 69.83, 51.29 ppm; LC_{90} = 335.26, 245.63 ppm, respectively) (Kamaraj et al. 2009).

The leaf ethyl acetate and flower methanol extracts of *C. auriculata* exerted highest mortality of the larvae of cattle tick *Rhipicephalus (Boophilus) microplus*; the leaf methanol exhibited antiparasitic activity against adult hematophagous fly, *Haemaphysalis bispinosa* (Kamaraj et al. 2010).

Safety/Toxicity Studies

Animal studies by Puranik et al. (2011) found that the traditional hydroalcoholic extract and technology-based supercritical extract of *Cassia auriculata* (CA) seeds to be pharmacologically safe and did not show any significant adverse reactions at the tested doses (250 mg to 1,000 mg/kg). The traditional hydroalcoholic extract did not show any significant effect on pharmacokinetics; however, the technology-based supercritical extract caused a significant reduction in absorption of metformin when co-administered. No rat mortality was observed during the treatment period of 12 weeks in either the control or treated groups. No significant change in total bilirubin, TC, TG, glucose and creatinine was observed. There was no significant difference between both systolic and diastolic blood pressure between CA extract-dosed animals and controls. ECG variables like heart rate (R-R interval), QT interval (diastolic dysfunction) and ventricular hypertrophy (R wave amplitude) were normal in all the groups.

Cassia auriculata was found to have pyrrolizidine alkaloids (Arseculeratne et al. 1981). Feeding trials in rats with materials from the plant produced liver lesions—disruption of the centrilobular veins, congestion or haemorrhage in the centrilobular sinusoids, and centrilobular or focal hepatocellular necrosis—and histopathology in the lungs and kidneys which were in accord with the action of pyrrolizidine alkaloids. The researchers suggested that the consumption of herbal medicines that contain pyrrolizidine alkaloids could contribute to the high incidence of chronic liver disease including primary hepatocellular cancer in Asian and African countries.

Traditional Medicinal Uses

The leaves, flowers, seeds, roots and bark are used for medicinal purposes in traditional medicine. The plant is used for the treatment of skin diseases, asthma, conjunctivitis and renal disorders by the tribal communities of the Chittoor district of Andhra Pradesh (Vedavathy et al. 1997). The Lambadis use the leaves for bone fractures; the Chenchus use the seeds to treat inflammations, diarrhoea, infertility, fever, migraine, night blindness, scorpion sting, leucorrhoea, ulcers and fissures in the mouth, and the stem and root for renal ailments; the Yanadis use the root bark and stem bark for stomach ache and earache. The leaves and fruit are ground into a paste and given as pills orally with limewater for leucorrhoea and menorrhoea in women by the Adivasis tribe of the Eastern Ghats, Andhra Pradesh (Ratnam and Raju 2005). The leaves are used in folk medicine for scorpion bites by the Chencu and Yanadi tribes in Gundla Brahmeswaram Wildlife Sanctuary, Andhra Pradesh (Ratnam and Raju 2008). They also use the whole plant for leucorrhoea and menorrhoea, similarly prepared and the pills are taken orally with milk. In South Travancore, India, the tribal communities use the leaves as a paste with vinegar for external application for various skin diseases (Jeeva et al. 2007). The indigenous communities of Kanyakumari district of Tamil Nadu use a dried leaf paste in vinegar as application on skin diseases once a day till cured (Kingston et al. 2009). In the Haveri district of Karnataka state, India, the village folks use tender cassia leaves mixed with lime in tablet form for stomach ache (Nagnur et al. 2009). Leaves and flowers are used for diabetes and

religious function by the community in the sacred grove of Pallapatti in the Madurai district of Tamil Nadu, India (Ganesan et al. 2009). Traditional healers in the Kancheepuram district of Tamil Nadu prescribe ingestion of the dried flower powder mixed with goat milk to prevent white discharge (Muthu et al. 2006).

The roots and bark are astringent and are used for gargles, as an alterative, and to cure skin diseases, eye troubles and rheumatism (CSIR 1950; Chopra et al. 1986; Duke 1981; Rahmansyah 1991). A decoction of the flowers and the seeds is recommended for diabetes; seeds are used to cure eye diseases, gonorrhoea and gout. In Tanzania the plant is used to treat impotence, which may be related to diabetes (Jansen 2005). Leaves and fruits serve as an anthelmintic and diuretic.

Other Uses

The plant is utilized for green manuring in India and is used for revegetating erodible and sodic soils. The bark is used in India to stupefy fish. The bark yields a valuable tanning material for heavy hides, and goatskin and sheepskin, a black dye and bast fibres can be made into ropes. Handles of small tools can be made from the wood. Branches are used as chewing sticks and toothbrushes. In southern India the flowers are used as a fast yellow dye for leather. In Gujarat, India, the flower buds are used with madder roots (*Rubia cordifolia*) in the galling process prior to dyeing cotton cloth and chintzes red, pink or purple. Boiled seeds are an important ingredient in indigo vats where bacterial fermentation converts the insoluble indigo into soluble leuco-indigo, facilitating the impregnation of the dye by textile fibres.

Comments

The plant is propagated from seeds. Acid scarification or manual scarification of seeds will facilitate germination. The tree also produces root suckers freely.

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Senna siamea

Scientific Name

***Senna siamea* (Lam.) Irwin & Barneby**

Synonyms

Cassia arayatensis sensu Naves, non Litv., *Cassia arborea* Macfad., *Cassia florida* Vahl, *Cassia gigantea* DC., *Cassia siamea* Lam., *Cassia siamea* Lam. var. *puberula* Kurz , *Cassia sumatrana* DC., *Cassia sumatrana* Roxb., *Chamaefistula gigantea* G. Don, *Sciacassia siamea* (Lam.) Britt. ex Britt. & Rose, *Senna sumatrana* Roxb.

Family

Fabaceae, also placed in Caesalpiniaceae

Common/English Names

Blackwood Cassia, Bombay Blackwood, Cassod, Cassod Tree, Iron Wood, Kassod Tree, Pheasant Wood, Siamese Cassia, Siamese Senna, Siamese Shower, Thai Cassia, Thai Copper Pod, Thailand Shower, Yellow Cassia

Vernacular Names

Amharic: Yeferenji Digita
Bangladesh: Minjiri
Brazil: Cássia-Do-Sião, Cássia-Siâmica, Cássia-Siamesa (Portuguese)
Burmese: Mezali
Chinese: Guo Mai Xi Li, Tie Do Mu
Creole: Kasya
French: Bois Perdrix, Casse Du Siam
German: Kassodbaum
India: Seemia, Kassod (Hindi), Hiretangedi, Motovolanyaro, Sima Tangedu (Kannada), Manjakonna, Manjakonnei (Malayalam), Kassod (Marathi) Sima Tangedu, Tangedu (Telugu), Mancal Konrai, Manjal Konrai, Manje-Konne, Celumalarkkonrai, Cimaiyaviri, Cuvarnakam, Karunkonnai, Karunkonrai, Kotakkini, Macantakatukkai, Makaraciya, Mampalakkonrai, Mancalkonrai, Mancatkonrai, Manga Konnei, Mulateciyam, Perumalarkkonrai, Pirampukkonnai, Ponnavirai, Vakai, Visakkini, (Tamil), Kurumbi, Sima Tangedu (Telugu)
Indonesia: Bujak, Dulang, Johar, Juhar, Juwar (Javanese), Jnar, Johor, Juwah (Sumatra)
Ivory Coast: Ando, Akassia
Japanese: Tagayasan
Khmer: Ângkanh
Laotian: Khi ‘Lek, ‘Khi:Z Hlek
Malaysia: Busok-Busok, Guah Hitam, Jaha, Jahor, Jeragor, Johor, Jual, Petai Belalang, Sebusok
Nepal: Casia
Pakistan: Minjri
Philippines: Robles
Sierra Leone: Mende Sheku Turay
Spanish: Flamboyán Amarillo

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*,
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Sri Lanka: Aramana, Wa (Sinhala), Manga Konnei, Vakai (Tamil)
Swahili: Mjohoro
Taiwan: Tie Dao Mu
Thai: Khi Lek, Khi Lek Ban, Khi Lek Kaen, Khi Lek Luang, Khi Lek Yai, Phak Chili
Tongan: Kasia
Vietnamese: Muồng Đen, Muồng Xiêm

Origin/Distribution

The species is native to South and Southeast Asia from India through to Malaysia and much of Malesia. It has been introduced to other humid tropical countries.

Agroecology

S. siamea will grow in a range of climatic conditions but is particularly adapted to the warm lowland tropics with a monsoon climate, with mean annual temperatures of 20–31°C and mean annual rainfall of 500–2,800 mm. It is found growing from sea level to 1,000 m altitude. It does not grow well in at altitudes above 1,300 m and will not survive in areas where the temperate falls below 10 °C. It tolerates seasonal flooding and exposure to strong winds but is cold, drought and salinity intolerant. It thrives on deep, well-drained soil rich in organic matter but will grow on degraded lateritic soils provided drainage is not impeded.

Edible Plant Parts and Uses

The young leaves have a bitter taste; young tender pods and inflorescences (buds/open flowers) are edible (Facciola 1990; Padumanonda and Gritsanapan 2006; Maisuthisakul et al. 2008; Kaisoon et al. 2011). The young leafy shoots (Plate 3) and young inflorescences are bundled and sold in markets as vegetables (Jacquat 1990). The leaves and flowers are popularly used in soups and in the Thai curry dish known as 'kaeng khi-lek' which is prepared with and without coconut milk (Monkheang et al. 2011). The fresh young leaves are boiled with water 2–3 times to get rid of the bitterness and to reduce the toxic barakol content before the boiled mush is used for curry. They are also pickled in brine. In Sri Lanka, the flowers and young fruits are used in curries.

Botany

A medium-sized, evergreen, much-branched perennial tree to 30 m tall with a straight trunk of 30 cm diameter with gray bark and a spreading crown of dense foliage (Plate 1). The leaves are alternate and pinnate, 23–33 cm long, and made up of 5–14 pairs of lanceolate, oblong or ovate-elliptic leaflets (Plates 1, 2 and 3), 3–7 cm long and 12–20 mm wide, abaxially finely pubescent, adaxially smooth and glabrous, base rounded and apex obtuse, borne on 25–40 mm long, terete petioles with caducous, minute subulate stipules.

Plate 1 Flowers, leaves and pods

Plate 2 Pinnate leaves

Plate 3 Tender leafy shoots sold as vegetables

Flowers occur in many-flowered, axillary or terminal, 40 cm long, racemose panicles (Plate 1). Flower 3 cm across, pedicellate, bisexual, zygomorphic, pentamerous, hypogynous; sepals imbricate, suborbicular, obtuse at the apex, pubescent outside; petals subequal, broadly obovate, bright yellow, shortly clawed; stamens 10, 7 fertile, accrescent towards the abaxial side of the flower, anther with apical pores; ovary superior, sessile, pubescent, linear and slightly curved. The fruits are pendant, linear, flat and often slightly curved legumes, 5–30 cm long, 12–20 mm wide, coriaceous or subwoody, and dark brown and dehiscent when ripe. Each fruit contains about 25 subglobose to ovate and laterally flattened seeds with a glossy, smooth, dark-brown testa.

Nutritive/Medicinal Properties

Flower Nutrient/Phytochemicals

Proximate nutrient composition of the edible flowers was reported in g/100 g edible portion as moisture 74.8 %, ash 5.6 g, protein 19.4 g, fat 1.6 g, carbohydrate 34.9 g, energy 231.7 kcal, dietary fibre 38.5 g, Ca 55.6 mg, Fe 6.93 mg and vitamin C483.3 mg (Maisuthisakul et al. 2008). Antioxidant activity (DPPH radical scavenging activity) was 2.4 ($1/EC_{50}$), total phenolics 51.5 mg GAE/g dry basis (db) and total flavonoids 24.8 mg RE/g db. The soluble phenol acids (per g dry weight) identified in *Cassia siamea* flower extract were gallic acid 30.3 µg, protocatechuic acid 638.4 µg, *p*-hydroxy benzoic acid 29.4 µg, vanillic acid 4.2 µg, chlorogenic acid 20.64 µg, caffeic acid 14.93 µg, syringic acid 16.0 µg, *p*-coumaric acid 17.5 µg, ferulic acid 11.6 µg, sinapic acid 10.4 µg and total phenolic acids 793.3 µg (Kaisoon et al. 2011). The flowers contained 455.5 µg total bound phenolic acids made up of *p*-hydroxy benzoic acid 8.8 µg, vanillic acid 3.4 µg, syringic acids 4.7 µg, *p*-coumaric acid 93.3 µg, ferulic acid 128.6 µg and sinapic acid 216.8 µg. The flowers contained 133.7 µg total soluble flavonoid made up of rutin 64 µg, myricetin 4.56 µg, quercetin 61.9 µg and kaempferol 3.21 µg and bound flavonoid 52.9 µg made up of rutin 32 µg, quercetin 10.9 µg and apigenin 10 µg. The DPPH radical scavenging activity (% inhibition) of soluble and bound phenolic fraction of the flower was 97.64 and 38.30 %, respectively. Bound phenolics exhibited lower antioxidant activity than soluble ones. The reducing potential of the soluble and bound phenolic fraction of the flower as evaluated by FRAP (ferric reducing antioxidant power) assay (mmol $FeSO_4$/100 g dry weight) was 7.30 and 26.6 mmol, respectively.

A chromone named chromone 1 was isolated from the flowers (Arora et al. 1971). Cassiadinine, a chromone alkaloid, and (+)-6-hydroxy-mellein, a dihydroisocoumarin, were isolated from the flowers (Biswas and Mallik 1986). Three new alkaloids, cassiarins C–E, and a new chromone, 10,11-dihydroanhydrobarakol, were isolated from the flowers (Oshimi et al. 2009). Cassiarin D was a dimeric compound consisting of 5-acetonyl-7-hydroxy-2-methylchromone and cassiarin C, and cassiarin E was a dimer of cassiarins A and C. The alkaloid cassiarin F was isolated from the flowers (Deguchi et al. 2011).

Seed/Fruit Phytochemicals

A water-soluble polysaccharide composed of D-galactose, D-mannose and D-xylose in a molar ratio 3:6:2 was isolated from *C. siamea* seeds (Khare et al. 1980). Hydrolysis of the methylated polysaccharide furnished five methylated sugars (I) 2, 3 di-*O*-methyl D-xylose, (II) 2, 3 di-0-methyl

D-mannose, (111)2, 3, 4-tri-0-methyl D-galactose, (IV) 2, 3, 6-tri-0-methyl D-mannose and (V) 2, 3, 4, 6-tetra-0-methyl D-galactose in the molar ratio 4:4:2:8:4, while partial acidic hydrolysis yielded five oligosaccharides (I) epimelibiose, (II) mannobiose, (III) mannotriose, (IV) mannosylgalactobiose and (V) xylotetraose. *Cassia siamea* seed oil was found to be a minor source of vernolic and cyclopropenoid fatty acids; it contained palmitic (19.0 %), stearic (7.6 %), oleic (11.6 %), linoleic (42.7 %), malvalic (2.0 %), sterculic (3.1 %) and vernolic (14.0 %) acids (Daulatabad et al. 1988).

A sodium salt of a natural 2-methylchromone was isolated from pods of *C. siamea* (Reddy et al. 1976). An anthraquinone, 1-desmethylchrysoobtusin-2-*O*-glucoside, was isolated from the fruit (Abdallah et al. 1994).

Leaf Nutrients/Phytochemicals

Leaves of *Cassia siamea* together with leaves of 3 other species out of 127 species were classified in the very high class group for both TEAC (Trolox equivalent antioxidant capacity) and SOS (superoxide scavenging) activity. TEAC values on a dry weight basis ranged from 0 to 2,105 μmol TE/g, and SOS values ranged from 0 to 6,206 μmol ascorbate equivalent (AE)/g (Yang et al. 2006). Kuo (2002) reported the young leafy shoot of *C. siamea* to have 20 g dry matter, 1.29 g fibre, 0.92 g sugar, 5.92 g protein, 3.48 mg vitamin C, 97 mg β-carotene, 26 mg Ca and 1.26 mg Fe. The proximate nutrient composition of cassod leaves was reported as follows: moisture content 46.01 %, protein 4.01 %, crude fibre 12.36 %, ash 17.93 %, carbohydrate 7.67 %, crude fat 12.02 % and minerals in ppm, potassium 812, calcium 932, sodium 612, magnesium 876, manganese 35.10, phosphorus 10.84, iron 112, copper 0.84 and lead 0.34 ppm (Smith 2009). Saponins, anthraquinones, phlobatannins and alkaloids were detected in the ethanol leaf extract and also present were antinutrients phytate, tannin and oxalate in trace amounts.

A dioxaphenalene derivative was isolated from *Cassia siamea* leaves and named barakol and its structure determined as 3α,4-dihydro-3α,8-dihydroxy-2,5-dimethyl-1,4-dioxaphenalene (Hassanali et al. 1968). From the leaves were isolated β-sitosterol, cassiamin A, physcion, chrysophanol, *p*-coumaric acid, apigenin-7-*O*-galactoside (thalictiin), and a new chromone cassiachromone with the structure 2-methyl-5-acetonyl-7-hydroxy-chromone (Wagner et al. 1978). Barakol, apigenin and β-sitosterol were isolated from the leaves (Krishna Rao and Murthy 1978). Isoquinoline alkaloids, siamine and siaminines A, B and C, were isolated from the leaves (El-Sayyad et al. 1984). An isoflavone glycoside 2′,4′,5,7-tetrahydroxy-8-*C*-glucosylisoflavone (2′-hydroxygenistein 9-*C*-glucoside) was isolated from the leaves (Shafiullah et al. 1995).

Luteolin; cassia chromone (5-acetonyl-7-hydroxy-2-methylchromone);5-acetonyl-7-hydroxy-2-hydroxymethyl-chromone; 4-(*trans*)-acetyl-3,6,8-trihydroxy-3-methyldihydronaphthalenone; and 4-(*cis*)-acetyl-3,6,8-trihydroxy-3-methyl-dihydronaphthalenone were isolated from the leaves (Ingkaninan et al. 2000). Two alkaloids cassiarins A and B were isolated from the leaves (Morita et al. 2007). Chrobisiamone A, a new bischromone, was isolated from the leaves (Oshimi et al. 2008). Cyclization of 5-acetonyl-7-hydroxy-2-methylchromone in the presence of ammonium acetate resulted in generation of cassiarin A. Six compounds were isolated from the leaves and identified as 2-methyl-5-acetonyl-7-hydroxy-chromone (1), 4-*cis*-acetyl-3,6,8-trihydroxy-3-methyl-dihydronaphthalenone (2), emodin (3), physcion (4), β-amyrin (5) and β-sitosterol (6) (Xue et al. 2010). A triterpene, lup-20(29)-en-1β-3β-diol, was isolated from the plant (Tripathi et al. 1992).

Fresh young leaves of *S. siamea* contained 0.4035 % w/w barakol (Padumanonda and Gritsanapan 2006). Barakol was extracted as pure lemon-yellow crystals from young *S. siamea* leaves with 0.1 % yield (Padumanonda et al. 2007). Barakol content in young leaves, mature leaves and young flowers were 1.67, 0.78 and 1.43 % dry weight, respectively. Total anthraquinone glycosides and total anthraquinones, calculated as rhein, in the fresh young leaves were

0.0523 and 0.0910 % w/w, respectively (Sakulpanich and Gritsanapan 2009). The first and second boiled filtrates contained total anthraquinone glycosides 0.0334 and 0.0031 % fresh weight, respectively. The first boiled leaves contained 0.0161 % fresh weight, and the second boiled leaves contained non-detected amount. Total anthraquinone contents in the first and second filtrates and the first and second boiled leaves were found to be 0.0721, 0.0069, 0.0167 % fresh weight and non-detected amount, respectively. Four new alkaloids, cassiarins G, H, J and K (1–4), were isolated from the leaves, (Deguchi et al. 2012).

Stem/Wood Phytochemicals

From heartwood, a new bianthraquinone, 4,4′-bis(1,3-dihydroxy-2-methyl-6,8-dimethoxy anthraquinone), along with 1,1′-bis(4,5-dihydroxy-2-methyl anthraquinone), chrysophanol and emodin were isolated (Singh et al. 1992). From the stem bark, 19α, 24-dihydroxyurs-12-ene-28-oic acid- 3-*O*-β-D-xylopyra-noside along with anthraquinones, namely, chrysophanol and physcion, were isolated (Singh and Agrawal 1994).

From the stem, three anthraquinone compounds were isolated and identified as chrysophanol, chrysophanol-1-*O*-β-D-glucopyranoside and 1-[(β-D-glucopyranosyl-(1→6)-0-β-D-glucopyranosyl) oxy]-8-hydroxyl-3-methy-9,10-anthraquinone (Lü et al. 2001b), and a chromone glycoside, 2-methyl-5-propyl-7, 12-dihydroxy chromone-12-*O*-β-D-glucopyranoside (Lü et al. 2001b). Five additional compounds were isolated from the stem and identified as β-sitosterol, sucrose, *n*-octacosanol, 2-methyl-5-(2′-hydroxypropyl)-7-hydroxy-chromone-2′-*O*-β-D-glucopyranoside and piceatannol (Lü et al. 2003). Emodin and lupeol were isolated from the ethyl acetate fraction of the stem bark extract (Ajaiyeoba et al. 2008). Triterpenes (lupeol, oleanolic acid, ursolic acid, friedelin, betulin), flavonoids (apigenin, kaempferol, luteolin), anthraquinones (emodin) and phytosterols (stigmasterol, β-sitosterol) were reported in the stem bark (Nsonde Ntandou et al. 2010).

Root Phytochemicals

Anthraquinones, chrysophanol, emodin, and two bianthraquinones, cassiamin A and cassiamin B (Koyama et al. 2002a), another two bianthraquinones(1,1′,3,8,8′-pentahydroxy-3′,6-dimethyl[2,2′-bianthracene]-9,9′,10,10′-tetrone and 7-chloro-1,1′,6,8,8′-pentahydroxy-3,3′-dimethyl[2,2′-bianthracene]-9,9′,10,10′-tetrone, respectively (Koyama et al. 2001a), were isolated from the root bark.

Antioxidant Activity

The alcoholic flower extract of *C. siamea* was found to contain a large amount of polyphenols and also exhibited an immense reducing ability (Kaur et al. 2006). At a concentration of 250 µg/mL, 96 % of DPPH radicals and at 500 µg/mL, 42.7, 32.7 and 64.5 % of O^{2-}, H_2O_2 and NO, respectively, were scavenged by the extract. The extract also inhibited OH radical-induced oxidation of protein (bovine serum albumin) and lipid peroxidation in murine hepatic microsomes. The extract displayed significant antioxidant activity in acute oxidative tissue injury animal model caused by CCl_4-induced hepatotoxicity. Oral administration of the extract at a dose of 50–150 mg/kg of body weight significantly protected from CCl_4-induced elevation in aspartate aminotransaminase (AST) and alanine aminotransaminase (ALT), in the serum; elevation in hepatic lipid peroxidation; depletion of hepatic glutathione (GSH); and decrease in the activities of hepatic antioxidant enzymes: superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT). The extract also protected against histopathological changes produced by CCl_4 such as necrosis, fatty changes and ballooning degeneration. The findings suggested that the alcoholic extract of *C. siamea* flowers had potent antioxidant activity against free radicals, prevented oxidative damage to major biomolecules and afforded significant protection against oxidative damage in the liver.

Antitumour Activity

Anthraquinone monomers isolated from *Cassia siamea* showed higher antitumour-promoting activity than that of bianthraquinones in inhibiting Epstein–Barr virus activation (Koyama et al. 2001b). Emodin and cassiamin B, isolated from *Cassia siamea,* exhibited marked antitumour-promoting effect on two-stage carcinogenesis test of mouse skin tumours induced by 7,12-dimethylbenz[*a*]anthracene as an initiator and 12-*O*-tetradecanoylphorbol-13-acetate (TPA) as a promoter by topical application (Koyama et al. 2002b). In addition, emodin exhibited potent inhibitory activity on two-stage carcinogenesis test of mouse skin tumours induced by nitric oxide donor, (+/−)-(*E*)-methyl-2-[(*E*)-hydroxyimino]-5-nitro-6-methoxy-3-hexeneamide as an initiator and TPA as a promoter.

Antiplasmodial Activity

Crude hot water extracts of *Cassia siamea*, *Jatropha gossypifolia* and *Pavetta crassipes* exhibited 100 % inhibition in vitro against *Plasmodium falciparum* (Gbeassor et al. 1989). Two alkaloids cassiarins A and B isolated from the leaves showed antiplasmodial activity; cassiarin A showed potent activity (Morita et al. 2007). Cassiarin A isolated from *C. siamea* leaves exhibited potent antimalarial activity against *Plasmodium falciparum* in vitro as well as *P. berghei* in vivo (Morita et al. 2009). Based on the premise that interactions of parasitized red blood cells (pRBCs) with endothelium in aorta were especially important in the processes involved in the pathogenesis of severe malaria, they found that cassiarin A showed vasorelaxation activity against rat aortic ring, which may be related with nitric oxide (NO) production. NO had been reported to reduce cytoadherence of pRBC to vascular endothelium. Similarly, a series of a hydroxyl and a nitrogen-substituted derivatives and a dehydroxy derivative of cassiarin A having potent antimalarials against *P. falciparum* with vasodilator activity reduced cytoadherence of pRBC to vascular endothelium. These derivatives showed more potent vasorelaxant activity but not higher inhibition of *P. falciparum* in vitro. The results suggested that cassiarin derivatives may be promising candidates as antimalarials with different mode of actions.

Emodin and lupeol, isolated from the stem bark, were found to be the active principles responsible for the antiplasmodial property with IC_{50} values of 5 μg/mL, respectively, against the multi-resistant strain of *Plasmodium falciparum* (K1) (Ajaiyeoba et al. 2008). Chrobisiamone A, a new bischromone isolated from the leaves, exhibited antiplasmodial activity (Oshimi et al. 2008). Three new alkaloids, cassiarins C–E (1–3), and a new chromone, 10,11-dihydroanhydrobarakol (4) isolated from the flowers, showed moderate antiplasmodial activity against *Plasmodium falciparum* 3D7 (Oshimi et al. 2009). The alkaloid cassiarin F from the flowers showed antiplasmodial activity against *Plasmodium falciparum* (Deguchi et al. 2011). Four new alkaloids, cassiarins G, H, J and K (1–4), isolated from the leaves, showed moderate antiplasmodial activity against *Plasmodium falciparum* 3D7 (Deguchi et al. 2012).

Cardioprotective Activity

Pretreatment with barakol (10 mg/kg i.v.) from *C. siamea* leaves reduced the incidence of aconitine-induced ventricular fibrillation (VF) and ventricular tachycardia (VT) as well as mortality of rats (Chen et al. 1999). It was found that the mechanisms of the protective effects of barakol on aconitine-induced cardiac toxicity may relate to the prevention of intracellular Na + accumulation.

Vasodilating Activity

In rings cut from rat superior mesenteric arteries precontracted with phenylephrine, cassiarin A from *C. siamea*, induced a concentration-dependent relaxation (Matsumoto et al. 2010).

It was found that that the vasodilating effect of cassiarin A may be mediated by endothelial nitric oxide and may occur partly via BK(Ca)-channel activation.

CNS (Anti-insomnia, Analgesic, Anxiolytic) Activities

Animal studies showed that barakol, active compound from *S. siamea*, had anxiolytic properties similar to diazepam but differed from diazepam in that it also increased exploratory and locomotor behaviour, as shown by the number of rears and total arm entries in the elevated plus-maze test (Thongsaard et al. 1996). However, studies by Fiorino et al. (1998) found that barakol (0–20 mg/kg) exhibited no evidence of its anxiolytic effects in either of two pharmacologically validated tests of rat anxiety: the plus-maze or shock-probe burying tests.

Luteolin from *Senna siamea* was found to be an antagonist at the adenosine A(1) receptor binding activity with a *K*(i) value in the low micromolar range (Ingkaninan et al. 2000). Abundant evidence showed that the sleep-inducing effects were mediated locally in the basal forebrain through the adenosine A1 receptor (Alanko et al. 2004). They found that G-protein activity was increased in the cortex but not in the basal forebrain during the first hours of sleep deprivation, suggesting different A1 receptor-mediated responses to increasing adenosine concentrations in different brain areas.

Studies showed that barakol, from *C. siamea*, reduced spontaneous locomotor activity, increased the number of sleeping mice and prolonged the thiopental-induced sleeping time, indicating a sedative effect (Sukma et al. 2002). At a high dose (100 mg/kg, i.p.), barakol slightly prolonged the latency of clonic convulsion induced by the convulsant, picrotoxin, suggesting that the sedative effect may not be induced via the GABA or glycine systems. There was no evidence of an anxiolytic effect of barakol in the plus-maze test. However, barakol (25–100 mg/kg, i.p.) could suppress methamphetamine (1 mg/kg, i.p.)-induced hyperlocomotor activity in a dose-dependent manner, indicating an effect on the dopaminergic system. The results indicated that the CNS inhibitory effect of barakol on dopamine release may account for the blocking effect of barakol on the striatum-related behaviour induced by methamphetamine. Acute and chronic oral administration of barakol (10, 30 and 100 mg/kg, p.o.) had no anxiolytic and locomotor effects on male Wistar rats (Deachapunya and Thongsaard 2009). However, it exerted a sedative effect as shown by a reduction in the directed exploratory behaviours.

Studies showed that intraperitoneal administration of low-dose (25 mg/kg) and high-dose (100 mg/kg) barakol resulted in sleeping behaviour in Long-Evans hooded rats, substantiating the use of the cassod leaves for insomnia commonly prescribed in Thai traditional medicine (Bulyalert 2011). The acetic acid-induced writhing test in mice showed that ethanol leaf extract of *Senna siamea* at the dose of 500 mg/kg exhibited significant inhibition of writhing reflex by 61.98 % while the standard drug diclofenac Na inhibition was found to be 85.95 % at a dose of 25 mg/kg body weight (Momin et al. 2012).

Antiinflammatory and Analgesic Activity

At the doses used (100, 200 and 400 mg/kg), ethanol and water extracts of *Cassia siamea* stem bark showed significant and dose-dependent analgesic and antiinflammatory effects in the hot-plate test, paw pressure and carrageenan-induced paw oedema tests (Nsonde Ntandou et al. 2010). None of the extracts had cytotoxic activity on KB and Vero cell lines, and the most active extracts (CSE3 and CSE4) had no acute toxicity. These activities were attributed to the presence of triterpenes (lupeol, oleanolic acid, ursolic acid, friedelin, betulin), flavonoids (apigenin, kaempferol, luteolin), anthraquinones (emodin) and phytosterols (stigmasterol, β-sitosterol) in the stem bark.

Antiviral Activity

Seven new chromones, siamchromones A–G (1–7), and 12 known chromones (8–19) were isolated from *Cassia siamea* stems (Hu et al. 2012). Compound 6 showed anti-tobacco mosaic virus (anti-TMV) activity with an inhibition rate of 35.3 % and IC_{50} value of 31.2 μM, which was higher than that of the positive control, ningnamycin. Compounds 1, 10, 13 and 16 showed anti-TMV activities with inhibition rates above 10 %. Compounds 4, 6, 13 and 19 showed anti-HIV-1 (anti-human immunodeficiency virus-1) activities with therapeutic index values above 50.

Antimicrobial Activity

The ethanol extracts of *C. siamea*, *Syzygium jambolanum* and alga *Caulerpa scalpelliformis* exhibited antifungal activity at 100 mg/mL against *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida krusei*, *Candida parapsilosis* and *Candida guilliermondii* (Prabhakar et al. 2008). The ethanol leaf extracts showed the highest activity at 40 mg/mL concentration against *Salmonella typhi* followed by acetone extracts, while the aqueous extracts showed the lowest activity (Doughari and Okafor 2008). The MIC and MBC values of the crude extracts (1–3 mg/mL) were comparable to those of the tested antibiotics (ampicillin, chloramphenicol, cotrimoxazole and ciprofloxacin). Purification of the ethanol extract showed that the ethyl acetate fraction possessed the highest activity followed by *n*-butanol fraction while the chloroform fraction did not show any activity at 20 mg/mL. The ethanol leaf extract of *Senna siamea* exhibited antibacterial activity against *Pseudomonas aeruginosa* at concentration of 500 μg/disc in comparison with the standard kanamycin (Momin et al. 2012).

Secretagogue Activity

Studies demonstrated that barakol stimulated bumetanide-sensitive chloride secretion in rat colon (Deachapunya et al. 2005a). The effect of barakol was partly mediated by the stimulation of submucosal nerves and through the release of cyclooxygenase metabolites. The results elucidated the underlying mechanism of barakol as a secretagogue in mammalian colon.

Purgative Activity

Barakol was found to have purgative effects (Deachapunya et al. 2005b). Barakol extract increased the force of spontaneous muscle contractions in the rat ileum in a concentration-dependent manner. Pretreatment of muscle strips with barakol (1 mM) significantly decreased the inhibitory effect of norepinephrine by 60 %, but not that of dopamine. Its ability to potentiate atropine- and saxitoxin-sensitive contractions and inhibit the antimotility actions of norepinephrine suggested that barakol may increase longitudinal smooth muscle contractions by decreasing the inhibitory effect of norepinephrine on excitatory cholinergic motor neurons. The authors concluded that barakol may produce a purgative action in small intestine which may be clinically important in patients with intestinal hypomotility disorders.

Antidiabetic Activity

Oral administration of cassod leaf extracts at doses of 250 and 500 mg/kg for 3 weeks significantly improved blood glucose levels and body weights in normal and streptozotocin-induced diabetic rats (Kumar et al. 2010). Daily oral treatment with the extract also resulted in significantly reduction of serum cholesterol and triglycerides and improvement in HDL cholesterol level.

Mosquitocidal Activity

The leaf methanol extract of *C. siamea* exhibited 100 % mortality against *Anopheles stephensi* (malaria vector) and *Culex quinquefasciatus*

(filariasis vector) after 48-hour exposure, suggesting that the extract has the potential to be used as an ideal eco-friendly approach for the control of both mosquito vectors (Kamaraj et al. 2011).

Laxative Activity

Studies showed that the process of preparation of Khi Lek curry by boiling *S. siamea* young leaves twice with water reduced total anthraquinone glycosides content by more than 75 %, confirming the traditional use of Khi Lek curry as a very mild laxative drug (Sakulpanich and Gritsanapan 2009). The fresh or dried leaves are used traditionally for constipation in Thailand (Monkheang et al. 2011).

Barakol Toxicity Studies

Studies showed that the process of preparation of Khi Lek curry by boiling *S. siamea* young leaves twice with water was found to reduce barakol content up to 90 % and thus lowering the tendency to cause liver toxicity (Padumanonda and Gritsanapan 2006). Fresh young leaves contained 0.4035 % w/w barakol. The contents of barakol in the first and second boiled filtrates were 0.2052 and 0.1079 % fresh weight, while the first and second boiled leaves samples were 0.1408 and 0.0414 % fresh weight, respectively. This may explain the reason why Thai Khi Lek curry had not caused hepatotoxicity, unlike *S. siamea* leaves consumed as a powdered capsule.

Hongsirinirachorn et al. (2003) studied the adverse effects of barakol in 12 healthy Thai patients, aged 29–81 years (mean 52.5) with neither a history of chronic liver disease nor known hepatotoxic substance ingestion, who took barakol for 3–180 days (mean 76.9). Eight of them were admitted with the first episode of anorexia and jaundice for 4–60 days after taking 20–40 mg/day (2–4 tablets) of barakol. The mean total bilirubin was 5.7 mg/dL, and liver function test revealed moderate to severe hepatitis (aspartate amino transferase (AST) range 111–1,473 U/L: mean = 692). Histopathological findings were in accord with interface hepatitis. Their symptoms and liver function completely improved within 2–20 weeks (mean 5.9) after barakol abstinence.

Barakol was hepatotoxic in mice, causing liver injury when administered in a single dose (100, 200, 300 and 400 mg/kg, p.o.) and repeated doses (100, 200 and 300 mg/kg/day, p.o., 28 days) for acute and subacute toxicity studies, respectively (Devakul Na Ayutthaya et al. 2005). The acute and subacute hepatotoxic findings included the increase in total bilirubin, AST and ALT concentrations and the decrease in cholesterol, triglyceride and glucose levels which corresponded to the histopathological examination showing the hydropic swelling of hepatocytes, scattered degree of necrotic cells around central vein spreading to periportal zone and finally apoptotic cell death around centrilobular zone spreading to periportal area. The degree of the severity of barakol-induced liver injury was dose and time dependent. There were signs of liver regeneration and recovery in all doses of barakol treatment. A 6-month chronic toxicity study of powdered cassod leaves in Wistar rats showed that at the doses of 200 and 2,000 mg/kg bw/day, the levels of bilirubin were significantly increased compared to control rats (Chavalittumrong et al. 2012). A dose-dependent increase of the incidence of hepatic lesion, namely, degeneration and necrosis, was found at every dose level in both male and female animals. It appeared that male rats were more susceptible to the hepatotoxic effect of cassod than female rats. Reduction of the hepatic damage of the recovery group suggested that the hepatotoxic effect of *C. siamea* was reversible when the drug was stopped for only 14 days.

Treatment with barakol decreased cell viability in a concentration- and time-dependent manner with an IC_{50} value of 1.5 mM in 24-h-treated mouse embryonal carcinoma P19 cells (Wongtongtair et al. 2011). Barakol-induced cytotoxicity was due to a significant increase in the number of apoptotic cells. The mechanism of barakol-mediated toxicity in P19 cells was mainly attributed with the ROS generation, followed by the imbalance of the Bax/Bcl-2 ratio,

and caspase-9 activation leading to apoptotic cell death. Pretreatment of cells with *N*-acetyl-l-cysteine could antagonize the toxicity produced by barakol.

Subchronic toxicity studies showed that *S. siamea* stem extract significantly increases the body weight and feed intake of the male Wistar rats but did not significantly affect haematological parameters, total protein and albumin levels, serum glucose, triglycerides, cholesterol and the markers of kidney function (creatinine, urea, potassium, sodium and chloride) (Mohammed et al. 2012). However, levels of serum liver enzymes (alkaline phosphatase (ALP), alanine aminotransaminase (ALT) and aspartate aminotransaminase (AST)) were significantly different from the normal control group. The quantitative determination of saponins, alkaloids, total polyphenolics and flavonoids in (g/g) were found to be 0.07, 0.05, 0.92 and 0.06, respectively. These results may explain the use of *S. siamea* stem bark in folk medicine due its less toxic effect.

Traditional Medicinal Uses

The plant is commonly used in traditional medicine to treat hypertension, malaria and diabetes mellitus (Mohammed et al. 2012). In Burkina Faso, a decoction of the leaves with lemon juice is used for the treatment of fevers (Fowler 2006). In northern Nigeria, the tree is very popular for its local usage in the treatment of typhoid fever. In Kampuchea, a hardwood decoction is used against scabies. The fruit and seeds have been used to treat intestinal worms. In Thailand, the leaves and flowers are used as a remedy for insomnia, as laxative for constipation and as appetite stimulant and digestive stimulant; flower and root decoctions are used to treat anxiety, nervousness and stress, and wood decoction for fever (Thongsaard et al. 1996; Sukma et al. 2002; Deachapunya et al. 2005a; Sakulpanich and Gritsanapan 2009; Bulyalert 2011; Monkheang et al. 2011). The flowers are used to treat insomnia and asthma in traditional medicine (Kaur et al. 2006).

Other Uses

Senna siamea is cultivated as windbreaks, shelterbelts, live fence, boundary markers, ornamental in parks and gardens, wayside tree and shade tree for tea, cocoa and coffee plantings. The tree is also used for erosion control, for land reclamation in former tin/aluminium mining sites and in alley cropping systems in agroforestry, largely because of its coppicing ability and high biomass production shade besides also for its nitrogen-fixing capability. In India, it is used as a host for the semiparasitic sandalwood (*Santalum* spp.). In China, it has been cultivated as fuelwood by the Dai people since 400 years ago and as a host plant for lac insects. Its foliage is rich in nitrogen and organic matter and is used as green manure. The foliage can be used as browse or fodder for cattle, sheep and goats but are toxic to poultry and swine. The flower is an important nectar source for bees.

The tree afford a hard, heavy, dense, durable, dark blackish brown and termite-resistant wood that is used in joinery, cabinet making, furniture, inlaying, tool handles, walking sticks, posts, bridges, mine poles and beams and other decorative carvings. All parts of the tree including the bark can be used for tanning.

Comments

Cassod is easily and readily propagated from seeds, although stumps can be used.

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Senna timoriensis

Scientific Name

***Senna timoriensis* (DC.) H. S. Irwin & Barneby**

Synonyms

Cassia arayatensis Litv., *Cassia exalta* Blume, *Cassia goensis* Dalzell, *Cassia montana* Naves & Villar, *Cassia montana* auct.non Roth, *Cassia timoriensis* DC., *Cassia timoriensis* DC. basionym, *Senna glauca* Roxb.

Family

Fabaceae also placed in Caesalpiniaceae

Common/English Names

Arremene, Golden Bird, Limestone Cassia

Vernacular Names

Burmese: Taung-Mezali, Taw-Mezalie
Indonesia: Eheng, Hing, Ihing, Nyinging, Ture, Waringinan (Javanese), Haringhin (Sundanese) Kayu Pelen (Timor)
Malaysia: Beresksa, Beksa, Babatai, Bebatai, Sinteng Hutan (Malay)
Philippines: Malamalunggai
Thai : Khi Lek Daeng, Khi Lek Lueat, Khi Lek Pa
Vietnamese: Muồng Đỏ, Muồng Tía, Khỉ Pọi

Origin/Distribution

The species is native to India, Ceylon, Myanmar, Thailand and through the Malay Peninsula to Northern Australia.

Agroecology

It is a drought-tolerant species naturalized in low elevations from sea level to 200 m. It usually occurs in disturbed sandy sites, sandstone outcrops, stony slopes or in thickets in limestone areas in its native range. It is also cultivated as ornamental and avenue trees.

Edible Plant Parts and Uses

The bitter young leaves and inflorescence/flowers are edible, cooked as vegetables in Thailand (Pongpangan and Poobrasert 1985). Young leaves and flowers can be used as vegetable by soft boiling and eating with chilli sauce (Monkheang et al. 2011). Both plant parts are sold in local markets in Thailand.

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Botany

A small, evergreen, perennial tree or shrub usually 2–6 m but may grow to 10 m high, pubescent on vegetative parts, inflorescence, sepals and ovary, otherwise glabrous. Leaves pinnate, 14–20 cm long with a terete 10–15 mm long petiole, acicular stipules and comprising 10–20 pairs of narrowly oblong to narrowly elliptic, 1.5–5.5 cm long by 0.8–1.7 cm wide leaflets, obtuse, apiculate and eglandular (Plates 1 and 2). Inflorescence corymbose paniculate, axillary or terminal, bract linear, flowers pedicellate, pentamerous with five unequal sepals, five yellow obovate, clawed petals and ten stamens (seven fertile and three staminodes) with subequal filaments and unequal anthers, ovary superior with 1 style and stigma (Plate 1). Fruit a long narrow, flat, legume, 6–15 cm long by 1–1.5 cm wide, septate with 10–20 shiny brown, suborbicular seeds.

Plate 1 Flowers, pods and leaves

Plate 2 Young tender leafy shoots sold as vegetables in the local markets

Nutritive/Medicinal Properties

Aloe emodin and 2,5-dimethyl-3α*H*-pyrano [2,3,4-de]-l-benzopyran-3α,8-diol (barakol) were isolated from *Cassia timoriensis* leaves (Gritsanapan et al. 1984).

Cassia timoriensis plant extract was one of several Thai medicinal plants that exhibited good antioxidant activity and could completely inhibit Heinz body formation at the dilution of 1:20 (Palasuwan et al. 2005). Heinz bodies are intracellular precipitates formed by damage to the haemoglobin component molecules in erythrocytes, usually through oxidant damage.

Traditional Medicinal Uses

C. timoriensis is used for scabies and itch and as a vermifuge (Toruan-Purba 1999). The plant is used as medicine for menstrual disorders, tonic, antitumour, blood stasis and cough in Thailand (Palasuwan et al. 2005); the heartwood is used as a traditional medicine by women to stimulate menstrual blood flow (Monkheang et al. 2011).

Other Uses

The plant is commonly grown as ornamental tree in parks and gardens or as shade trees along roads. The wood is used for matchsticks, matchboxes, joinery, cement casks and decorative items.

Comments

The plant is propagated from seeds or stem cuttings.

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Sesbania grandiflora

Scientific Name

***Sesbania grandiflora* (L.) Pers.**

Synonyms

Aeschynomene coccinea L. f., *Aeschynomene grandiflora* (L.) L., *Agati coccinea* (L. f.) Desv., *Agati grandiflora* (L.) Desv., *Coronilla coccinea* (L. f.) Willd., *Coronilla grandiflora* (L.) Willd., *Coronilla grandiflora* Boiss, *Dolichos arborescens* G. Don, *Dolichos arboreus* Forssk., *Emerus grandiflorus* (L.) Kuntze, *Resupinaria grandiflora* (L.) Raf., *Robinia grandiflora* L., *Sesban coccinea* (L.f.) Poir, *Sesban grandiflora* (L.) Poir., *Sesban grandiflorus* Poir., *Sesbania coccinea* (L.f.) Pers.

Family

Fabaceae, also placed in Papilionaceae

Common/English Names

Agathi, Agati Sesbania, August Flower, Australian Corkwood Tree, Corkwood Tree, Flamingo Bill, Grandiflora, Hummingbird Tree, Scarlet Wisteria Tree, Sesban, Sesbania, Swamp Pea, Tiger Tongue, Vegetable-Hummingbird, West Indian Pea, West Indian Pea Tree, White Dragon Tree

Vernacular Names

Arabic: Saysabān
Burmese: Pauk-Pan, Pauk-Pan-Hpyu
Caribbean: Colibri Vegetal, Fleur Papillon
Chamorro: Caturay, Katurai
Chinese: Ta-Hua, Tien-Tsing, Da Hua Tian Jing, Mu Tian Jing
Creole Patois: Pwa Valet, Pwa Valye
Czech: Sesbánie Velkokvětá
Dutch: Agati
French: Agati A Grandes Fleurs, Fagotier, Colbri Vegetal, Fagotier, Fleur Papillon, Papillon, Pois Valette, Pois Vallier, Pois Valliere
German: Kolibribaum, Turibaum, Scharlach Baumwisterie
Hawaiian: Ohai Ke‘Oke‘O
India: Bak Phool (Assamese), Agasthi, Agati, Agusta, Bagphal, Bak, Bak, Bak Phool, Bake, Bakphool, Buko (Bengali), Agathio (Gujarati), Agasati, Agast, Agasti, Agastoya, Agust, Agusta, Bak, Balmota, Basma, Basna, Chogache, Gaach-Munga, Hadaga, Hadga, Hathia, Hathya, Hatiya, Jalt, Jayanti, Jhijan (Hindi), Agace, Agache, Agaci, Agase, Agasemara, Agashi, Agasi, Agastya, Bakapushpa, Chinna Daare, Chogache, Kempagase (Kannada), Agati, Agatti, Agaty, Akatti, Argati, Argatti, Athi, Atti (Malayalam), Houwaimal (Manipuri), Agasta, Agastha, Agasthi, Agasthiya, Agasti, Agastiya, Agathi, Agati, Agosto, Akatti, Chopchini, Haadga, Hatga, Jainti, Shevari, Shewari, Sirimonta (Marathi), Vranari (Oriya), Agasthya, Agasta,

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Agasti, Agastih, Agastivaka, Agastya, Agastyah, Agati, Anari, Buka, Dirghaphalaka, Dirghashimbi, Kanali, Kharadhvansi, Kumbhayoni, Kumbhayonih, Kusuma, Muni, Munidruma, Munidrumah, Munipriya, Munipushpa, Munitaru, Pavitra, Raktapushpa, Shighrapushpa, Sthulapushpa, Surapriya, Vaka, Vakrapushpa, Vakrapuspa, Vakrapuspah, Vamari, Vangasena, Vangasenah, Vranapaha, Vranari (Sanskrit), Acaiyam, Accam, Acci, Acham, Acokam, Acotakatti, Agathi, Agathi Keerai, Agaththi, Agati, Agatti, Akacam, Akaci, Akaddi, Akatti, Akattikkirai, Alakiyal, Alakucivappi, Alakucivappimaram, Ampalacai, Ampalakaimaram, Anali, Aracamiyam, Argati, Arokkiyamatar, Arpakaimaram, Arrokkiyamatar, Athi, Attikkirai, Avappittaniti, Avappittanti, Cakanpanni, Cantirantankacci, Cayanti, Cenkutamaram, Cevvakatti, Cevvakattimaram, Chittakathi, Civappakatti, Civappi, Iyaktam, Kacikavakatti, Kakanaman, Karikam, Karikamaram, Kariram, Karunchempa, Kilimukkumaram, Kilimukkumram, Kiraiyakattimaram, Kopavairini, Kotikkalmaram, Kunali, Kunkumapperikamaram, Malaiyinmunimaram, Malaiyinmunivam, Malaiyinmunivanmara, Malaiyinmunivanmaram, Mayilmunimaram, Mayilmunivam, Mayilmunivan, Mulakariyam, Mulakiyam, Muni, Munipattiri, Munippuntu, Munitalam, Munittorumam, Munitturumam, Mutanki, Nattakatti, Paluppuccarruccattukkati, Pantukam, Pantukamaram, Pattiyamuriccan, Pavalaakatti, Pavalavakatti, Pavalavakattimaram, Peragatti, Pintaputpam, Piraimalar, Pocaki, Pocakimaram, Pocam, Pukal, Pukalmaram, Sevvagatti, Tanavakamaram, Tetcanamuli, Tetcanamurtti, Tirakkappalakam, Tirkkappalakam, Turucu, Tuvatacipattiri, Tuvatecipattiri, Ullulattitam, Uppi, Utumparam, Vaka, Vakai, Vanitam, Vankacenakam, Vellakatti, Vinpakam, Vinpakavakatti, Vintai, Vittari, Vittaru, Vitteri, Vittineruppu, Vittutti, Vittuttimaram, Yatakam (Tamil), Agasi, Agathi, Agise, Agisi, Anaga, Aneesay, Anisay, Aushika, Avasinara, Avesi, Avise, Avisey, Avishi, Avisi, Bakapushpam, Bakku-Pushapamu, Erraagasi, Erraavisi, Erragise, Ettagise, Patta, Suka Nasam, Sukanaasamu, Sukanasamu, Tella-Suiminta, Tellaavesi, Tellaavisi, Tellayavise, Thellayavise, Yerraavesi (Telugu), Agast (Urdu)

Indonesia: Bunga Turi, Kembang Turi (Flowers), Daun Turi, Turi, Tuwi, Toroy (Leaves), Turi Bang (Javanese for red-flowered form), Turi Berem (Sundanese for red-flowered form), Turi Putih (Javanese for white-flowered form), Turi Bodas (Sundanese for white-flowered form), Toroj (Madurese)

Japanese: Agachi, Shiro-Gochou

Khmer: Ângkiëdèi, Pka Angkea Dey

Korean: A Ga Ti, We-Seu-Teu-In-Di-An-Kong-Na-Mu

Laotian: Kh'ê: Kha:W

Malaysia: Turi, Geti, Kacang Turi, Petai Belalang, Sesban, Sesban Getih

Nepali: Agasti

Palauan: Katurai

Persian: Sīsabān

Philippines: Diana (Bagobo), Katurai, Katudai (Ibanag), Katudia, Katodai (Iloko), Gauai-Gauai (Panay Bisaya), Katurai (Pangasingan), Kambang-Turi (Sulu), Katuray, Katurai

Portuguese: Agasto, Sesbânia

Russian: Sesbania Krupnotsvetkovaia

Samoan: Sepania

Slovakian: Sezbánia Veľkokvetá

Spanish: Baculo, Cresta De Gallo, Gallito, Paloma, Pico De Flamenco, Zapaton Blanco

Sri Lanka: Katurumurunga Kolle (Leaves, Sinhalese), Katurumurunga Mala (Flowers, Sinhalese), Attikkirai (Tamil)

Tahitian: Afai, Ofai, Ouai, Oufai

Thailand: Khae Daeng (Chiang Mai), Dok Khae Baan, Kae-Ban, Khae, Ton Kae (Central)

Tibetan: A Ga Sta

Vietnamese: So Đũa

Origin/Distribution

The species is native to South Asia and Southeast Asia with possibly Indonesia as the centre of diversity. It is closely related to the Australian species, *Sesbania formosa*. The species is now distributed pantropically in Africa, Central America, Florida, Hawaii, Southwest China, Northern Australia, the Caribbean and the Pacific Islands.

Agroecology

The tree is found in open fields, near roadsides or waterways, and dikes between the rice fields from sea level to occasionally 1,200 m altitude in its native range. The plant is cultivated in orchards or as backyard trees in remote areas as an ornamental but has a tendency to naturalize. It is adaptable to tropical conditions in areas with mean annual temperatures of 22–30 °C and mean annual rainfall of 2,000–4,000 mm. It prefers a bimodal rainfall distribution, with rapid growth in the wet, but is drought tolerant withstanding extended dry periods of up to 9 months. It is frost sensitive and is intolerant of protracted period of low cool temperatures. It grows on a wide range of soils including alkaline, saline, acid soils with pH down to 4.5, heavy clays and poorly drained and low fertility soils. It is tolerant to brief periods of flooding.

Edible Plant Parts and Uses

In Asia, young leaves, flowers and young pods are used in curries and soups, lightly fried, steamed or boiled (Burkill 1966; Ochse and Bakhuizen van den Brink 1980; JIRCAS 2010). The young, tender pods are cooked similarly to other green beans. The leaves and young tender pods are used as flavouring items in the cuisine of South India (Yadav et al. 2010). In Sri Lanka, the leaves are sometimes added to 'sodhi', a widely eaten, thin coconut gravy. In India, the tender leaves, young green pods and flowers are eaten alone as a vegetable or mixed into curries or salads. The young leaves are chopped and sautéed, perhaps with spices, onion or coconut milk. Seeds are high in protein (33.7 %) and are eaten as famine food in India.

In India, flowers may be dipped in batter and fried in butter. Flowers after removal of the bitter stamens are eaten as vegetables raw or cooked in Southeast Asian countries, namely, Thailand, Laos, Kampuchea, Vietnam, Malaysia, Indonesia and the Ilocos region of the Philippines and also in Bihar, India. In Thailand young shoots and leaves are blanched and eaten with chilli paste '*nam prik kapi*' or 'nam prik plaa raa' (JIRCAS 2010). Young flowers are used as an ingredient in sour curry soups such as 'kaeng som'. The flowers are also consumed raw. They are also fried with pork or shrimps or mixed with flour and fried. In the Philippines, unopened white flowers are a common vegetable, steamed or cooked in soups and stews after removal of the stamen and calyx (Stuart 2012). In Vietnam the flowers are used in soups or stir-fry with meat (Tanaka and Nguyen 2007). In Peninsular Malaysia, the leaves are cooked in coconut milk (lemak) or curry (Saidin 2000), and the flowers are commonly used raw in 'ulam' (Mackeen et al. 1997) or cooked as vegetables as are the young pods (Saidin 2000). In Sarawak, one popular dish is 'duan turi' cooked in coconut gravy with shrimp paste, dried pounded shrimps, pumpkin and chillies (Voon et al. 1988). In Indonesia young leaves and pods eaten as sepan (steamed vegetables) and the flowers are used for making sayor or lalab. 'Petjel' (sauce) can be made of the flowers by adding 'sambal kacang' (Ochse and Bakhuizen van den Brink 1980).

Botany

A small, open-branched, unarmed, perennial tree 5–9 m tall with drooping branches (Plates 1 and 2) and 30 cm trunk with heavily nodulated roots. Leaves glaucous, deep green, pinnately compound to 30 cm long with 20–40 pairs of opposite to alternate leaflets (Plates 1, 2, 3 and 4). Leaflet oblong, to elliptical, obtuse apex, about 2–3 cm long. Inflorescences arise from leaf axils in lax racemes of 2–4 flowers, bracts lanceolate, deciduous, 3–6 mm long. Flowers white or deep pink to red, quite large, 7–9 cm long, corolla with standard and wings, staminal tube and glabrous ovary and style (Plates 1, 2, 3, 4, 5 and 6). Pods pendent, slender, long, 30–55 cm, cylindric, green, indehiscent containing 15–50 seeds. Seed sub-reniform, 6.5 mm × 5 mm × 3 mm, dark brown.

Plate 1 Leaves, fruit and white flowers

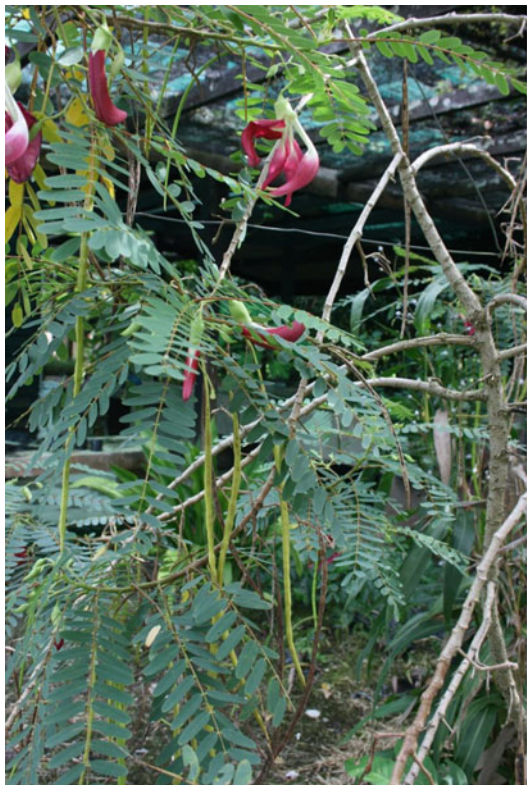

Plate 2 Leaves, fruit and red flowers

Plate 3 Close view of flower and leaf

Plate 4 Tender, leafy shoot used as vegetable

Plate 5 Red and white flowers sold as vegetables

Nutritive/Medicinal Properties

Leaf Nutrients and Phytochemicals

The leaves and flowers of agathi (*Sesbania grandiflora*) were found to be rich in minerals and vitamins. The leaves were reported to contain per 100 g edible portion, 8.4 g protein, 11.8 g carbohydrate, 3.1 g fat, 2.2 g fibre,

Plate 6 Mass of white flowers sold in local markets as vegetables

5,400 µg carotene, 169 mg vitamin C, 0.21 mg vitamin B1, 0.09 mg vitamin B2, 1.2 mg niacin, 3.1 g minerals, 1,130 mg Ca, 80 mg P and 3.9 mg Fe (Devi et al. 2007). Duke (1983) reported that per 100 g ZMB (zero-moisture basis), the leaves contained 321 cal, 36.3 g protein, 7.5 g fat, 47.1 g carbohydrate, 9.2 g fibre, 9.2 g ash, 1,684 mg Ca, 258 mg P, 21 mg Na, 2,005 mg K, 25,679 µg β-carotene equivalent, 1.00 mg thiamine, 1.04 mg riboflavin, 9.17 mg niacin and 242 mg ascorbic acid. The flowers contain per 100 g ZMB, 345 cal, 14.5 g protein, 3.6 g fat, 77.3 g carbohydrate, 10.9 g fibre, 4.5 g ash, 145 mg Ca, 290 mg P, 5.4 mg Fe, 291 mg Na, 1,400 mg K, 636 µg β-carotene equivalent, 0.91 mg thiamine, 0.72 mg riboflavin, 14.54 mg niacin and 473 mg ascorbic acid (Duke 1983). Voon et al., (1988) reported the leaves to contain per100 g edible portion energy 85 kcal, moisture 78.2 %, protein 6 g, fat 0.9 g, carbohydrate 10.9 g, fibre 2.1 g, ash 2 g, P 2 mg, K, 308 mg, Ca 96 mg, Mg 65 mg, Fe 164 µg, Mn 33 µg, Cu 33 µg, Zn 6.6 mg and vitamin C 15.5 mg.

Physicochemical studies of the leaves revealed loss on drying (0.6 %), total ash (10.75 %), acid-insoluble ash (0.045 %), alcohol-soluble extractive (21.7 %) and water-soluble extractive (30.72 %) (Yadav et al. 2010). The leaves were reported to contain alkaloids, saponins, phenols and proteins.

Flower Phytochemicals

The flowers were reported to contain ZMB per 100 g, 345 cal, 14.5 g protein, 3.6 g fat, 77.3 g carbohydrate, 10.9 g fibre, 4.5 g ash, 145 mg Ca, 290 mg P, 5.4 mg Fe, 291 mg Na, 1,400 mg K, 636 µg β-carotene equivalent, 0.91 mg thiamine, 0.72 mg riboflavin, 14.54 mg niacin and 473 mg ascorbic acid (Duke 1983).

Raj and Nagarajan (1984) isolated kaempferol-3-rutinosides from the flowers. Kalyanagurunathan et al. (1985) isolated three active compounds: methyl ester of oleanolic acid, nonacosan-6-one and flavonol glycosides type of molecules, kaempferol-3-rutinosides from the flowers. The flowers were found to have various chemical compounds that could be grouped as flavonoid, anthraquinone, and glycoside (Krasaekoopt and Kongkarnchanatip 2005). Red agati petal (rose-pink to red) of 3 cm length was found to have the highest total anthocyanin content (455 µg/g FW) while hypocotyl of 7-day-old, light-grown Red Agati seedlings also had high anthocyanin content (290 µg/g FW) (Bodhipadma et al. 2006). It was concluded that the hypocotyl of light-grown Red Agati seedlings would be an attractive alternative source of anthocyanins to the petal as the seedlings can be raised and be made available throughout the year.

Yang et al. (2008) found the edible red and white flowers to contain 10.6 %, 10.6 % DM, and 20.4, 22.4 mg/100 g FW of total flavonoids, respectively. The red flower contained (per 100 g FW) 10.1 mg quercetin and 10.3 mg kaempferol while the white flowers contained only 22.4 mg kaempferol and no quercetin. It was found that 70 % alcoholic extract of flowers of *Sesbania grandiflora* had 64.0 mg/g of total phenol equivalent to catechol and 28.80 mg/g of flavonoid content equivalent to quercetin (Shanmukha et al. 2012). The methanol flower extract was found to contain abundant flavonoids, and tannins, alkaloids and anthraquinone glycosides, triterpenes, gums and mucilage (Arthanari et al. 2012). The total polyphenolic content in the acetone flower extract was found to be 49.1 µg/mg and the flavonoid content was 12.86 µg/mg (Munde-Wagh et al. 2012).

Seed Phytochemicals

Seeds (ZMB) were reported to contain 36.5 % CP, 7.4 % fat, 51.6 % total carbohydrate and 4.5 % ash (Duke 1983). The seed oil contains 12.3 % palmitic, 5.2 % stearic, 26.2 % oleic and 53.4 % linoleic acids. The seed testa, which constitutes 20 % of the seed, contains 5.2 % moisture, 1.3 % ash, 0.8 % fat, 2.7 % crude fibre, 0.1 % free reducing sugars, 1.4 % sucrose, 2.8 % nitrogen, 6.3 % pentosans and 65.4 % carbohydrates.

The seed was found to have a galactomannan, with a D-galactose-D-mannose ratio of 1:2 (Srivastava et al. 1968). Methylation of the polysaccharide, followed by hydrolysis, afforded 2,3,4,6-tetra-*O*-methyl-D-galactose, 2,3,6-tri-*O*-methyl-D-mannose and 2,3-di-*O*-methyl-D-mannose in equimolecular proportions. Periodate oxidation of the polysaccharide, followed by reduction and hydrolysis, gave glycerol (1 mol) and erythritol (1.8 mol). The seeds were found to contain kaempferol 3,7-diglucoside, (+)-leucocyanidin and cyanidin 3-glucoside (Andal and Sulochana 1986). The seeds were reported to contain alkaloids, a cyanoglucoside and canavanine (Wenas 1989).

The seed oil of *S. grandiflora* was found to contain (mg/100 g) 258.21 mg total tocopherol, 47.04 mg α-tocopherol, 2.09 mg β-tocopherol, 201.06 γ-tocopherol and 8.02 mg δ-tocopherol, and 74.06 % β-sitosterol, 9.21 % campesterol, 2.06 % Δ^7-avenasterol, 3.02 % stigmasterol, 7.65 %Δ^5-avenasterol and 4 % unidentified sterol (Shareef et al. 2012).

Root Phytochemicals

The roots were found to contain indole acetic acid (IAA), gibberellic acid-like substances (GAs), cytokinin-like substances (CKs) and abscisic acid-like substances (ABA) (Bhowmick and Basu 1984). A steroid was isolated from the roots (Mandey et al. 2003). Three isoflavonoids, isovestitol, medicarpin and sativan, along with another known compound, betulinic acid, were isolated from the root (Hasan et al. 2012). A new biaryl natural product, l,l′-binaphthalene-2,2′-diol, and two known isoflavonoids, isovestitol and sativan, were isolated from the roots (Noviany et al. 2012).

Gum exudates from *S. grandiflora* were found to compose of strongly dextrorotatory, acidic arabinogalactans (Anderson and Wang 1990).

Antioxidant Activity

Studies by Ramesh and Begum (2008) suggested that supplementation with aqueous suspension of *S. grandiflora* reversed the cigarette smoke-induced oxidative damage in rats through its antioxidant potential. Cigarette smoke-enhanced levels of protein carbonyl and activities of cytochrome P450, NADPH oxidase and xanthine oxidase and cigarette smoked-induced decreases in levels of total thiol, protein thiol, non-protein thiol, nucleic acids and tissue protein in the lung, liver, kidney and heart of cigarette smoke-exposed rats were altered and normalized by the extract. The results provided further support for the traditional use of *S. grandiflora* in the treatment of smoke-related diseases. The methanol flower extract of *S. grandiflora* exhibited maximum radical scavenging activity in vitro on nitric oxide, superoxide and hydroxyl radical, and these values were significantly higher over positive standards butylated hydroxyanisole and butylated hydroxytoluene (Loganayaki et al. 2012).

Antidiabetic Activity

Two alpha-glucosidase inhibitors named SGF60 and SGF90 were isolated from the *Sesbania grandiflora* flowers (Boonmee et al. 2007). SGF90 matched a beta-glucosidase from *Arabidopsis thaliana.* SGF60 was similar to p27SJ, a protein from *Hypericum perforatum* and found to suppress HIV-1 gene expression.

Anticancer Activity

Studies showed that a protein fraction, SF2 (Sesbania Fraction 2), isolated from *S. grandiflora*

flowers inhibited cell proliferation and induced apoptosis as evidenced by DNA fragmentation and externalization of phosphatidyl serine in Dalton's lymphoma ascites (DLA) and colon cancer cells (SW-480) (Laladhas et al. 2010). In-vivo studies using ascites and solid tumour models strongly confirmed in-vitro findings as SF2 administration increased the life span and decreased the tumour volume in mice bearing tumour. In-vivo toxicological evaluation revealed the pharmacological safety of SF2, suggesting that it may serve as a potential anti-cancer drug candidate. Administration of *Sesbania grandiflora* ethanol leaf and flower extracts exerted significant decrease in tumour volume, viable cell count and tumour weight and elevated the life span of Ehrlich ascites carcinoma-bearing mice (Sreelatha et al. 2011). Haematological profile such as RBC, haemoglobin and lymphocyte count reverted to normal level in the extract-treated mice. The extracts significantly decreased the levels of lipid peroxidation and significantly increased the levels of GSH, SOD and CAT. The flower extract of *S. grandiflora* inhibited proliferation of human leukaemic cells by inducing autophagy and apoptosis (Roy et al. 2012).

Seven 'ulam' (raw traditional vegetables) extracts, namely, *Anacardium occidentale*, *Garcinia atroviridis*, *Sesbania grandiflora*, *Barringtonia racemosa*, *Polygonum minus*, *Kaempferia galanga* and *Etlingera elatior* displayed cytotoxic activity against the HeLa (human cervical carcinoma) cell line with CD_{50} values in the range of 10–30 μg/ml (Mackeen et al. 1997). The 'ulam' vegetables demonstrated potential as 'functional food' in view of the significant therapeutic and nutritive benefits. The methanol flower extract of *S. grandiflora* exhibited potential cytotoxic activity against human cervical cancer cell line HeLa (IC50 value of 0.13 mg/ml) (Loganayaki et al. 2012).

Antibacterial Activity

Aqueous flower extract exhibited into antibacterial activity against *Bacillus cereus*, *Escherichia coli* and *Staphylococcus aureus* (Krasaekoopt and Kongkarnchanatip 2005). The methanol flower extract of *Sesbania grandiflora* in combination with oxytetracycline exhibited synergistic antibacterial activity against 12 different Gram-positive and Gram-negative bacteria, namely, *Shigella sonnei*, *Escherichia coli*, *Shigella boydii*, *Rhodococcus terrae*, *Micrococcus flavum*, *Flavobacterium devorans*, *Brevibacterium leuteum*, *Bacillus licheniformis*, *Salmonella typhi*, *Klebsiella pneumonia*, *Micrococcus luteus* and *Shigella flexneri* (Kumar et al. 2008). The MIC values ranged from 62.5 to 1,000 μg/ml. The highest synergism effect was attained against *Shigella boydii*. The flower extracts showed good activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escherichia coli* (Munde-Wagh et al. 2012). Polyphenolic extracts (PE) of edible flower of *Sesbania grandiflora* exhibited in-vitro inhibitory effect against *Staphylococcus aureus*, *Shigella flexneri*, *Salmonella typhi*, *Escherichia coli* and *Vibrio cholerae*. The Gram-positive organism *S. aureus* was the most sensitive to the extract with minimum inhibitory concentration (MIC) of 0.013 mg/ml, where *V. cholerae* was not sensitive with a high MIC of 0.25 mg/ml (China et al. 2012).

The butanol fraction of the crude ethanol extract of the stem bark was found to possess the most pronounced antibacterial activity against Gram-negative bacteria (Anantaworasakul et al. 2011). Isovestitol (1), medicarpin (2), sativan (3) and betulinic acid (4) isolated from the roots exhibited antituberculosis activity against *Mycobacterium tuberculosis* H37Rv, with MIC values of 50 μg/ml for compounds 1–3 and 100 μg/ml for compound 4, whereas the methanol root extract exhibited antituberculosis activity of 625 μg/ml.

Das et al. (2013) developed a simple, rapid and effective method for the green synthesis of silver nanoparticles (AgNPs) using leaf extract of *Sesbania grandiflora* and demonstrated their in-vitro potent antibacterial activity against multidrug-resistant (MDR) bacteria such as *Salmonella enterica* and *Staphylococcus aureus*.

Antiviral Activity

Of all the flower extracts (petroleum ether, chloroform, ethyl acetate, ethanol, methanol and water) of *S. grandiflora*, the methanol flower extract exhibited the strongest antiviral activity against the following viruses grown in different cell lines like Hel, HeLa, Crandell Reus feline kidney and Vero cell (Arthanari et al. 2012). *S. grandiflora* flower extracts were found not to be toxic with MIC at 20 μg/ml in Vero cells and 100 μg/ml in the other cell lines. The methanol extract exhibited potent activity against herpes simplex 1 and 2, respiratory syncytical, parainfluenza, reo-1, sindbis, coxsackie and Punta Toro viruses with EC_{50} = 20 and 45 μg/ml and moderate activity against vaccinia, vesicular stomatitis, feline corona, feline herpes and viruses (EC_{50} = 100 μg/ml).

Probiotics Stimulating Activity

Polyphenolic extracts of edible flower of *Sesbania grandiflora* exhibited growth-promoting effect on the common probiotic bacterium *Lactobacillus acidophilus* (China et al. 2012). *S. grandiflora* extract induced a significant biomass increase of *L. acidophilus* grown in liquid culture media.

Antiurolithiatic Activity

The leaf juice of *S. grandiflora* showed significant antiurolithiatic activity against calcium oxalate-type stones as evaluated by a calculi-producing diet model in rats (Doddola et al. 2008). It also exhibited antioxidant properties in scavenging of nitric oxide and 2-diphenyl-2-picrylhydrazyl-free (DPPH) radicals. The leaf juice of *S. grandiflora* was safe orally and exhibited no gross behavioural changes except for an increase in urination.

Antihyperlipidaemic Activity

Administration of a dose of 200 μg/kg (p.o.) aqueous leaf extract of *S. grandiflora* to the triton-induced hyperlipidaemic rats significantly decreased levels of serum cholesterol, phospholipid, triglyceride, LDL and VLDL and significantly increased serum HDL level (Saravanakumar et al. 2010).

Anticonvulsant and Anxiolytic Activities

Studies showed that the benzene:ethyl acetate fraction (BE) of a petroleum ether leaf extract of *S. grandiflora* significantly delayed the onset of convulsions in pentylenetetrazol- and strychnine-induced seizures in mice and reduced the duration of tonic hindleg extension in the maximum electroconvulsive shock (MES)-induced seizures in mice (Kasture et al. 2002). The BE fraction was found to contain a triterpene as a major component. BE also suppressed electrically induced kindled seizures in mice and lithium-pilocarpine-induced status epilepticus in rats. It prolonged the duration of sleep induced by pentobarbital and antagonized the effect of D-amphetamine. Mice treated with BE preferred to remain in the open arm of the elevated plus maze indicating anxiolytic activity. The BE raised the brain contents of gamma-aminobutyric acid and serotonin. Thus, the triterpene containing fraction of *S. grandiflora* exhibited a wide spectrum of anticonvulsant profile and anxiolytic activity.

Hepatoprotective and Nephroprotective Activities

Oral administration of an ethanol extract of *S. grandiflora* leaves (200 mg/kg/day) for 15 days produced significant hepatoprotection against erythromycin estolate (800 mg/kg/day)-induced hepatotoxicity in rats (Pari and Uma 2003). The increased level of serum enzymes (aspartate transaminase, alanine transaminase, alkaline phosphatase), bilirubin, cholesterol, triglycerides, phospholipids, free fatty acids, plasma thiobarbituric acid-reactive substances and hydroperoxides observed in rats treated with erythromycin estolate was significantly decreased

in rats treated concomitantly with sesbania extract and erythromycin estolate. The sesbania extract also restored the depressed levels of antioxidants to near normal. The results of the study reveal that sesbania could afford a significant protective effect against erythromycin estolate-induced hepatotoxicity.

The ethanol extract at doses of 250 and 500 mg/kg, p.o. and aqueous extract at a dose of 500 mg/kg, p.o. of *Sesbania grandiflora* flowers exhibited significant hepatoprotective effect against carbon tetrachloride-induced hepatotoxicity in the liver of Swiss Albino rats (Kale et al. 2012). Both extracts were effective in bringing about functional improvement of hepatocytes.

The petroleum ether extract of *Sesbania grandiflora* fruit exhibited significant dose-dependent (100 mg, 200 mg/kg p.o.) protective effect against thioacetamide- and ranitidine-induced hepatotoxicity in Wistar albino rats (Ramakrishna et al. 2012). The fruit extract completely prevented the toxic effects of thioacetamide and ranitidine on biochemical parameters like serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, alkaline phosphatase, total bilirubin, total cholesterol, total protein and histopathological alterations.

The results of studies by Ramesh et al. (2010) indicated that *S. grandiflora* aqueous leaf suspension significantly decreased the elevated hepatic, renal and lipid peroxidation markers and ameliorated the diminished antioxidant levels while restoring the hepatic and renal architecture in cigarette smoke-exposed rats. They concluded that *S. grandiflora* leaves ameliorated cigarette smoke-induced oxidative damage in liver and kidney of rats.

Studies by Kumaravel et al. (2011) found that *Sesbania grandiflora* protected kidney against alcohol and polyunsaturated fatty acid-induced oxidative stress. The elevated levels of thiobarbituric acid-reactive substances (TBARS) and lipid hydroperoxides induced by oxidative stress were reduced by treatment with the extract. The decreased levels of both enzymatic and non-enzymatic antioxidants were restored on treatment with *S. grandiflora.* The authors attributed this nephroprotective effect to the phenolic compounds and anthocyanins present in the plant.

Cardioprotective and Pulmoprotective Activities

Treatment of adult male Wistar-Kyoto rats (exposed to cigarette smoke for a period of 90 days) with *S. grandiflora* aqueous suspension (SGAS, 1,000 mg/kg bw per day orally) for a period of 3 weeks restored the antioxidant status and retained the levels of micronutrients (Ramesh et al. 2008). In contrast rats exposed to cigarette smoke had significantly increased lactate dehydrogenase activity in serum and cardiac lipid peroxidation product level, and the levels of cardiac superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione-S-transferase and glucose-6-phosphate dehydrogenase and levels of reduced glutathione, vitamin C and vitamin E were significantly decreased. Besides, copper level was elevated, whereas zinc, manganese and selenium levels were significantly diminished in the heart of rats exposed to cigarette smoke. The results suggested that *S. grandiflora* protected the heart from the oxidative damage through its antioxidant potential. Similarly, they found that *S. grandiflora* protected the lungs of cigarette smoked-exposed rats against chronic oxidative stress and damage through its antioxidative potential (Ramesh et al. 2007).

Analgesic and CNS Depressant Activities

The leaf extract of *S. grandiflora* was found to have analgesic and CNS depressant activity (Sutradhar and Choudhury 2012). In the acetic writhing test, a dose-dependent reduction in the number of abdominal constriction was observed in animals treated with different concentration of methanol leaf extract of *S. grandiflora*. At the dose of 250 and 500 mg/kg, 68.13 and 85.56 % inhibition of writhing response was observed, respectively. In the tail-flick method, the duration

of heat tolerance was dependent on the dose of the extract, and the onset of action was very rapid, faster than diclofenac Na. The tail-flick test and acetic acid writhing test were used to elucidate central and peripheral antinociceptive effect, which were both central and peripheral, and the results indicated the extract to have analgesic activity. In the open field and whole cross tests, both 250 and 500 mg/kg leaf extract of *S. grandiflora* gave rapid onset of action and produced rapid sleeping, indicating the extracts had neurological activity, namely, CNS depressant activity.

Antiinflammatory and Analgesic Activities

S. grandiflora flower extract exhibited antiinflammatory activity in the rat paw oedema test (Tamboli 1996), and the flower extracts also demonstrated analgesic (tail-flick test) and antipyretic activity (Brewer's yeast-induced pyrexia assay) (Tamboli 2000).

The methanol flower extracts of *S. grandiflora* showed significant inhibitory activity against inflammation in the carrageenan and cotton pellet-induced animal models and analgesic activity in hot-plate pain model (Loganayaki et al. 2012). The inhibitory values were comparable with positive standards.

Increased paw oedema of the injected paw measured on 1st to 12th hours, a feature of carrageenan-induced inflammation in Wistar arts, was significantly reduced after prophylactic oral administration of petroleum ether, chloroform and methanol extracts of bark of *Sesbania grandiflora* (300 mg/kg bw) and *Sesbania sesban* (300 mg/kg bw) (Patil et al. 2010). Increased swelling of the non-injected paw (secondary paw) measured on days 14 and 21; injected paw swelling (primary paw) measured on days 3, 14 and 21; splenomegaly; thymic involutions; and loss in body weight, all features of adjuvant-induced arthritis, were effectively reduced after prophylactic administration of extracts of bark of *Sesbania grandiflora* and *Sesbania sesban*. Albino rats treated with the ethanol stem bark extract of *S. grandiflora* showed significant increase in the tail-flick latency compared to control, and the ethanol extract suppressed carrageenan-induced oedema in rats when compared to control (Swetha et al. 2012).

Antiulcerogenic Activity

Animal studies showed that the ethanol bark extract of *S. grandiflora* had antiulcer potential (Serti et al. 2001). The extract significantly prevented stress and nonsteroidal antiinflammatory drug-induced gastric lesions in rats. At a dose of 36.75 mg/kg (ED_{50}) p.o., the extract did not modify the volume, pH and hydrochloric acid contents of gastric secretion. The ethanol leaf extract of *S. grandiflora* at a dose of 400 mg/kg produced a significant reduction in the ulcer index of rats with gastric injury induced by aspirin, ethanol and indomethacin (Bhalke et al. 2010). The extract significantly suppressed gastric mucosal damaged induced by aspirin, ethanol and indomethacin. In pylorus-ligated Shay rats, the extract significantly reduced basal gastric secretion. The antiulcer effect was further confirmed histologically.

Wound Healing Activity

Both concentrations (2 and 4 % w/w ointment) of ethanol flower extract of *S. grandiflora* showed significant wound healing (wound closure) and tensile strength increase in both excision and incision wound models tested in Wistar rats when compared with control group (Sheikh et al. 2011). The effects were comparable to the standard nitrofurazone ointment (0.2 %w/w).

Anthelmintic Activity

S. grandiflora seed oil exhibited high anthelmintic activity in both paralysis and time of death of test earthworm, *Pheretima posthuma* (Jalalpure et al. 2010).

Adverse Haemolytic Activity

Aqueous leaf extract of *Sesbania grandiflora* produced haemolysis of human and sheep erythrocytes even at very low concentrations (Kumar et al. 1982). Haemolysis was greater when the pH was acidic. The liberation of phospholipids and sterols into the supernatant as a result of haemolysis indicated possible damage to the erythrocyte membrane. The aqueous flower extracts *S. grandiflora* produced haemolysis of human and sheep erythrocytes even at low concentration (Kalyanagurunathan et al. 1985). The active principle responsible for the haemolytic effect was characterized as the methyl ester of oleanolic acid.

Traditional Medicinal Uses

Various parts of the tree have been used in folkloric medicine in south and Southeast Asian countries (Burkill 1966; CSIR 1972; Stuart 2012; Kirtikar 1993; Tanaka and Nguyen 2007; Wagh et al. 2009). According to Duke and Wain (1981), *S. grandiflora* is reported to be aperient, diuretic, emetic, emmenagogue, febrifuge, laxative, and tonic and used as a folk remedy for bruises, catarrh, dysentery, eyes, fevers, headaches, smallpox, sores, sore throat and stomatitis. Bark, roots, leaves, gum and flowers are considered medicinal.

Sesbania grandiflora is widely used in Ayurveda for the treatment of diseases and for processing of various formulations in Rasashastra (Yadav et al. 2010). It is used for its astringent, antihistaminic, anxiolytic, anticonvulsive and febrifugal properties. Ayurvedics, believing the fruits to be alexeteric, laxative and intellectually stimulating, prescribe them for anaemia, bronchitis, fever, pain, thirst, ozena and quartan fever (Ramakrishna et al. 2012). Yuani considers the tonic levels useful in biliousness, fever and nyctalopia. In local folk medicine, it is applied as aperients, diuretic, emetic, emmenagogue, febrifuge, laxative and tonic (Wagh et al. 2009). In the indigenous system of medicine in India, *Sesbania grandiflora* is claimed to be useful for various ailments, and one such use is for the treatment of renal calculi (Doddola et al. 2008). One traditional use of *S. grandiflora* is in the treatment of smoke-related diseases (Ramesh and Begum 2008). *Sesbania grandiflora* is widely used in Indian folk medicine for the treatment of liver disorders (Pari and Uma 2003). Various parts of this plant are used in Indian traditional medicine for the treatment of a broad spectrum of illness including leprosy, gout, rheumatism and liver disorders. The bark is reported to cure diarrhoea, dysentery, paludism, snakebite, malaria, smallpox, eruptive fever, scabies, ulcer and stomach disorders in children; in high doses it causes vomiting and mild diarrhoea (Kirtikar 1993). Indians apply the roots in rheumatism and the juice of the leaves and flowers for headache and nasal catarrh (Saravanakumar et al. 2010). The Yanadi tribe in the Chittoor District of Andhra Pradesh used the flowers for cataract, conjunctivitis, kidney and bladder stones and alopecia (Vedavathy et al. 1997).

Burkill (1966) has reported on its medicinal uses in Malaysia, Java and also in India. The bark is considered tonic and is bitter the bark extract acts as aperient and larger doses are emetic, and small doses are prescribed for dysentery and other bowel complaints. Bark extract is also prescribed for ulceration of the tongue and alimentary tract. In Java, it is used for thrush and infantile disorders of the stomach. Dried powdered bark is used as cosmetic in Java. An infusion of the leaves is used as aperients, leaf juice prescribed for dim vision and the leaves boiled in vinegar or arrack applied to sprains. In Amboina, flower juice is squeezed into the eye to correct dim vision. The bark is used in infusions for smallpox. An herbal preparation of dried powered leaves mixed with leaves of *Citrus* lime, *Parkia* seeds and wood ash moistened with vinegar is rubbed on the abdomen for a fortnight after confinement. Consumption of large quantities of leaves can cause diarrhoea. Saidin (2000) reported that the leaf juice is taken to reduce nose inflammation and cough and to expel mucus in Malaysia. The cortex has been used to treat dysentery, indigestion and diarrhoea in Vietnam (Tanaka and Nguyen 2007). In the Philippines, the pounded bark is employed for haemoptysis;

the powdered bark is also recommended for ulcers of the mouth and alimentary canal (Stuart 2012). Cambodians consider the flowers emollient and laxative and the bark for diarrhoea, dysentery and paludism.

Other Uses

According to NAS (1979, 1980), *S. grandiflora* is an important source of firewood, forage, pulp and paper, food, medicine, green manure and shade tree and has potential for reforesting eroded and grassy wastelands throughout the tropics. The tree combines well with agriculture (agroforestry) in areas where trees are not normally grown and becomes an important fuel-wood source. The small tree is often grown as a light shade tree for companion plants such as turmeric, galangal and ginger and as a live support tree for climbing plants such as black pepper and betel vine. It is also grown as an ornamental in home gardens, as living fences and as windbreak. The tree is also grown around fields, eroded hill slopes and wastelands as it is planted to ameliorate soils and improve their fertility, especially their nitrogen content. In South Asia and Southeast Asia, its foliage is valued as fodder for cattle and goats. The fast-growing seedlings and the tree foliage make excellent green manure. In Java, the tree is extensively used as a pulp source. The trunks may be used for light construction like bamboos and have been used as poles for temporary shelters and sheds, but they may not last very long due to rots and insect infestation. The bark yields a tanning agent. The gum exuding from a cut in the bark has properties of gum Arabic and is used by fisher-folks for toughening nets and lines. An aqueous extract of bark is said to be toxic to cockroaches. The inner fibrous bark and the white, soft wood can be used for cork.

Comments

The toxic compound, sesbanimide, was detected in seeds of *Sesbania drummondii*, *S. punicea* and *S. vesicaria* but not detected in seeds of *S. grandiflora*, *S. emerus*, *S. exaltata*, *S. sesban*, *S. speciosa* and *S. sonorae* (Powell et al. 1990) and has been erroneously reported in literature to be present in the seeds of *S. grandiflora*.

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Sesbania javanica

Scientific Name

***Sesbania javanica* Miq.**

Synonyms

Aeschynomene paludosa Roxb., *Sesbania aculeata* (Willd.) Pers. var. *paludosa* (Roxb.) Baker, *Sesbania aculeata* var. *paludosa* Baker, *Sesbania cochinensis* Kurz, *Sesbania cochinchinensis* (Lour.) DC., *Sesbania paludosa* (Roxb.) Prain, *Sesbania paludosa* (Roxb.) King, *Sesbania roxburghii* Merr.

Family

Fabaceae also in Papilionaceae

Common/English Names

Marsh Sesbania, Yellow Wisteria

Vernacular Names

Chinese: Yan Sheng Tian Jing, Zhao Wa Tian Jing
French: Sesbanie De Java
German: Gelbe Wisterie
Hawaiian: Kathsola
India: Kathsola (Hindi, Sanskrit)
Khmer: Snaô(r)
Laotian: Sanô; Sanô:Sanô, Kho:Ng Kh'wa:Y
Russian: Sesbanya Yavanskaya
Thai: Sano Kin Dok, Phak Hong Haeng, Si Pree Laa, Sano Hin
Vietnamese: Dien Dien Phai, Dien Thanh Hat Thron

Origin/Distribution

The species is found in India, Bangladesh, Sri Lanka, Indonesia (Java), Malaysia, Papua New Guinea, Philippines, Cambodia, Laos, Myanmar, Thailand, Vietnam, South China and Taiwan.

Agroecology

It thrives in subtropical to tropical regions, occurring naturally in wet marshy lands or banks of waterways, ditches and rice fields.

Edible Plant Parts and Uses

The young leaves and flowers are used as a green vegetable in Thailand and Vietnam boiled in soup and curries, fried with meat or added to steamboat dishes. Seed sprouts are used as mung bean sprouts (Tanaka and Nguyen 2007; Loedsaksaesakul 2007; Wetwitayaklung et al. 2008; JIRCAS 2010). In Thailand, the young shoots are cooked and eaten with 'nam phrik'.

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The flowers are eaten either raw in salad, blanched, fried with egg or fermented and are served with 'nam phrik kapi'. As the flowers contain a carotenoid substance, they are used to impart a yellow colour to various desserts such as 'kanom bua loi', which are coloured balls of sticky rice flour cooked in sweetened coconut milk.

Botany

Shrub 1–4 m high, erect, with cylindrical green or purplish much-branched stem. Leaves compound paripinnate with 10–30 pairs of narrow linear leaflets arranged subalternately or opposite along the rachis. Leaflets 20–25 mm long and 2–44 mm wide, stipules 5–6 mm long. Inflorescences racemose, pendant 5–12 flowered, pendant from leaf axils, 5–12 cm long with 5–12 moderately large yellow flowers 2.5 cm wide with 5 fused petals, 5 sepals and many stamens (Plate 1). Pods brown or purplish 20 cm long and 0.5 cm wide, linear, straight pendant, with many globular (3 mm diameter) brown seeds.

Nutritive/Medicinal Properties

Nutrient composition (g/100 DM) of the flower had been reported by Kijparkorn et al. (2010) as crude protein 23.46 g, ether extract 2.27 g, crude fibre 15.05 g, ash 8.47 g, Ca 0.83 g P 1.02 g and energy 2790 kcal/kg. Amino acids composition of Sano based on dry matter basis was 1.11, 0.34, 0.63, 0.88, 0.96, 0.95, 1.46, 1.17, 0.61, 0.92, 0.92, 1.19, 1.37, 4.08 and 2.08 for lysine, methionine, methionine plus cystine, threonine, arginine, isoleucine, leucine, valine, histidine, phenylanine, glycine, serine, alanine, aspartic acid and glutamic acid, respectively. Pigment composition of sano flowers were reported as total carotenoids 307 mg/kg, *b*-carotene 63.19 %, b-cryptoxanthin 16.73 %, *cis*-lutein 5.45 %, *trans*-lutein 9.695, epoxide-lutein 3.74 % and *trans*-zeaxanthine 1.21 % (Kijparkorn et al. 2010).

β-sitosterol, prunetin, genistein, 4-hydroxycinnamic acid and sistosterol-3-*O*-β-D-glucopyranoside were isolated from the flowers and leaves of *S. javanica* (Loedsaksaesakul 2007). Prunetin, genistein and 4-hydroxycinnamic acid exhibited antioxidant activity using DPPH assay.

Plate 1 Flowers of Marsh Sesbania

The flower and crude extract was found to have low total polyphenol contents (0.31 g/100 g dried flowers or 2.39 g/100 g crude extract), and the antioxidant activity in terms of TEAC (trolox equivalent antioxidant capacity) is low (TEAC = 0.2, IC_{50} = 500.35 ug) when compared to trolox (TEAC = 1) (Wetwitayaklung et al. 2008). In Thailand, the flowers are used for stomachache and burned tree ash as diuretic.

Flowers were reported to have antimutagenic activity (Tangvarasittichai et al. 2005). Dimethyl sulfoxide extract of the flower showed a strong inhibitory effect against aflatoxin B1 (AFB1) and benzo(a)pyrene [B(a)P], mutagens. The flavonol glycoside, quercetin 3-2G-rhamnosylrutinoside, was confirmed by its physicochemical properties as a major constituent of the flower. Quercetin 3-2G-rhamnosylrutinoside (207 μg/plate) also showed a strong inhibitory effect against AFB1 and B(a)P with more than 70 % inhibition rate.

Other Uses

Its soft stems are used to make cork. The plant is used also for animal fodder and as green manure for soil improvement.

Studies showed that using dried sano flowers in the diet of layers had a beneficial effect in enhancing egg yolk colour (Kijparkorn et al. (2010).

Moreover the high content of β-carotene with pro-vitamin activity and high protein content make it suitable as poultry feedstuff.

Comments

Studies by Gross (2010) found the names *Sesbania javanica* Miq. and *S. sesban* (L.) Merr. do not apply to species native to Australia and *Sesbania benthamiana* has been misapplied. The name *Sesbania burbidgei* is proposed to account for specimens previously identified as *Sesbania sesban*, and *Sesbania muelleri* is proposed to account for specimens previously assigned as *Sesbania benthamiana*. The name *Sesbania benthamiana* is reapplied to material previously known as *Sesbania javanica*.

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Wetwitayaklung P, Phaechamud T, Limmatvapirat C, Keokitichai S (2008) The study of antioxidant activities of edible flower extracts. Acta Hort (ISHS) 786:185–192

Styphnolobium japonicum

Scientific Name

***Styphnolobium japonicum* (L.)Schott.**

Synonyms

Anagyris chinensis Spreng., *Macrotropis foetida* DC., *Ormosia esquirolii* H. Lév., *Pongamia chinensis* DC., *Robinia mitis* Lour., *Sophora angustifoliola* Q.Q. Liu & H.Y. Ye, *Sophora chinensis* hort. ex Zabel, *Sophora japonica* L., *Sophora japonica* f. *columnaris* Schwer., *Sophora japonica* f. *hybrida* Carrière, *Sophora japonica* f. *oligophylla* Franch., *Sophora japonica* f. *pendula* Loudon, *Sophora japonica* var. *praecox* Schwer., *Sophora japonica* var. *pubescens* (Tausch) Bosse, *Sophora japonica* f. *variegata* Nichols, *Sophora japonica* var. *vestita* Rehder, *Sophora japonica* var. *violacea* Carrière, *Sophora japonica* var. *violacea* Dippel, *Sophora korolkowii* Dieck, *Sophora mairei* H. Lév., *Sophora pendula* Spach, *Sophora pubescens* Tausch, *Sophora sinensis* Forrest, *Sophora vanioti* H. Lév., *Styphnolobium japonicum* var. *pubescens* hort. ex Kirschner

Family

Fabaceae

Common/English Names

Chinese Scholar Tree, Japanese Pagoda Tree, Pagoda Tree, Scholar Tree, Umbrella Tree

Vernacular Names

Brazil: Sôfora Do Japão (Portuguese)
Chinese: Huái Hua, Huái Hua Mo, Huái Jiao, Huái Mi, Huái Shu
Czech: Jerlín Japonský
Danish: Pagodetræ
Eastonian: Jaapani Keepuu
French: Arbre Aux Pagodes, Arbre De Miel, Arbre Des Pagodes Du Japon, Sophora Du Japon
German: Japanischer Perlschnurbaum, Japanischer Schnurbaum, Pagodenbaum Sophore
Hungarian: Japánakác
Indonesia: Sari Cina
Italian: Sofora, Sofora Del Giappone
Japanese: Enju
Korean: Hoe-Wha-Na-Moo
Polish: Perełkowiec Japoński, Szupin Chiński, Szupin Japoński
Portuguese: Acácia-Do-Japão
Slovencina: Sofora Japonská
Spanish: Acacia Del Japón, Arbol De Las Pagodas, Sófora

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Swedish: Pagodträd
Turkish: Japon Soforası
Vietnamese: Hoè

Origin/Distribution

The species is indigenous to East Asia—Central and Northern China and Korea. It is now widely cultivated in temperate and subtropical regions of the world and infrequently in the highlands in the tropics, e.g. in Southeast Asia, in Vietnam and Thailand.

Agroecology

A cool climate species, being native to the temperate and subtropical regions of Eastern Asia will withstand warm but not hot temperatures. It is frost tolerant down to –25 °C when mature except when young. It will grow in the cooler and drier areas of the highlands in the tropics as it is drought tolerant. The tree is found in wasteland and open country between 300 and 1,000 m altitude in its native range. The tree is well adapted to wide range of soil types including poor soils, but thrives best in well-drained, moderately fertile, sandy loams in full sun.

Edible Plant Parts and Uses

The young tender leaves, shoots and twigs, flowers and seeds are edible cooked (Uphof 1968; Read 1982; Kunkel 1984; Facciola 1990; Hu 2005). Leaves are cooked with rice and consumed (Uphof 1968; Read 1982). Shoots are sun-dried and boiled several times to remove the bitter elements before eating. The twigs are thoroughly boiled in water into which an egg is poached; the liquid is then drunk and the poached egg consumed as a home remedy for stopping haemorrhages (Hu 2005). Flowers and buds are gathered and used as an important ingredient in the traditional Five Flower Tea ('Wu Hua Cha') for the hot summer season in Hong Kong. The leaves can also be made into tea and an edible starch is obtained from the seed (Facciola 1990). The seed endosperm is cooked with sugar to prepare a dessert that is eaten in Northern China (Hu 2005).

Botany

A small to medium-sized, deciduous perennial tree, up to 5–15(−30) m tall with a short stout bole, rough, greyish-brown, fissured bark and upright, spreading branches and glabrous, terete, pale green, lenticillate twigs and broad round crown (Plates 1 and 2). Leaves are arranged spirally, imparipinnate, 15–25 cm long with caducous stipules; leaflets are subopposite and shortly petiolulate, 13–17, elliptical to ovate-lanceolate (Plates 2 and 5), 1.5–6 cm by 1–2.5 cm, acute to subacute apex, obtuse at the base, margin entire, sparsely pubescent below, bright green tuning to yellow in autumn. Flowers are bisexual, papilionaceous, mildly fragrant, small pentamerous, in terminal, 15–35 cm long upright panicles (Plates 3 and 4), bracteoles present, calyx campanulate, 3–4 mm long with 5-teeth, corolla 5 white or greenish-white petals, standard broad and cordate, 12–15 mm long with curled margins (Plate 5), stamens 10 free but filaments joined near the base, ovary superior and pilose. Fruit an indehiscent, terete leguminous pod, 3–12 cm by 7–12 mm, green turning to yellow when mature, constricted between the seeds, stipitate, glabrous, distinctly beaked, 2–5-seeded. Seeds

Plate 1 Tree habit with a short stout bole (Nguyen VT)

Plate 2 Ascending slender branches and twigs

Plate 3 Large panicle with flower buds (Nguyen VT)

ellipsoid to ovoid, 8 mm × 4–5 mm, slightly compressed, yellowish-brown.

Nutritive/Medicinal Properties

Flower Phytochemicals

Blossoms were found to contain sophorin (A,B, C) (Brauns and Schmidt 1904; Vo 1997) and four to five times as much rutin as does buckwheat, the best domestic source (Couch et al. 1952). Rutin content declined as the bud opened and continued to fall as the seed pod formed. No rutin was found in the seed while traces occurred in the leaves. Sophoroflavonoside, kaempferol-3-rhamnodiglucoside, genistein-7-D-cellobioside, sophoricoside, sophorabioside, betulin and sophoradiol were isolated from the flower buds (Kariyone et al. 1956; Takahashi et al. 1960; Ishimasa 1960), flavonoids: quercetin, rutin and isorhamnetin-3-rutinoside, kaempferol-3-rutinoside (Kimura and Yamada 1984); andisorhamnetin2-(3-methoxy-4-hydroxyphenyl)-3,5,7-trihydroxy-4*H*-1-benzopyran-4-one were isolated from the flower buds (Ishida et al. 1998). Three new glucuronide saponins, named kaikasaponin I, kaikasaponin II and kaikasaponin III,

Plate 4 Panicle with some opened flowers (Nguyen VT)

Plate 5 Pinnate leaves and inflorescence with white flowers (Nguyen VT)

were isolated from buds of *Sophora japonica* together with five known glucuronide saponins soyasaponin I, soyasaponin III, azukisaponin I, azukisaponin II and azukisaponin V (Kitagawa et al. 1988). The structures of kaikasaponins I, II andIIIwereelucidatedas3-*O*-[β-D-galactopyranosyl-(1 → 2)-β-D-glucuronopyranosyl]sophoradiol, 3-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl-(1→2)-β-D-glucuronopyranosyl]sophoradiol and 3-*O*-[α-L-rhamnopyranosyl-(1 → 2)-β-D-galactopyranosyl-(1 → 2)-β-D-glucuronopyranosyl]sophoradiol, respectively.

Accumulation of rutin started with initiation of the flower buds, reaching a maximum content of 287 mg/g (dry weight) during the earliest stages of flower development (Gevrenova et al. 2007). A further decline in the amount of rutin up to 44 mg/g was found proportionally with the decline of flavonoids throughout and after the flowering period. Rutin was the predominant glycoside and accounted for up to 90 % of flavonoid glycoside mixture in young buds, whereas sophorabioside (64.7 mg/g, calculated as rutin equivalent) and kaempferol 3-rutinoside (46.8 mg/g) dominated at later development stages of the fruits. Balbaa et al. (2009) reported that rutin reached its maximum in the flower buds (23 %). Maximum yield and efficiency of extraction of rutin from *Sophora japonica* flowers was improved by the application of ultrasound to methanol extraction but was dependent on the solvent employed (Paniwnyk et al. 2001). Rutin being a compound with antioxidant activity and aqueous solvents appeared to be unsuitable for ultrasonic extractions due to the formation of free radicals from the insonation of the solvent. The flower buds (Huai Mi) and flowers (Huai Hua) of *S. japonicum* (collectively Flos Sophorae) contained rutin as the main flavonoid and lacked the flavone glycosides that were present in flower buds and flowers of *Sophora flavescens* (Kite et al. 2009).

Fruit/Seed Phytochemicals

Sophorobioside, a glycoside, was isolated from the fruit (Farkas et al. 1968). Flavonoids isolated from the fruit included rutin, quercetin, genistein, kaempferol, sophorobioside, sophoricoside and sophoroflavonoloside (Tulaganov and Gaibnazarava 2001). Two kaempferol triglycosides: kaempferol 3-*O*-β-D-sophoroside-7-*O*-α-*L*-rhamnoside and kaempferol 3-*O*-(2″-*O*-β-D-glucosyl)-β-D-rutinoside (Tang et al. 2001a), four isoflavone triglycosides, genistein 7-*O*-β-D-glucopyranoside-4′-*O*-[(α-L-rhamnopyranosyl)-(1 → 2)-β-D-glucopyranoside], genistein 7-*O*-β-D-glucopyranoside-4′-*O*-[(β-D-glucopyranosyl)-(1 → 2)-β-D-glucopyranoside], genistein 7-*O*-α-L-rhamnopyranoside-4′-*O*-[(α-L-rhamnopyranosyl)-(1 → 2)-β-D-glucopyranoside] and genistein 7-*O*-α-L-rhamnopyranoside-4′-*O*-[(β-D-glucopyranosyl)-(1 → 2)-β-D-glucopyranoside], together with nine known compounds, namely, genistein 7-*O*-β-D-glucopyranoside-4′-*O*-β-D-glucopyranoside, sophorabioside, prunetin 4′-*O*-β-D-glucopyranoside, sophoricoside, genistin, rutin, kaempferol 3-*O*-β-rutinoside, quercetin 3-*O*-β-D-glucopyranoside and kaempferol 3-*O*-β-D-glucopyranoside (Tang et al. 2001b); new flavonol triglycoside, kaempferol 3-*O*-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside (1), as well as two known kaempferol 3-*O*-[α-L-rhamnopyranosyl-(1 → 6)]-[β-D-glucopyranosyl-(1 → 2)]-β-D-glucopyranoside (2) and kaempferol 3-*O*-β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranoside-7-*O*-α-L-rhamnopyranoside (3) (Tang et al. 2002b); a coumaronochromone derivative, sophorophenolone, along with 13 known compounds, l-maackiain, medicagol, 7-*O*-methylpseudobaptigenin, pseudobaptigenin, 7,3′-di-*O*-methylorobol, genistein, prunetin, daidzein, formononetin, di-*O*-methyldaidzein, quercetin, kaempferol and isorhamnetin (Tang et al. 2002a) were isolated from the fruit. Flavone compounds genistein-7,4′-di-*O*-β-D-glucoside (I), genistein-7-*O*-β-D-glucopyranoside-4′-*O*-[(α-L-rhamnopyranosyl)-(1 → 2)-β-d-glucopyranoside] (II), kaempferol-3-*O*-β-D-sophoroside(III), quercetin-3-*O*-β-L-ramnopyranosyl-(1 → 6)-β-D-glucopyranoside (IV), genistein-4′-β-L-rhamnopyransoyl-(1 → 2)-α-d-glucopyranoside(V)andkaempferol-3-*O*-β-L-ramnopyranosyl-(1 → 6)-β-D-glucopyranoside (VI) were purified from the fruit crude extract using high-speed

countercurrent chromatography combined with macroporous resin column separation (Sun et al. 2007). The purities of compounds I, II, III, IV, V and VI were 98.7, 98.2, 97.8, 98.5, 99.3 and 98.9 %, respectively, as determined by HPLC. The flavonoids kaempferol glycosides—kaempferol 3-*O*-β-glucopyranosyl(1 → 2)-β-galactopyranoside-7-*O*-α-rhamnopyranoside and kaempferol 3-*O*-β-xylopyranosyl(1 → 3)-α-rhamnopyranosyl(1→6)[β-glucopyranosyl(1 → 2)]-β-glucopyranoside and two tetraglycosides: kaempferol 3-*O*-β-glucopyranosyl(1 → 2)[α-rhamnopyranosyl(1→6)]-β-glucopyranoside-7-*O*-α-rhamnopyranoside and kaempferol 3-*O*-β-glucopyranosyl(1 → 2)[α-rhamnopyranosyl(1 → 6)]-β-galactopyranoside-7-*O*-α-rhamnopyranoside—were identified in the fruit; the latter was the main flavonoid in mature seeds (Kite et al. 2009). Three flavonoids were isolated from the fruit: sophorabioside, genistin, quercetrin (Kim and Yun-Choi 2008). Flavonoids sophorabioside, sophora-flavanoloside and genistein glucoside appeared at the beginning of the fruit formation, while sophoricoside appeared only at the stage of its maturation (Balbaa et al. 2009). Rutin was found in the fruit reaching a minimum in the ripe fruits (4.3 %).

Phytoestrogens genistin, genistein, rutin, kaempferol and quercetin were determined in the fruit and seed of *S. japonica* by high-performance capillary electrophoresis with electrochemical detection (CE-ED) method (Chu et al. 2005). Detection limits ranged from 1.1×10^{-7} to 2.8×10^{-7} g/ml for all five analytes.

Seed Phytochemicals

Cytisine, *N*-methylcytisine, sophocarpine and matrine were isolated from the epigeal parts of the seed (Abdusalamov et al. 1972). Stizolamine were found in the seeds (Toshida and Hasegawa 1977). Triterpene glycosides: soyasapogenol B-3-[*O*-β-D-glucopyranosyl-(1 → 2)-*O*-β-D-glucopyranuronoside] (adzukisaponin II), soyasapogenol B [3-*O*-β-galactopyranosyl-(1 → 2)-*O*-β-L-glucopyranuronoside] (soyasaponin III), soyasapogenol B 3-(*O*-α-L-rhamnopyranosyl-(1 → 2)-*O*-β-L-glucopyranosyl-(1 → 2)-*O*-β-D-glucopyranuronoside) (adzukisaponin V), soyasapogenol B 3-(*O*-β-D-rhamnopyranosyl-(1 → 2)-*O*-β-D-galactopyranosyl-(1 → 2)-*O*-β-D-glucopyranuronoside (soyasaponin I) and the new glycoside (**1**)—soyasapogenol B 3-[*O*-β-D-glucopyranuronoside] were isolated from the seeds (Grishkovets and Gorbacheva 1995). Five triterpene glycosides with soyasapogenol B as the aglycone were isolated from the seeds (Gorbacheva et al. 1996). A new saponin 3-*O*-β-D-glucuronopyranosyl-soyasapogenol B was identified as s a minor component.

Six compounds were isolated from the seed alcohol extract and identified as follows: genistein 7-*O*-β-D-glucopyranoside-4′-*O*-β-D-glucopyranoside, genistein 7-*O*-β-D-glucopyranoside-4′-*O*-[α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranoside],tectorigenin,tectoridin,1,6-di-*O*-galloyl-β-D-glucose and ethyl gallate (Wang et al. 2002).A flavonoltetraglycosideandkaempferol3-*O*-α-L-rhamnopyranosyl(1 → 6)-β-D-glucopyranosyl(1 → 2)-β-D-glucopyranoside-7-*O*-α-L rhamnopyranoside, together with nine known compounds, were isolated from the seeds (Wang et al. 2003).

Total extractive from ground ripe *S. japonica* seeds consisted of neutral lipids, polar lipids, carbohydrates, amino acids, pigments, etc. (Mukhamedova and Glushenkova 1997). Total yield of neutral lipids was 7 %, phospholipids 1.1 % of seed weight and phosphorus content of the total neutral lipids was 3.3 %. Nine phospholipid classes were detected:

lysophosphatidylcholines (lyso-PCs), phosphatidylcholines (PCs), phosphatidylinositols (PIs), phosphatidylethanolamines (PEs), *N-acyl-phosphatidylethanolamines* (*N*-acyl-PEs), *N*-acyl-lysophosphatidylethanolamines (*N-acyl-lyso* PEs), phosphatidic acids (PAs), phosphatidylglycerols (PGs) and D-phosphatidylglycerols (DPGs).

A high level of 16:0 and 18:2 fatty acids were found in all phospholipid samples. In the (*N*-acyl-lyso PEs), 18:2 made up 51.7 % of total acid weight. In total phospholipid, trace amount of 21:0 fatty acids were found, mainly localized in the *N*-acyl-PEs. PGs contained a higher level of SFA (64.5 %) than other phospholipids, while *N*-acyl-lyso

PEs contained the least (15.1 %) In sequence of decreasing unsaturation, the individual phospholipids were ranked as follows: *N*-acyl-lyso PEs → PCs → PEs → *N*-acyl-PEs → lyso-PCs → PIs → DPGs → PAs → PGs.

A haemagglutinin protein was purified from the seeds (Poretz et al. 1974). It was found to contain relatively large amounts of hydroxyl and acidic amino acids, no methionine and about five residues of half-cystine/mol. The presence of covalently bound carbohydrates was determined as 14–15 residues of 2-amino-2deoxyglucose and 5.9 % neutral saccharide of mannose and xylose. Seeds were found to contain *N*-acetylgalactosamine-specific lectins, glycoproteins with molecular weights of about 130,000 and possessing substantial sequence homology (Mcpherson et al. 1987). The lectin isolated from *Sophora japonica* seeds was found to be a glycoprotein, its carbohydrate moiety comprising fucose, xylose, mannose and *N*-acetylglucosamine (Fournet et al. 1987). The lectin was found to bind oligosaccharides with nonreducing terminal Gal beta(1-3/4)GlcNac beta 1 units. *S. japonica* seeds contained a GalNAc-specific lectin which was highly homologous to though not identical with the GalNAc-specific lectin from the bark (Van Damme et al. 1997). *Sophora japonica* seed was found to contain an incomplete partial phytohaemagglutinin anti-B2 of the blocking type (Potapov 2004).

Leaf Phytochemicals

Two flavonol tetraglycosides 3-*O*-α-rhamnopyranosyl(1 → 2)[α-rhamnopyranosyl(1 → 6)]-β-glucopyranoside-7-*O*-α-rhamnopyranosides of quercetin and kaempferol were isolated from the leaves of *Styphnolobium japonicum* (Kite et al. 2007). The 3-*O*-α-rhamnopyranosyl(1 → 2)[α-rhamnopyranosyl(1 → 6)]-β-galactopyranoside-7-*O*-α-rhamnopyranoside of kaempferol, the 3-*O*-α-rhamnopyranosyl(1 → 2)[α-rhamnopyranosyl(1 → 6)]-β-glucopyranosides of kaempferol and quercetin and the 3-*O*-α-rhamnopyranosyl (1 → 2)[α-rhamnopyranosyl(1 → 6)]-β-galactopyranoside of kaempferol were also isolated. An additional constituent obtained was identified as the maltol derivative, 3-hydroxy-2-methyl-4*H*-pyran-4-one 3-*O*-(4′-*O*-*p*-coumaroyl-6′-*O*-(3-hydroxy-3-methylglutaroyl))-β-glucopyranoside.

Two isoflavone tetraglycosides genistein 7-*O*-β-D-glucopyranoside-4′-*O*-(6″′-*O*-α-L-rhamnopyranosyl)-β-sophoroside and genistein 7-*O*-α-L-rhamnopyranoside-4′-*O*-(6″′-*O*-α-L-rhamnopyranosyl)-β-sophoroside and six known compounds (genistein 7-*O*-β-D-glucopyranoside-4′-*O*-α-D-glucopyranoside, sophorabioside, genistin, rutin, quercetin3-*O*-β-D-glucopyranoside and kaempferol 3-*O*-β-D-glucopyranoside) were isolated from *S. japonica* leaves (Tang et al. 2008a, b). Three flanoids were isolated from the leaves genistein, tectoridin rutin (Kim and Yun-Choi 2008).

The rutin content decreased from young (8.7 %) to mature leaves (4.1 %) and then remained without significant changes all over flowering and fruiting seasons (Balbaa et al. 2009). Two new flavanones with a C15 isoprenoid group, japonicasins A and B (1 and 2), were isolated from the leaves (Zhang et al. 2013a) and represented the first report on the presence of the (2*E*,7*E*)-6-isopropyl-3,9-dimethyldeca-2,7,9-trien-1-yl group (C15 isoprenoid group) in isoprenylated flavonoids. The quinolizidine alkaloid, lupanine, was found in the leaves and cell cultures (Wink et al. 1983).

Two lectins, Leaf Lectin I and Leaf Lectin II (LLI and LLII), were purified from the leaves (Hankins et al. 1987). Like the *Sophora* seed lectin, LLI and LLII were found to be tetrameric glycoproteins containing a single subunit with respect to size. The subunits of LLI (32 kDa) and LLII (34 kDa) were slightly larger than those of the seed lectin (29.5 kDa). The three Sophora lectins displayed indistinguishable specificities, amino acid compositions, specific haemagglutinin activities and extinction coefficients. Although very closely related to the seed lectin, the leaf and seed lectins were not immunologically identical, and they differed in subunit molecular weights, carbohydrate content and in the pH sensitivity of their haemagglutinin activities. The leaf lectins

were found to be exclusively sequestered in the protein-storage vacuoles of these tissues (Herman et al. 1988).

Stem/Bark Phytochemicals

Two isoflavone triglycosides, genistein 4′-*O*-(6″-*O*-α-L-rhamnopyranosyl)-β-sophoroside and genistein 4′-*O*-(6‴-*O*-α-L-rhamnopyranosyl)-β-sophoroside, together with five known compounds, namely, sophorabioside, genistin, rutin, quercetin 3-*O*-β-D-glucopyranoside and kaempferol 3-*O*-β-D-glucopyranoside, were isolated from the small branches of *Sophora japonica* (Tang et al. 2008b). Four flavonoids were isolated from the stem: biochanin A, iridolidone, sissotrin and apigenin (Kim and Yun-Choi 2008). A new isoflavone glycoside, 6-methoxy-7-hydroxy-4′-*O*-β-D-glucosyl isoflavone, glycitein-4′-*O*-β-D-GLUCOSIDE, along with known flavonoids (daidzein, calycosin, trifolirhizin, puerol A, ononin, 5-hydroxypseudobaptigenin-7-*O*-glucoside, glycitin, calycosin-7-*O*-glucoside, paratensein-7-*O*-glucoside), were isolated from the stem bark of *Sophora japonica* (Park et al. 2010).

Five *N*-acetyl-galactosamine-specific lectins were isolated from the bark but were absent in other tissues (Hankins et al. 1988). These lectins were immunologically and structurally very similar, but not identical, to the *Sophora* seed and leaf lectins. The carbohydrate specificities and haemagglutinin activities of these lectins were indistinguishable at pH 8.5 but their activities differed markedly at pH values below 8. All five lectins were found to be tetrameric glycoproteins made up of different combinations of subunits of about 30,000, 30,100, 33,000 *M*(r) containing 3–5 % covalently attached sugar. Mannose/glucose-specific lectins were found in the bark (Van Damme et al. 1997). The bark lectins were found to be exclusively sequestered in the protein-storage vacuoles of these tissues (Herman et al. 1988). Sophoragrin, a D-mannose/D-GLUCOSE-SPECIFIC lectin (B-SJA-II), was isolated from the bark of *S. japonica (*Ueno et al. 1991). It was found to have 4subunits a-1 (*M*r = 19,400), a-2 (*M*r = 18,200), b-1 (*M*r = 15,000) and b-2 (*M*r = 13,200). Each subunit had a sugar-binding site for the mannosyl core of N-linked oligosaccharide chains and recognized each other sugar specifically to form aggregates. Further studies showed that self-aggregation of sophoragrin was shown to be a unique homopolymerization due to the sugar-specific interaction (Ueda et al. 2004). Sophoragrin was found to sequester endogenous glycoprotein ligands via sugar-specific interactions.

Unidentified Plant Parts Phytochemicals

A new compound, *N*-feruloyl-*N*′-*cis*-feruloyl-putrescine, together with four flavonoids (rutin, quercetin, 3-methylquercetin, orobol) and three putrescine derivatives (*N,N*′-diferuloyl-putrescine, *N,N*-dicoumaroyl-putrescine and *N*-coumaroyl-*N*-feruloyl-putrescine), was isolated from *S. japonica* (Lo et al. 2009).

Root Phytochemicals

DL-maackiain and D-maackiain—mono-β-D-glucoside under the proposed name sophojaponicin, a diastereomer of trifolirhizin, were isolated from the roots (Shibata and Nishikawa 1963). *Sophora japonica* roots were found to contain anhydropisatin (flemichapparin B); irisolidone; 5,7-dihydroxy-3′, 4′-methylenedioxyisoflavone; biochanin A; D-maackiain and β-sitosterol (Komatsu et al. 1976); and oxymatrine (Gan et al. 2011). An aromatic glycoside, named sophoroside A with the structure puerol B 5-*O*-β-D-glucopyranoside together with puerol A and puerol B, was isolated from the roots (Shirataki et al. 1987). Oxymatrine and matrine were found in the roots (Cheng et al. 2008).

Antioxidant Activity

A flavonol triglycoside, kaempferol 3-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranoside,

and kaempferol 3-*O*-[α-L-rhamnopyranosyl-(1 → 6)]-[β-D-glucopyranosyl-(1 → 2)]-β-D-glucopyranoside and kaempferol 3-*O*-β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranoside-7-*O*-α-L-rhamnopyranoside isolated from the fruit, exhibited antioxidant activity in DPPH (2,2-diphenyl-1-picrylhydrazyl) and cytochrome-c assay using HL-60 cell system (Tang et al. 2002b). It was found that rutin administration sharply suppressed free radical production in liver microsomes and by phagocytes of iron-overloading rats and only slightly affected these processes in normal rats (Afanas'ev et al. 1995). The selective inhibitory effect of rutin under pathologic conditions induced by iron overload was thought to be due to the formation of inactive iron–rutin complexes which were unable to catalyze the conversion of superoxide ion into reactive hydroxyl radicals, a process responsible for the free-radical-mediated toxic effects of iron overload. In cholesterol-enriched erythrocytes and control erythrocytes, quercetin provided greater protection against lipid peroxidation and reactive oxygen species (ROS) formation, and it preserved better cellular integrity than rutin (López-Revuelta et al. 2006). Both antioxidants suppressed the alterations in membrane fluidity and lipid losses with similar efficiency, reducing haemoglobin oxidation by 30 % and GSH losses by 60 % in the above-mentioned erythrocytes. Cholesterol depletion reduced the efficiency of the antioxidant power of both flavonoids against oxidative damage induced in the erythrocyte membrane, while a stronger degree of protection of GSH and haemoglobin contents was observed, mainly in the presence of rutin.

Wang et al. (2008) found that the polysaccharides of *Sophora japonica* scavenged hydroxyl and superoxide anion free radicals. Of four plants, *Sophora japonica* showed significant antioxidant activity in both yeast model and also DPPH free radical scavenging methods. The ethanol extract of *S. japonica* showed highest levels of phenolics and flavonoids (91.33 GAE mg/g and 151.86 QE mg/g, respectively). A positive linear correlation between antioxidant activity and the total phenolics and flavonoid contents indicates that these compounds are likely to be the main antioxidants contributing to the observed activities (Zhang et al. 2011).

Two new flavanones japonicasins A and B isolated from the leaves exhibited potential antioxidant DPPH radical scavenging activities, with IC_{50} values of 35.1 and 88.7 μM, respectively (Zhang et al. 2013a).

Antiinflammatory Activity

Five plant extracts including *S. japonica* and *S. flavescens* exhibited significant antiinflammatory activity by in-vitro inhibition of the production of NO and TNF-α with low IC_{50} values (Zhang et al. 2011). Sophoricoside, an isoflavone glycoside isolated from immature fruits of *Sophora japonica* when administered orally at >100 mg/kg or injected intravenously at >10 mg/kg, exerted significant reduction of carrageenan-induced paw oedema in mice (Kim et al. 2003a). The anti-inflammatory effect of sophoricoside was found to be through selective inhibition of cyclooxygenase (COX)-2 activity with an IC_{50} value of 3.3 μM. Sophoricoside from immature *S. japonica* fruit inhibited the interleukin (IL)-6 bioactivity with an IC_{50} value of 6.1 μM but had no effects on IL-1beta and TNF-alpha bioactivities (Kim et al. 2003b). Sophoricoside was identified as a selective inhibitor of cyclooxygenase (COX)-2 activity with an IC_{50} value of 4.4 μM, but did not show inhibitory effect on the synthesis of COX-2. However, sophoricoside had no effect on the production of reactive oxygen species including superoxide anions and nitric oxide. The results revealed that in-vitro antiinflammatory action of sophoricoside was significantly different from that of genistein a known phytoestrogen.

Antiplatelet Activity

An antihaemostatic principle was isolated from dried buds and identified as isorhamnetin (Ishida et al. 1998). Isorhamnetin increased capillary permeability and reduced platelet aggregation. Among the flavonoid compounds, biochanin A, genistein and tectoridin showed approximately

2.5–6.5-fold greater inhibitory effects on arachidonic acid (AA) and U46619-induced platelet aggregation (IC_{50}: 19.9 and 99.8 μM; 20.3 and 53.8 μM; 25.9 and 123.4 μM, respectively) than acetylsalicylic acid (ASA, IC_{50}: 63.0 and 350.0 μM) (Kim and Yun-Choi 2008). Irisolidone was an approximately 22–40-fold stronger inhibitor than ASA on AA and U46619-induced aggregation (IC_{50}: 1.6 and 15.6 μM, respectively). All crude, parched and carbonized forms of the flowers and its extracts were found to have a haemostatic effect (Li et al. 2004). All the samples could lower capillary permeability, bleeding time and coagulation time in mice and also decreased the plasma prothrombin time in rats. All three forms of Flos Sophorae could increase fibrinogen in rats, while the three extracts inhibited the platelet aggregation rate in rats. In addition, rutin had the effect of raising the platelet count.

Immunopharmacological Activity

The isoflavone sophoricoside isolated from *Sophora japonica* at dosages of 3 and 10 mg/kg, ameliorated 2,4-dinitrochlorobenzene-induced acute and chronic contact dermatitis by 50–70 % (Lee et al. 2013). Sophoricoside mainly affected the functions of B cells rather than T cells, macrophages and dendritic cells. As signalling targets, sophoricoside inhibited the phosphorylation and degradation of IκBα/β and the nuclear translocation of NF-κB p65 in B cells, but not in dendritic cells and macrophages.

The haemagglutinin seed lectin was found to require eightfold greater concentration to agglutinate human type A erythrocytes than required for the agglutination of type B cells (Poretz et al. 1974). It was unable to agglutinate type O cells at a concentration 500 times greater than needed for agglutination of type B erythrocytes. The optimum pH for agglutination of type B cells was 8.3–9.0. The lectin was found to be inhibited by *N*-acetyl-D-galactosamides more easily than D-galactosides and displayed a preference for binding β anomers of these saccharides. *S. japonica* seed lectin, which demonstrated blood group specificity, was found to be more active than concanavalin A (from *Canavalia ensiformis*) with human erythrocytes, but had a much lower reactivity than concanavalin A with murine red blood cells (Poretz and Barth 1976). Ficin treatment of human erythrocytes resulted in an increase in agglutinability by the lectin as well as causing the appearance of *S. japonica* lectin receptors on type O cells. The *S. japonica* lectin appeared to be devoid of mitogenic and immunosuppressive activity, in contrast to concanavalin A which suppressed the T helper-dependent antibody response to sheep erythrocytes. They found the native lectin to be composed of the non-covalent association of two dissimilar subunits, one subunit consisted of two identical polypeptide chains attached by two disulphide bonds and the other subunit of two identical polypeptide chains stabilized by a single cysteine bridge (Timberlake et al. 1980). *Sophora japonica* seed lectin agglutinated human B erythrocytes strongly and A_1 erythrocytes weakly (Wu et al. 1981) Bivalent metal ions such as Ca^{2+}, Mn^{2+} or Mg^{2+} were shown to be essential for haemagglutinating and precipitating activities. At optimal concentrations of bivalent metal ions, haemagglutinating activity was highest between pH 8.5 and 9.0 and decreased sharply below pH 8.5, whereas precipitating capacity was maximal between pH 6.7 and 9.5. The combining site of the *S. japonica* lectin was explored by quantitative precipitin and precipitin inhibition assays.

Cardioprotective Activity

Studies showed that administration of oxymatrine to rat with acute myocardial infarction relieved myocardial injuries during ischaemia, and this was achieved by protecting cardiomyocytes from apoptotic death (Sun et al. 2008). The beneficial effects of oxymatrine were likely mediated by an inhibition of lipid peroxidation (MDA production) and an increase in endogenous antioxidant activity (SOD), activation of the survival signalling molecule (Bcl-2) and a reduction of apoptotic mediator (Fas) and intracellular Ca^{2+} overload. Intragastric administration of oxymatrine (alkaloid of *S. japonica*) to rats with acute myocardial

infarction induced by ligation of left anterior descending branch, significantly ameliorated haemodynamics, inhibited the expression of transforming growth factor beta 1 TβR(1) mRNA and Smad3 mRNA and reduced the left ventricle weight/body weight (Shen et al. 2011). The results indicated that oxymatrine might protect against myocardial fibrosis and the mechanism may involve modulation of the TGF-β(1)-Smads signal pathway. Pretreatment with oxymatrine main alkaloid component of the root markedly increased the dose of aconitine required to induce arrhythmias in rats (Gan et al. 2011). Additionally, oxymatrine significantly delayed the initial time and shortened the duration time of rat arrhythmias induced by coronary artery ligation. Cardiac mortality rate in coronary artery ligation-induced arrhythmias was also effectively decreased by oxymatrine in rats. Oxymatrine could significantly inhibit sodium and calcium currents in isolated rat cardiomyocytes in a concentration-dependent manner. It was concluded that oxymatrine played a remarkably preventive role in rat arrhythmias through the inhibition of sodium and calcium currents. Another animal study showed that oxymatrine exhibited substantial therapeutic potential for the treatment of septic shock-induced myocardial injury through inhibition of the janus kinase-signal transducer and activator of transcription (JAK/STAT) signalling pathway (Zhang et al. 2013b). It also attenuated the expression of proinflammatory cytokines, including interleukin-1β and tumour necrosis factor-α. Moreover, oxymatrine exhibited antiinflammatory properties as heart function and myocardial contractility were improved and pathological and ultrastructural injury were prevented in myocardial tissue induced by septic shock.

Neuroprotective/Cerebral Protective Activity

Studies in rats with cerebral infarct induced by ischaemia–reperfusion showed that pretreatment with 100 or 200 mg/kg *Sophora japonica* and posttreatment with 200 mg/kg *S. japonica* significantly reduced the grade of neurological deficit and the ratio of cerebral infarction area (Lao et al. 2005). Further, pretreatment with 200 mg/kg *S. japonica* also significantly reduced ED1 (mouse anti rat CD68) and interleukin-1beta immunostaining positive cells, and apoptotic cells in ischaemia–reperfusion cerebral infarct rats. The study demonstrated that *S. japonica* could reduce the cerebral infarction area and neurological deficit induced by ischaemia–reperfusion in rats by its suppressive action of microglia, interleukin-1beta and apoptosis, suggesting its potential as a treatment for cerebral infarct in humans. Pu et al. (2007) found both rutin and quercetin (50 mg/kg × 2) improved spatial memory impairment in the 8-arm radial maze task and neuronal death in the hippocampal CA1 area induced by repeated cerebral ischaemia in rats; however, catechin (200 mg/kg × 2) and (−)-epigallocatechin gallate (EGCG) (50 mg/kg × 1) did not. Administration of EGCG (50 mg/kg × 2) resulted in a high mortality rate. These results suggested that in this repeated cerebral ischaemia model, the 4-oxo group and the 2,3-double bond in the C ring of rutin and quercetin were related to their neuroprotective action.

Studies found that *Sophora japonica* flower extract reduced the size of cerebral infarction and neurological deficits and reduced microglial activation, interleukin-1β release and number of apoptotic cells in ischaemia–reperfusion injured Sprague–Dawley rats (Chen and Hsieh 2010). Studies suggested that *S. japonica* contained both antihaemorrhagic and antihaemostatic substances and reduced cerebral infarction partly as a result of its antioxidative and antiinflammatory activities. The results of animal studies suggested that the neuroprotective effect of rutin on trimethyltin-induced spatial memory impairment could be attributable to its inhibitory effect against microglial activation and its role in synapse formation via neurotrophic factors in the hippocampus (Koda et al. 2009).

Pulmoprotective Activity

Pretreatment of mice with oxymatrine (*S. japonica* alkaloid) significantly alleviated oleic

acid-induced acute lung injury which was characterized by prominent atelectasis, intra-alveolar and interstitial patchy haemorrhage, oedema, thickened alveolar septum, formation of hyaline membranes and the existence of inflammatory cells in alveolar spaces (Xu et al. 2005). This attenuation was accompanied by reduction of lung index and wet-to-dry weight ratio, decreases in serum TNF-alpha level and inhibition of phosphorylated p38 MAPK. The findings suggested that oxymatrine had a beneficial effect on acute lung injury induced by oleic acid in mice and may inhibit the production of proinflammatory cytokine, TNF-alpha, by means of the inhibition of p38 MAPK. In another study, administration of oxymatrine to mice with bleomycin-induced lung fibrosis inhibited the proliferation of murine lung fibroblasts, arrested the cells at G(0)/G(1) phase and reduced the expression of cell-cycle regulatory protein, cyclin D1 (Chen et al. 2008). In addition, the steady-state production of collagen and the expression of alpha1(I) pro-collagen and alpha2(I) pro-collagen mRNA in fibroblasts were inhibited by oxymatrine in a dose-dependent manner. The results suggested that oxymatrine may attenuate pulmonary fibrosis induced by bleomycin in mice, partly through inhibition of inflammatory response and lipid peroxidation in lung induced by bleomycin and reduction of fibroblast proliferation and collagen synthesis.

Antitumour Activities

Among 11 isoflavones of *Sophor*a species tested, genistein produced high cytotoxic activity against human oral tumour cell lines (HSC-2, HSG; CC_{50} = 31,54 μg/ml, respectively) than against normal cells (human gingival fibroblast, HGF; CC_{50} = 401 μg/ml), suggesting its tumour-specific action (Shirataki et al. 2001). Biochanin A also showed high cytotoxicity activity against human oral tumour cell lines (HSC-2, HSG; CC_{50} = 26, 125 μg/ml). Daidzein and formonetin showed weak cytotoxic activity against human oral tumour cell lines (HSC-2, HSG; (CC_{50} = 114, 117; 596,584 μg/ml, respectively) but much weaker cytotoxicity against normal cells HGF (CC_{50} = 625, 726 μg/ml respectively) indicating their tumour-specific action. Calycosin (HSC-2, HSG; CC_{50} = 179,142 μg/ml) and 7,4′-dihydroxy-3′-methoxyisoflavone (HSC-2, HSG; CC_{50} = 500,524 μg/ml) showed weak activity comparable to daidzein and formonetin. Licoisoflavone A (HSC-2, HSG; CC_{50} = 25,31 μg/ml) and 6,8-diprenylgenistein (HSC-2, HSG; CC_{50} = 10,13 μg/ml) highest cytotoxic activity but lower tumour specificity. Sophoraisoflavone (HSC-2, HSG; CC_{50} = 26,26 ug/ml) and licoisoflavone A (HSC-2, HSG; CC_{50} = 11, 19 μg/ml) also showed higher cytotoxicity but reduced tumour specificity. Matrine-induced apoptosis in human hepatoma Hep G2 cells in a time- and dose-dependent manner through the mitochondrial pathway, and oxidative stress via depletion of glutathione (GSH) directly involved in the apoptotic process (Cheng et al. 2008). Matrine induced the release of cytochrome c from mitochondria to cytoplasm and then stimulated the cleavage of Caspase-9 in a time-dependent manner.

Both collagen synthesis and Smad3 production in human keloid fibroblasts were significantly suppressed in a dose-dependent administration of oxymatrine, alkaloid extracted from *S. japonica* (Fan et al. 2012). Oxymatrine reversed phosphorylation and nuclear translocation of Smad3 induced by TGF-β1. Oxymatrine inhibitory effect in collagen synthesis might be associated with TGF-β/Smad signalling pathway. The results suggested that oxymatrine may be a promising candidate to prevent keloid and other fibrotic diseases. Keloids are benign dermal tumours characterized by fibroblastic proliferation and excessive accumulation of collagen.

Antiviral Activity

Of 11 *Sophora* isoflavones, licoisoflavone A (CC_{50} = 33 μg/ml) and sophoraisoflavone A (CC_{50} = 55 μg/ml) showed high higher anti-*Helicobacter pylori* activity but lower than clarithromycin (CC_{50} = 10 μg/ml) (Shirataki et al. 2001). Other isoflavones were inactive. All 11 isoflavones failed to induce antihuman immunodeficiency virus (HIV) activity.

In 22 patients with chronic hepatitis B treated with oxymatrine 0.4 g/daily by intramuscular injection for 3 months, the seroconversion rate of HBV (hepatitis B virus) DNA and HBeAg (hepatitis B early antigen) in the treated group was 43.47 and 43.47 %, respectively, which was way better than those in the untreated control group respectively (Chen et al. 2002). The study showed that oxymatrine effective in treating chronic hepatitis B. The therapeutic effect was better for patients with lower quantity of serum HBV DNA. In another randomized clinical trial, 253 patients with chronic hepatitis B treated with intravenous or intramuscular injection of oxymatrine and oral oxymatrine capsule showed improvement in liver function, and the negative rate of HBeAg and HBV DNA were increased (Yu et al. 2001). The therapeutic effect of oxymatrine persisted after the cessation of treatment. In a randomized double-blind and placebo-controlled multicenter trial of 199 patients with chronic hepatitis B, administration of oxymatrine injection or oral capsule was found to be safe and efficacious (Lu et al. 2003). In the capsule-treated patients, 76.47 % became normal in ALT level and 38.61 and 31.91 % became negative both in HBV DNA and in HBeAg. In the injection-treated patients, 83.33 % became normal in ALT level and 43.33 and 39.29 % became negative both in HBV DNA and in HBeAg. In the placebo-treated patients, 40.00 % became normal in ALT level and 7.46 and 6.45 % became negative both in HBV DNA and in HBeAg. The rates of complete response and partial response were 24.51 and 57.84 % in the capsule-treated patients, 33.33 and 50.00 % in the injection-treated patients and 2.99 and 41.79 % in the placebo-treated patients, respectively.

Hepatoprotective Activity

Xiang et al. (2002) showed that oxymatrine protected mice from fulminant hepatitis induced by GalN/LPS (galactosamine/lipopolysaccharide) and may block hepatocyte apoptosis and subsequent necrosis through downregulating the production of serum tumour necrosis factor alpha and the expression of Fas and Fas ligand in liver tissue. Similarly in another study, Jiang et al. (2005) reported that the antiapoptotic activity of oxymatrine protects the liver from warm ischaemia–reperfusion injury in rats mainly by downregulation of Fas and Fas ligand in liver tissues. Similar results were also obtained by Meng et al. (2005), wherein oxymatrine protected rats against ischaemia–reperfusion injury of liver by antiapoptotic activity via downregulation of Fas protein expression.

Intestinal Protective Activity

Studies showed that oxymatrine could attenuate intestinal ischaemia–reperfusion injury induced in rats (Zhao et al. 2008). The oxymatrine-treated group had a significantly lower histological score and apoptosis index than the saline group, demonstrating that the pre-administration of oxymatrine attenuated gut damage. Moreover, oxymatrine inhibited the production of lipid peroxides (LPO), decreased the serum levels of tumour necrosis factor (TNF)-alpha and downregulated expression of phosphorylated p38 mitogen-activated protein kinase, Fas and FasL, which had been elevated by ischaemia–reperfusion.

Renoprotective Activity

Studies showed that matrine exhibited a renoprotective effect on experimental glomerulosclerosis in rats, probably through the reduction of the transforming growth factor-beta1 (TGF-beta1) negative function via connective tissue growth factor, which inhibited the activation and proliferation of glomerular intrinsic cells, and decreasing the secretion of extracellular matrix proteins accordingly (Zhang and Jin 2004). Administration of oxymatrine inhibited adriamycin-induced chronic renal fibrosis in rats and functional impairment by downregulating NF-kappaB expression, which may play a key role in protection against renal fibrosis (Chen and Jin 2007).

Antidiabetic Activity

Among compounds isolated from the stem bark, daidzein, puerol A and paratensein-7-*O*-glucoside exhibited potent aldose reductase inhibitory effects, with IC_{50} values of 3.2, 6.4 and 1.9 μM, respectively (Park et al. 2010).

Antibacterial Activity

The ethanol extract of *S. japonica* flower buds exhibited marked antibacterial activity against *Propionibacterium acnes*, *Propionibacterium avidum* and *Staphylococcus aureus* under weak acidic conditions (Kimura and Yamada 1984). The bioactive principles were found to be quercetin, rutin and isorhamnetin-3-rutinoside.

Oestrogenic Activity

Sophora japonica methanol extract showed oestrogenic effect only after naringinase treatment (El-Halawany et al. 2011). The naringinase-treated methanol extract of *Sophora japonica* seeds showed potent oestrogen agonist activity (El-Halawany et al. 2010). The aglycones genistein and kaempferol were found to be the main phytoestrogens in the naringinase-treated methanol extract. Additionally, kaempferol was nearly equipotent to genistein as an oestrogen agonist. Sophoricoside isolated from the untreated methanol extract showed weak oestrogenic activity on ERbeta only.

Antiobesity Activity

Administration of a diet containing *Sophora japonica* fruit to high-fat diet-induced obese mice for 4 weeks significantly decreased body weight gain (Park et al. 2009). *S. japonica* also reduced serum and hepatic triglyceride, serum total and high-density lipoprotein cholesterol, glucose level and fat mass and caused a decrease in the number of large adipocytes and a concomitant increase in the number of small adipocytes, which may explain at least in part the antiobesity effects. The results indicated a potential role of *S. japonica* in the control of body weight and obesity-related metabolic diseases. The ethyl acetate fraction fruit extracts inhibited morphological differentiation and lipid accumulation in the C3H10T1/2 mesenchymal stem cells and 3 T3-L1 preadipocytes (Jung et al. 2011). The fraction also reduced the expression of peroxisome proliferator-activated receptor γ and other adipocyte markers. The fraction was found to have the highest total phenol contents, suggesting that the polyphenols in the fraction mediated the anti-adipogenic effects. Genistein, a known anti-adipogenic compound, was identified in the fractions and suggested to be probable mediator of the anti-adipogenic effects of the ethyl acetate fractions. The results validated the beneficial roles of *S. japonica* in controlling body weight and obesity-related metabolic diseases.

Skin Whitening (Tyrosinase Inhibitory) Activity

Sophora japonica extract showed inhibition of mushroom tyrosinase activity in-vitro (Lee et al. 1997). Four herbs, *Pharbitis nil*, *Sophora japonica*, *Spatholobus suberectus* and *Morus alba*, exhibited potent inhibitory effects on tyrosinase (IC_{50} values 24.9, 95.6, 83.9 and 78.3 μg/ml, respectively) (Wang et al. 2006a). Melanin inhibition was not dose dependent. *Sophora japonica* (IC_{50}: 14.46 μg/ml, DPPH; 1.95 μg/ml, hydroxyl radical) and *Spatholobus suberectus* (IC(50): 10.51 μg/ml, DPPH; 4.36 μg/ml, hydroxyl radical) showed good antioxidative activities and high phenolic contents (255 and 189 mg of gallic acid/g extract, respectively). Among active anti-tyrosinase extracts, *Sophora japonica* and *Spatholobus suberectus* were especially potent in human epidermal melanocyte cells in terms of free radical scavenging effects and high phenol contents, making them the strongest candidates for cosmetic application found in the study. A putrescine compound, *N*-feruloyl-*N′*-*cis*-feruloyl-putrescine, was minimally cytotoxic (cell viability >90 % at 100 μM) and the IC_{50}

value for suppression of cellular tyrosinase activity in human epidermal melanocytes was estimated at 85.0 μM (Lo et al. 2009).

Antiosteoporotic Activity

Nine weeks after oral administration of *S. japonica* fruit extract to ovariectomized rats, elevated deoxypyridinoline level was significantly decreased and Ca levels were elevated compared to control (Shim et al. 2005). Further trabecular bone area (TBA) in the tibia and lumbar was also increased compared with control group. The preventive or treatment effects of Sophorae Fructus extracts on bone loss in ovariectomized rats appeared to be due to suppression of bone turnover.

Treatment of SD rats with a 4.5 or 9 mg/kg dosage of genistein (extracted from *S. japonica*) prevented osteoporosis significantly at the fourth week after treatment (Wang et al. 2006b). In comparison with the anti-osteoporosis effects of soybean genistein, the genistein extracted from Huaijiao had the same beneficial effect on anti-osteoporosis.

Interleukin-5 Inhibitory Activity

Fruits of *Sophora japonica* exhibited an inhibitory effect in the interleukin IL-5 bioassay of mIL-5-dependent Y16 proliferation; the isoflavonoids of sophoricoside, genistein, orobol and genistin were isolated as the IL-5 inhibitors from the fruits (Min et al. 1999). Among the IL-5 inhibitors, sophoricoside exhibited the highest inhibitory effect with 89 % inhibition at 12.5 μM, 82 % at 6.3 μM, 72 % at 3.1 μM, 59 % at 1.6 μM and 24 % at 0.8 μM where the 50 % inhibition (IC_{50}) was shown at the concentration of 1.5 μM. In the order of IC_{50} values, the inhibitory potency in the IL-5 bioassay was sophoricoside > orobol (9.8 μM) approximately equal to genistein (10.6 μM) > genistein (51.9 μM).

Analgesic Activity

Puerol A isolated from the roots, greatly inhibited 3 h-ethyl ketocycloazocine on the receptor-binding assay test and so may be developed as a nonaddictive analgesic (Shirataki et al. 1987).

Alleviation of Postmenopausal Symptoms

In a randomized double-blind placebo-controlled clinical trial, consumption of Rexflavone (*S. japonica* fruit extract) was found to possess beneficial effects on the postmenopausal symptoms in postmenopausal women (Lee et al. 2010). Rexflavone significantly improved 11 menopausal symptoms including hot flash, which was evaluated by the modified Kupperman Index (KI), while hormone level and lipid profile were little altered by consumption. Rexflavone had no adverse effect and appeared to be safe for long-term consumption.

Radioprotective Activity

A mixture of *Sophora japonica* and pantocrine exhibited the highest radioprotective effect in irradiated (2.5 Gy) human lymphoblastoid cells when injection 15 minutes after irradiation which was more effective than preinjection (Narimanov et al. 1990). *Sophora japonica* and pantocrine were shown to increase the survival rate of lethally exposed mice (LD90/30) when administered in a combination 5–15 minutes before irradiation. Similar radioprotective effects were found with *Sophora japonica* and its combination with an antioxidant vitamin complex administered enterally to mongrel male rats exposed to whole-body gamma-radiation (7, 9 and 11 Gy) (Sokol'chik et al. 1992).

Traditional Medicinal Uses

Sophora japonica is commonly used in traditional Chinese medicine and is considered to be one of the 50 fundamental herbs (Duke and Ayensu 1985). The flowers and flower buds are astringent, antibacterial, anticholesterolaemic, antiinflammatory, antispasmodic, haemostatic,

antihaemorrhagic, oestrogenic and hypotensive (Stuart 1979; Duke and Ayensu 1985; Bown 1995; Vo 1997; WHO 1998; Tran 1999; Le and Nguyen 1999). They have been reputed as therapeutic relief for various types of haemorrhages (e.g. haemoptysis, epistaxis, haematuria, haematochezia, haemorrhagic haemorrhoids, metrorrhagia) and are also useful for the treatment of hypertension, poor peripheral circulation, ophthalmia and intestinal worms. Flower buds and young pods are an important source of rutin, which has 'vitamin P'-like properties and is used in the treatment of conditions characterized by increased capillary permeability and fragility. The seedpods are abortifacient and the underlying reason for the second ranking of the plant in a study of 250 potential antifertility agents in China (Duke and Ayensu 1985). The seed is emetic and haemostatic and employed in the therapy of haemorrhoids, haematuria, uterine bleeding, constipation, stuffy sensation in the chest, dizziness, red eyes, headache and hypertension. The leaves are laxative and used in the therapy of epilepsy and convulsions. A stem decoction is employed for piles, sore eyes and skin problems. Oxymatrine an alkaloid from *Sophora japonica* has been used to treat inflammatory diseases and various types of cancer in traditional Chinese medicine (Zhang et al. 2013b).

Other Uses

In northern China it is used as component of agroforestry systems. In northern Indochina, the tree was planted in the villages for obtaining raw material for paper production. In temperate and subtropical regions around the world, the Japanese pagoda tree is commonly cultivated as an ornamental and shade trees in gardens and parks and as a road-side tree, in large parking lot islands, median strip plantings in highways or as a buffer strips around parking lots. The pagoda tree is also widely used in bonsai gardening. The shoots and leaves appeared to be suitable as fodder. The wood is durable and tough and can be used for window and door frames and for agricultural implements. The flower buds can be used for dyeing yellow or a beautiful granite grey. Mixed with indigo, the dye gives a green colour. In China and Vietnam this dye was formerly important for dyeing silk, embroidery thread and hat tassels. In Java, dried flower buds were imported from China for the batik industry. In the fine 'soga-batik' process, they were used in the last fixing and colouring bath after the real colouring process, in a mixture together with rice flour, camphor, lime juice, sugar and water. In China, extracts of the leaves and pods are used to adulterate opium.

Comments

The tree is propagated by seeds which germinate readily after scarification or soaking treatment with hot water. Grafting, layering, greenwood and root cuttings are used for the ornamental cultivars. Trees can be coppiced successfully.

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Trifolium pratense

Scientific Name

***Trifolium pratense* L.**

Synonyms

Trifolium borysthenicum Gruner, *Trifolium bracteatum* Schousb., *Trifolium lenkoranicum* (Grossh.) Roskov, *Trifolium pratense* var. *lenkoranicum* Grossh., *Trifolium ukrainicum* Opperman

Family

Fabaceae, also placed in Papilionaceae

Common/English Names

Beebread, Broad-Leaved Clover, Chilean Clover, Cow Clover, Cowgrass Clover, Early Blooming Clover, June Clover, King's Crown, Mammoth Clover, Mammoth Red Clover, Meadow Clover, Meadow Honeysuckle, Meadow Trefoil, Medium Red Clover, Multi-Cut Clover, Peavine Clover, Purple Clover, Red Clover, Sweet Clover, Sweet Kitty Clover, Wild Clover

Vernacular Names

Arabic: Barsym 'Āhamar
Brazil: Trevo Dos Prados
Chinese: Hong Che Zhou Cao, Hong San Ye Cao
Czech: Jetel Luční, Jetel Luční Červený
Danish: Rød-Kløver, Rødkløver
Dutch: Rode Klaver
Eastonian: Aasristik
Esperanto: Ruĝa Trifolio, Trifolio Ruĝa
Finnish: Nurmiapila, Puna-Apila
French: Trèfle Commun, Trèfle Des Prés, Trèfle Rouge, Trèfle Violet, Triolet
Gaelic: Seamair Dhearg
German: Feldknoppern, Fleischklee, Futterklee, Himmelsbrot Honigklee, Hummellust, Rot-Klee, Rotklee, Roter Wiesen-Klee, Steyrerklee, Sügerli, Wiesen-Klee, Weissklee, Zuckerblümli, Zuckerbrot
Greek: Trifilli To Limonio
Hebrew: Tiltan
Hungarian: Réti Here, Lóhere, Vörös Here
Icelandic: Rauðsmari
India: Laal Tipatiya Ghaas, Tripatra (Hindi)
Italian: Trifoglio Dei Prati, Trifoglio Pratense, Trifoglio Rosso, Trifoglio Violetta
Japanese: Aka Kurooba, Aka Tsume Kusa, Aka-Tsumekusa, Murasaki-Tsumekusa Murasaki Tsume Kusa, Reddo Kurooba
Korean: Bulgeuntokkipul
Mexico: Trébol De Los Prados
Norwegian: Raudkløver, Rødkløver Sukkertopp, Sukkertust, Søtekolle
Polish: Koniczyna Czerwona, Koniczyna Łąkowa
Portuguese: Pé-De-Lebre, Trevo-Comum, Trevo-Dos-Prados, Trébol Pratense, Trevo-Violeta
Russian: Klever Krasnyj, Klever Lugovoi
Slovaščina: Črna Detelja, Detelja Črna

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Slovencina: Ďatelina Lúčna
Spanish: Trébol Común, Trébol Morado, Trébol Rojo, Trébol Violeta
Swedish: Amerikansk Rödklöver, Rödklöve
Taiwan: Hong Shu Cao
Turkish: Çayır Dutu, Çayır Üçgülü, Dirfil, Yonca
Vietnamese: Chẽ Ba Đồng Cỏ; Ba Chẽ Đỏ
Welsh: Meillion Coch

Origin/Distribution

Red clover is indigenous to Europe, western Asia and northwest Africa but has been introduced and naturalized in many other parts of the world.

Agroecology

Red clover favours cool weather conditions. It is well-adapted to a wide range of soil types and conditions. It tolerate wet conditions but thrives best in well-drained fertile soils. It is found in meadows, wet and dry grassland, woodland, forest margins, field borders, roadsides and paths and widely planted as pastures.

Edible Plant Parts and Uses

Leaves and young flowering heads are edible raw or cooked (Hedrick 1972; Tanaka 1976; Launert 1981; Facciola 1990). The young leaves are harvested before the plant comes into flower and are used in salads and soups or cooked like spinach (Launert 1981) The leaves can be dried, powdered and sprinkled on foods such as boiled rice (Facciola 1990). The dried leaves impart a vanilla flavour to cakes (Schofield 2003) Young flowering heads can be eaten raw in salads (Cribb and Cribb 1976; Schofield 2003). Some recipes with clover flowers are lentil and clover risotto and cauliflower and clover cheese (Roberts 2000). Fresh or dried flowers can be made into a delicate sweet herbal tea (Lust 1974; Facciola 1990). Flowers and seed pods can be dried, ground into a powder and used as a flour. The seeds can be spouted and used in salads (Facciola 1990). Roots can be eaten cooked (Kunkel 1984; Schofield 2003).

The high quercetin concentration and soyasaponin occurrence make the seeds of some *Trifolium* species (*T. repens, T. pratense*) a potential source of health beneficial phytochemicals for use in human nutrition (Sabudak and Guler 2009).

Botany

A herbaceous pubescent to glabrescent perennial, with erect to ascending stems, 20–80 cm high and with a fairly deep tap root. Leaves are alternate, trifoliate, basal and cauline, long petiolate in lower leaves, shortly petiolate in upper leaves with membranous, ovate-lanceolate stipules (Plates 1, 2, 3, and 4). Leaflets ovate-elliptic or obovate, 15–30 mm long by 8–15 mm broad, green with a characteristic pale inverted v-pattern in the outer half of the leaflet, base broadly cuneate, margins obscurely serrulate, apex obtuse, rarely retuse. Flowers 30–70, in dense globose or ovoid, terminal, sessile to shortly pedunculate heads, subtended by involucre of stipules (Plates 2, 3, and 4). Calyx with subulate teeth, pubescent or glabrous. Corolla purple or dark pink, standard spatulate, ovary elliptic. Legume ovoid with one yellowish-brown ovoid seed.

Plate 1 Trifoliate leaves of red clover

Plate 2 Close view of flower head and trifoliate leaf (J. Holopainen)

Plate 3 Flower head, hairy leaves and peduncle (T. James)

Plate 4 Top view of flower head (David Llyod)

Nutritive/Medicinal Properties

Plant Phytochemicals

From the plant, glucose, galactose, arabinose, xylose and mannose and amino acids phenylalanine, leucine, isoleucine, methionine, aspartic acid, proline, alanine and histidine were found (Kazakov and Samokish 1980). Phytin and a mixture of Ca and Mg salts of inositol phosphate were also isolated. The amount of ash in the herbage of clover was 8.4 % and the amount insoluble in HC1 was 1.5 %. The amounts of macroelements (mg^{-}%) determined were K^{+} 1620, Na^{+} 310, Ca^{2+} 1240 and Mg^{2+} 1090. The oil yield for *T. pratense* was small 0.018 % (weight/fresh weight basis) (Tava et al. 2009). Several classes of compounds were found in the oil, including alcohols, aldehydes, ketones, terpenes, esters, hydrocarbons, phenolics and acids.

A total of eleven flavonoids were identified by liquid chromatography–electrospray mass spectrometry: genistin, isoquercitrin, ononin, daidzein, sissotrin, formononetin, biochanin A, pratensein, pectolinarigenin, pseudobaptigenin and hyperoside (He et al. 1996). The following isoflavones were isolated from red clover: prunetin, irilone, biochanin A, formononetin, pratensein, genistein, calycosin and daidzein (Huang and Tu 2004).

Isoflavone compounds identified in the methanol/water (7:3 v/v) extract of red clover included daidzein, genistin, daidzein, glycitein, orobol, calycosin, genistein, pratensein, pseudobaptigenin, formononetin, texasin, irilone, prunetin, biochanin A, trifoside (prunetin-4′-*O*-β-D-glucoside), daidzein-7-*O*-β-D-glucoside-6″-*O*-malonate, daidzein-7-*O*-β-D-glucoside-6″-*O*-acetate, glycetin-7-*O*-β-D-glucoside, genistein-7-*O*-β-D-glucoside-6″-*O*-malonate, calycosin-7-*O*-β-D-

glucoside, calycosin-7-*O*-β-D-glucoside-6″-*O*-malonate, prunetin-4′-*O*-β-D-glucoside-6″-*O*-malonate, prunetin-4′-*O*-β-D-glucoside-6″-*O*-acetate, pratensein-7-*O*-β-D-glucoside, pratensein-7-*O*-β-D-glucoside-6″-*O*-malonate, pseudobaptigenin-7-*O*-β-D-glucoside, pseudobaptigenin-7-*O*-β-D-glucoside-6″-*O*-malonate, pseudobaptigenin7-*O*-β-D-glucoside-6″-*O*-acetate, orobol-7-*O*-β-D-glucoside-6″-*O*-malonate, 3-methylorobol, 3-methylorobol-7-*O*-β-D-glucoside, 3-methyloronol-7-*O*-β-D-glucoside-6″-*O*-malonate, irilone-4′-*O*-β-D-glucoside, irilone-4′-*O*-β-D-glucoside-6″-*O*-malonate, irilone-4′-*O*-β-D-glucoside-6″-*O*-acetate, irilin B-5,7,2′-trihydroxy-6-methoxyisoflavon-7-*O*-β-D-glucoside, irilin B-5,7,2′-trihydroxy-6-methoxyisoflavon-7-*O*-β-D-glucoside-6″-*O*-malonate, sissotrin (biochanin A-7-*O*-β-D-glucoside), rormosin-7-*O*-β-D-glucoside, afrormosin-7-*O*-β-D-glucoside-6″-*O*-malonate, formononetin-7-*O*-β-D-glucoside-6″-acetate, formononetin-7-*O*-β-D-glucoside-6″-*O*-malonate, ononin (formononetin-7-*O*-β-D-glucoside), isomer (formononetin-7-*O*-β-D-glucoside-6″-*O*-malonate), isomer (formononetin-7-*O*-β-D-glucoside-6″-*O*-malonate), isomer (formononetin-7-*O*-β-D-glucoside-6″-*O*-acetate), texasin-7-*O*-β-D-glucoside-6″-*O*-malonate, biochanin A-7-*O*-β-D-glucoside-6″-*O*-malonate, and biochanin A-7-*O*-β-D-glucoside 6″-*O*-acetate (Klejdus et al. 2001).

Thirty-one isoflavones were found in red clover leaves and stem: daidzein-G (daidzein), glycitein-G (glycitin), genistein-G (genistin), daidzein-G–M, calycosin-G–M, pratensein-G–M, pseudobaptigenin-G, formononetin-G (ononin), genistein-G–M, pratensein-G–M, daidzein, glycitein, irilone-G, calycosin, pseudobaptigenin--G–M, formononetin-G–M, formononetin-G, biochanin A–G, prunetin-G, genistein, irilone-G–M, irilone-G–M, irilone-G–M, biochanin A–G–M, prunetin-G–M, pseudobaptigenin, biochanin A–G–M, formononetin, irilone, prunetin and biochanin A, where G represents glucosyl or galactosyl moiety, and M, malonyl (in general, glucosyl group, occasionally galactosyl group, was substituted on 7/4′ position of aglycone and malonyl group was linked to 6″ position of sugar moiety) (Wu et al. 2003). Twenty-five isoflavones were detected in the roots except for daidzein, daidzein-G-M, biochanin A-G-M, prunetin-G, prunetin and biochanin A. Twenty-six were found in the flowers except for daidzein, glycitin, genistin, daidzein-G-M and prunetin.

Different red clover cultivars showed significantly different concentrations of individual and total isoflavones (Tsao et al. 2001). The leaf contained the highest overall concentration, followed by the stem, petiole and flower. Biochanin A and formononetin were the predominant isoflavones in all cultivars and all parts, along with eight other minor aglycones, daidzein, genistein, glycitein, irilone, orobol, pratensein, pseudobaptigenin and prunetin, and four minor malonyl glycosides, genistein-7-glucoside-6″-malonate, orobol-7-glucoside-6″-malonate, formononetin-7-glucoside-6″-malonate and biochanin A-7-glucoside-6″-malonate. The isoflavone compositions and concentrations were also found to be different between red clover parts harvested at the early bud stage and the late flowering stage. Clover tissues were found to be rich in the isoflavonoids formononetin and biochanin A, particularly in plants left to wilt for 24 hours (Flythe and Kagan 2010).

The isoflavonoids prunetin, genistein, prunetin-4′-*O*-β-D-glucopyranoside, prunetin-4′-*O*-α-D-glucopyranoside, genistein-7-*O*-β-D-galactopyranoside and (+)-pinitol (1R,2S,3s,4S,5S,6r)-6-methoxycyclohexane-1,2,3,4,5-pentaol were isolated from the aerial parts (Drenin et al. 2011). Concentrations of isoflavones (μg/g) in red clover leaves were daidzein 42 μg, daidzein 0 μg, genistin 560 μg, genistein 0 μg, formononetin-7-*O*-β-D-glucoside-6″-*O*-malonate (FGM) 4900 μg, ononin 970 μg, formononetin 600 μg, biochanin A-7-*O*-β-D-glucoside-6″-*O*-malonate (BGM) 3300 μg, sissotrin 540 μg and biochanin A 330 μg (de Rijke et al. 2001). The two main isoflavones in red clover were FGM and BGM. Both were subject to decomposition according to formononetin-7-*O*-β-D-glucoside-6″-*O*-malonate (FGM) → ononin (FG) → formononetin (F) and biochanin A-7-*O*-β-D-glucoside-6″-*O*-malonate (BGM) → sissotrin (BG) → biochanin A (B). The main isoflavones in leaf extracts of *T. pratense* were biochanin A and formononetin, their 7-*O*-glucosides,

and two glucoside malonate isomers of each of them (de Rijke et al. 2004). The two formononetin glucoside malonate isomers were identified as 7-*O*-β-D-glucoside 6″-*O*-malonate and 7-*O*-β-D-glucoside 4″-*O*-malonate. The biochanin A glucoside malonate isomers had different structures. The main and later eluting isomer was biochanin A 7-*O*-β-D-glucoside 6″-*O*-malonate, and the minor and earlier eluting isomer is 5-hydroxy-7-methoxyisoflavone 4′-*O*-β-D-glucoside 4″-*O*-malonate. The most prominent isoflavones found in red clover were formononetin and biochanin A and their corresponding glucosides and malonyl glucoside esters (Swinny and Ryan 2005). They found that postharvest freeze-drying inhibited the conversion of the glycosides to the aglycones, while vacuum drying allowed for maximum conversion of the glycosides to their corresponding aglycones. Air drying produced a low level of the aglycones formononetin and biochanin A, and oven drying promoted decarboxylation of the malonyl glucosides to the acetyl glucosides. Exposure to enhanced UV-B radiation resulted in an increase in total formononetin and biochanin A isoflavone levels, indicating that harvest during a period of high ambient UV-B radiation may be appropriate for maximum yield. The levels of caffeic acid and flavonols also increased by about 40 and 250 %, respectively, on exposure to enhanced UV-B radiation.

The emission of 24 compounds comprising monoterpenes, homoterpenes, esters, hydrocarbons and aldehydes from red clover plant was quantified in the laboratory, of which eight showed increased emission rates after herbivory by *Spodoptera littoralis* caterpillars (Kigathi et al. 2009). The most abundant compounds included the monoterpene (*E*)-β-ocimene (30–50 % of the total), the isomeric monoterpene (*Z*)-β-ocimene, the monoterpene linalool, the sesquiterpene (*E*)-β-caryophyllene, the sesquiterpene-derived homoterpene 4,8-dimethyl-1,3,7-nonatriene (DMNT), (*E,E*)-α-farnesene, 1-octen-3-ol, and methyl salicylate. Other compounds included α-pinene, sabinene, β-pinene, limonene, 1,8-cienole, indole, (*Z*)-jasmone, (*E*)-β-farnesene, germacrene D, (*Z*)-3-hexenyl acetate, benzyl alcohol, dodecane, undecane, octylaldehyde, nonanal and decanal.

Volatile components of red clover hay and silage comprised alkanes, alkenes, aldehydes, alcohols, ketones, esters, acids, terpenes, unidentified compounds and others (Figueiredo et al. 2007). In hay, reductions of the percentages of alcohols, such as 3-methylbutanol and 1-hexanol, of aldehydes and of low boiling point ketones were observed A sesquiterpene (β-farnesene; ca. 10 %) and a phytol degradation product (6,10,14-trimethyl-2-pentadecanone; ca. 12 %) were the most abundant compounds detected in hay. In silage, as a result of the fermentation of fresh red clover, esters (ca. 46 %) were a more representative class of compounds. Silage esters included methyl esters, ethyl esters, acetates, non-linear esters, phenylethyl esters and others.

A synthetic pyridine derivate, 2-(2-fluoro-6-nitrobenzylsulfanyl) pyridine-4-carbothioamide, was found to be a good elicitor of isoflavonoid production in red clover suspension culture (Kašparová et al. 2012). After 48-hours application of 1 μmol/l concentration, maximum contents of genistin (11.60 mg/g DW), daidzein (8.31 mg/g DW) and genistein (1.50 mg/g DW) were recorded, and the production of these isoflavonoids was significantly increased, when compared with the control, by 152, 151 and 400 %. The tested substance showed to be an effective elicitor of phenylpropane metabolism.

Leaf Phytochemicals

The leaves were found to contain 81 % water, 4 % protein, 0.7 % fat, 2.6 % fibre and 2 % ash (Duke and Ayensu 1985). Based on over 500 analyses, Miller (1958) reported that green red clover forage had the following nutrient composition: 12.4–34.87 % protein (av. 18.2), 3.2–5.9 % fat (av. 4.0 %), 12.7–30.8 % crude fibre (av. 24.2), 7.0–13.6 % ash (av. 8.8), and 37.1–49.7 % N-free extract (av. 44.8 %), 0.58–3.21 % Ca (av. 1.76), 0.24–0.53 % P (av. 0.29), 1.49–2.94 % K (av. 2.10 %), 0.36–0.57 % Mg (av. 0.45), 0.016–0.032 % Fe (av. 0.03), 7.3–10.3 ppm Cu (av. 8.8 ppm), and 121–464 ppm Mn (av. 159 ppm). The leaf-protein concentrate (59 % protein) comprised 6.4 % arginine, 2.5 % histidine, 5.4 % threonine,

1.7 % tryptophan, 9.5 % leucine, 5.3 % isoleucine, 1.7 % methionine, 6.87. lysine, 6.1 % phenylalanine and 6.8 %. valine.

Major volatile components identified in red clover leaves were (*Z*)-3-hexenyl acetate, (*Z*)-3-hexenol and (*E*)-β-ocimene and (*Z*)-β-ocimene (Buttery et al. 1984). In red clover leaves, a total of 31 different phenolics were identified: *cis–trans*-phaselic acid, *cis*-clovamide, daidzein-G, daidzein-G-M, calycosin-G, calycosin-G-M, genistein, genistein-G, genistein-G-M, pratensein, irilone, irilin B, methylorobol, methylorobol-G, methylorobol-G-M, formononetin, formononetin-G, formononetin-G-M, afrormosin-G-M, maackiain, maackiain-G-M, biochanin A, biochanin A-G-M, prunetin, texasin, texasin-G-M, quercetin-glucoside, quercetin-galactoside, quercetin-G-M, kaempferol-G and pseudobaptigenin-G-M (Saviranta et al. 2010a). The most abundant isoflavones and flavonoids were biochanin A glycoside malonate (G-M), formononetin-G-M and quercetin-G-M. Elevated ozone (mean 32.4 ppb) increased the total phenolic content of leaves and also had minor effects on the concentrations of individual compounds. Elevated ozone increased the net photosynthesis rate of red clover leaves before visible injuries by 21–23 %.

The acetone-soluble lipids of red clover leaves largely comprised galactosyl-1-glycerol (I) and L linoleate (Weenink 1961). The fatty acids of the galactolipids contained (mole%) linolenic, 95.8 %; linoleic, 1.9 %; and palmitic, 2.3 %. Oleic, stearic and palmitoleic acids were not detected. Triglycerides were not found in the acetone-soluble lipid fraction. The hexane-soluble fraction contained galactose 4.2 %, glycerol 2.4 %, nonsaponifiable matter 43.3 % and fatty acids 26.0 %, the remainder being acidic, non-fatty material. Free sterols (0.8 %), sterol esters (0.57 %), triglycerides (1.5 %), diglycerides (0.6 %) and normal hydrocarbons (0.38 %) were isolated from the acetone-soluble lipids of red clover leaves (Weenink 1962). Free and combined sterol contained β-sitosterol, and the hydrocarbons consisted of homologous odd- and even-numbered series C_{15} to C_{25} with C_{25} predominating. The diglycerides contained over 50 % of palmitic acid, whereas the sterol esters and triglycerides contained linoleic and linolenic acids as the main components. The composition of the acetone-insoluble fraction (molar proportions) of red clover leaves comprised phosphatidycholine 37 %, phosphatidylglycerol 23 %, phosphatidylethanolamine 15 %, phosphatidylinositol 2 %, uncharacterized acidic compounds 13 % and unknown compounds 10 % (Weenink 1964). An unusual C_{14} unsaturated fatty acid was found in the phosphatidylglycerol fraction. *Trans*-Δ^3-hexadecenoic acid ($16:1^t$) was found to occur exclusively in the phosphatidylglycerol fraction of red clover leaves (Weenink and Shorland 1964). The fatty acid composition (mol %) of phosphatidylglycerol in red clover leaves comprised 16:0 (20 %), $16:1^t$ (40 %), 18:0 (1 %), 18:1 (7 %), 18:2 (13 %) and 18:3 (25 %) (Murata et al. 1982). In response to waterlogging, the concentrations of biochanin A and biochanin A-7-*O*-glucoside malonate, biochanin A-7-*O*-glucoside and genistein-7-*O*-glucoside in the leaves increased two- to threefold after a lag period of 3 weeks because of disturbed root nodulation (De Rijke et al. 2005). The other isoflavones detected—formononetin, formononetin-7-*O*-glucoside malonate and formononetin-7-*O*-glucoside—did not show any significant changes related to waterlogging. After restoring normal soil water conditions, the concentrations of biochanin A and its glucoside and glucoside malonate rapidly returned to the initial values, whereas the concentration of genistein-7-*O*-glucoside remained high.

Red clover leaves were found to accumulate several μmol of phaselic acid [2-*O*-caffeoyl-L-malate] per gram fresh weight (Sullivan and Zarnowski 2010). Their study found that phaselic acid was likely formed by transfer of a caffeoyl moiety to malic acid, although the existence of a second C3′H capable of hydroxylating p-coumaroyl-malate could not be definitively excluded. They identified coumarate 3′-hydroxylase (CYP98A44), a cytochrome P450 which was capable of hydroxylating p-coumaroyl-shikimate but not p-coumaroyl-malate in the biosynthesis of phaselic acid. The gene for cytochrome P450 C3′H (CYP98A44) was cloned from red clover.

Root Phytochemicals

Formononetin and the new isoflavonoid glycosides formononetin-7-*O*-*β*-D-galactopyranoside and inermin-3-*O*-*β*-D-galactopyranoside were isolated from *Trifolium pratense* roots (Drenin et al. 2008). The following volatile compounds were identified from red clover roots: butyl acetate, E-2-hexenal, α-pinene, benzaldehyde, 6-methyl-5-hepten-2-one, limonene, acetophenone, methyl benzoate, nonanal, octanoic acid and decanal (Tapia et al. 2007). The results showed that the clover root borer (*Hylastinus obscures*) was attracted to root volatiles of 1.5-year-old extracts but not to those from 2.5-year-old extracts. A 10 μg dose of methyl benzoate and E-2-hexenal attracted the insect, whereas the same dose of limonene repelled the red clover borer. The following volatiles and free fatty acids were detected in the dichloromethane extract of 9-month-old red clover roots: 1-nonene, 3-octanol, 2-pentyl furan, benzyl alcohol, limonene, maltol, benzoic acid, *o*-acetyl-*p*-cresol, eugenol, caryophyllene oxide, pentadecanal, lauric acid, palmitic acid, oleic acid and stearic acid (Manosalva et al. 2011). The four long-chain free fatty acids lauric, palmitic, oleic and stearic acids were found to be main components in the extract. Further studies on the response of clover root borer to volatiles emitted from red clover roots afforded the identification of ethanol, E-2-hexenal, hexanal, 3-octanone, limonene and α-pinene (Palma et al. 2012). For females, ethanol and E-2-hexenal were attractive at one or more of the tested doses, while hexanal, 3-octanone, R-limonene and S-limonene were repellent at one or more of the tested doses. In a much earlier study, of 15 root compounds, 10 were attractive to the borer clover root borer (*Hylastinus obscures)* (Kamm and Buttery 1984). None of the attractive compounds were competitive with crude extracts of diseased roots when tested individually. Certain combinations of ethyl laurate, ethyl benzoate, methyl salicylate, eugenol, hexadecanal and chavicol were competitive with crude extracts of diseased root in laboratory tests. Adult borers were not attracted to individual compounds or mixtures in preliminary field tests.

A total of 28 phenolic compounds were tentatively identified in red clover roots (Saviranta et al. 2010b). The most abundant phenolics in pot-grown roots were formononetin glycoside malonate (G-M) (1.51–4.26 mg/g), formononetin (2.21–3.57 mg/g) and biochanin A (1.73–2.17 mg/g), whereas field-grown roots were rich in formononetin-G-M (3.90–4.27 mg/g), maackiain-G-M (2.35–3.02 mg/g) and pseudobaptigenin-G-M (1.80–2.58 mg/g). Concentrations were affected by the growth stage and ozone exposure slightly affected the total phenolic content in roots and also had minor effects on individual compounds. The isoflavonoids formononetin, formononetin-7-*O*-β-D-galactopyranoside and inermin-3-*O*-β-D-galactopyranoside were isolated from the roots (Drenin et al. 2011).

Flower/Seed Phytochemicals

T. pratense seeds were found to contain quercetin, soyasaponin I, 22-*O*-glucoside and 22-*O*-diglucoside of soyasaponin I and astragaloside VIII (Oleszek and Stochmal 2002).

More than 50 compounds were identified in the essential oil samples of red and white Austrian clover flowers (Buchbauer et al. 1996). The main constituents (concentration >2 %) were maltol (8.2 %), linalool (4.2 %), 1-phenylethyl alcohol (3.2 %), phenol (2.9 %), phenylethyl acetate (2.7 %), acetophenone (2.4 %), and (*Z*)-3-hexenyl acetate (2.2 %) for red clover flowers and maltol (5.3 %), linalool (3.8 %), phenol (3.6 %), phenylethyl acetate (3.3 %) and 2-phenylethyl alcohol (2.8 %) for white clover flowers. Major volatile components identified in red clover flowers were acetophenone, methyl cinnamate and 1-phenylethanol (Buttery et al. 1984). Major volatile components identified in red clover seed pods were (*E*)-β-ocimene and (*Z*)-β-ocimene, longifolene and an unidentified sesquiterpene hydrocarbon (Buttery et al. 1984).

Twenty flavonoid glycoside malonates were detected in red clover flower extract (Lin et al. 2000). Eight were identified as genistin 6″-*O*-malonate (39), formononetin 7-*O*-β-D-glucoside 6″-*O*-malonate (40), biochanin A 7-*O*-β-D-glucoside 6″-*O*-malonate (41), trifoside

6″-*O*-malonate (42), irilone 4′-*O*-β-D-glucoside 6″-*O*-malonate (43), pratensein 7-*O*-β-D-glucoside 6″-*O*-malonate (44), isoquercitrin 6″-*O*-malonate (45), and 3-methylquercetin 7-*O*-β-D-glucoside 6″-*O*-malonate (46). About 15 other flavonoids and clovamides were present in this extract. Floral procyanidins of red clover comprised a range of oligomeric procyanidin ions (DP of 2–11) (Sivakumaran et al. 2004). The thiolysis reaction products indicated a mean degree of polymerization (mDP) of 9.3 with epicatechin (81 %) as the abundant flavan-3-ol extension unit and the terminating units dominated by catechin (95 %).

Antioxidant Activity

All *T. pratense* leaf extracts especially water and ethyl acetate extracts showed good antioxidant activity when evaluated using DPPH, hydroxyl, superoxide anion and nitric oxide radical scavenging and lipid peroxidation assays (Kaurinovic et al. 2012). In the DPPH assay, the IC_{50} (50 % of reduction) values in μg/ml were as follows: 17.47 μg for H_2O (water), 17.81 μg for EtOAc (ethyl acetate), 20.36 μg for Et_2O (diethyl ether), 29.47 μg for n-BuOH (n-butanol), and 34.19 μg for $CHCl_3$(chloroform) extract compared to synthetic antioxidants tert-butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA)BHT (14.31 μg) and BHA (11.08 μg). In scavenging of superoxide and NO radicals, H_2O extract demonstrated highest activity but was lower than that of BHT and BHA. The lowest antioxidant activity was expressed by the $CHCl_3$ (IC_{50}=92.37 μg/ml for superoxide and IC_{50}=58.46 μg/ml for NO radical) extract. Good antioxidant scavenging of OH radical was shown by the H_2O (IC_{50}=18.44 μg/ml) and EtOAc (IC_{50}=19.79 μg/ml) extracts, which showed higher ability than BHT and BHA (IC_{50}=22.17 μg/ml). The worst effect on the neutralization of all the radicals studied in-vitro was shown by the n-BuOH extract. In lipid peroxidation suppressing activity, H_2O extract exhibited the highest activity followed by EtOAc extract. In in-vivo experiments in the liver homogenate and blood of mice after their treatment with extracts of *T. pratense* leaves, or in combination with CCl_4, all the extracts decreased the GSH (reduced glutathione) and GSHPx (glutathione peroxidase) content compared with control. Treatment with the EtOAc extract yielded an increase in GSHR (glutathione reductase) activity, whereas the other four extracts caused a statistically significant decrease of this enzyme, which was in agreement with the action of this enzyme on GSH. Only H_2O extract produced a statistically significant increase in Px (peroxidase) activity. The LPx (lipid peroxidation activity) was lowered in the liver homogenate of animals treated with all extracts. The CAT (catalase) increased in the treatments with EtOAc, n-BuOH and H_2O extracts, but the other extracts caused no essential changes of CAT with respect to control. A statistically significant decrease of XOD (xanthine oxidase) activity was observed in the experimental animals treated with last three extracts (EtOAc, n-BuOH and especially H_2O). The amount of total phenolics in *T. pratense* leaf extracts ranged from 0.16 mg GAE/g d.e. ($CHCl_3$ extract) to 0.43 mg GAE/g d.e. (EtOAc extract) (Kaurinovic et al. 2012). A significant amount of these compounds were observed in the H_2O extract (0.34 mg GAE/g d.e.). Comparatively lower amount of total flavonoids was determined in the n-BuOH extracts, while the smallest quantity of was found in the Et_2O and $CHCl_3$ extracts. Quercetin glycosides and flavonoids (kaempferol-3-*O*-glucoside, quercetin-3-*O*- glucoside, luteolin-7-*O*- glucoside and apigenin-7-*O*-glucoside) were detected in EtOAc extract, while the presence of phenolic acids (such as caffeic acid) and flavonoids (luteolin, apigenin, naringenin and kaempferol) was confirmed in the H_2O extract. Additionally, two phytoestrogens (daidzein and genistein) were detected in the H_2O extract. The results suggested that the water and ethyl acetate leaf extracts afforded the best in-vitro and in-vivo antioxidant activity in protecting against carbon tetrachloride toxicity.

Anticancer Activity

Slater et al. (2002) found that in mice fed a diet supplemented with red clover isoflavones, the prostatic epithelium displayed a significant increase in the production of oestrogen receptor

beta and the adhesion protein E-cadherin but a decrease in transforming growth factor beta 1. These proteins were oestrogenically induced markers of proliferation, maintenance of histological architecture, preservation of cell phenotype and reduction of the potential for neoplastic and metastatic transformation. Their study suggested that red clover isoflavones presented a nontoxic dietary treatment for prostatic hyperplasia and a reduction in the potential for neoplastic transformation. Jarred et al. (2003) found that red clover-derived dietary isoflavones (RC) suppressed prostate growth in-vivo in the aromatase knockout (ArKO) mouse exhibiting lifelong elevation of androgens leading to prostate enlargement. Following 28 days of RC diet, ArKO ventral prostate (VP), anterior prostate, and seminal vesicle weights were reduced to wild-type mouse weights, although testis and body weights remained unaltered. Stereological analysis of VPs revealed a reduction in all components of the tissue, particularly the lumen. The RC diet reduced ArKO serum testosterone and dihydrotestosterone to WT levels. In comparison to castration and oestrogen administration, the dietary isoflavones were shown to be antiandrogenic rather than weakly oestrogenic. Engelhardt and Riedl (2008) found that 1-year treatment of 20 men (mean age 65 years) with isoflavone extract from red clover elicited a significant reduction of 33 % in prostate-specific antigen (PSA) level and a slight decrease in prostate volume. Sexual hormone levels (total testosterone, oestrogen, luteotropic hormone, follicle-stimulating hormone and dehydroepiandrosterone sulphate) did not changed throughout the study. However, a significant increase in all three liver transaminases after 3 months was recorded. The International Prostate Symptom Score showed a mean value of 7.9 at baseline and 6.68 after 12 months. Sexual function was not influenced by the treatment. Daily oral administration of 60 mg of an isoflavone extract was well tolerated and caused no side effects. In in-vitro studies, red clover isoflavones at 25.0 µg/ml significantly inhibited the proliferation by 18.86 % and promoted the apoptosis of human benign prostatic hyperplasia (BPH) stromal cells by 18.54 % compared to negative and blank control (Chen et al. 2010).

Studies by Ye et al. (2012) suggested that higher concentrations of formononetin inhibited the proliferation of prostate cancer cells (LNCaP and PC-3), while the most striking effect was observed in LNCaP cells. They further found that formononetin inactivated extracellular signal-regulated kinase1/kinase2 (ERK1/ERK2) mitogen-activated protein kinase (MAPK) signalling pathway in a dose-dependent manner, which resulted in increased the expression levels of BCL2-associated X (Bax) mRNA and protein, and induced apoptosis in LNCaP cells.

A series of cases in which *Trifolium pratense* was used in breast disease with hyperoestrogenic symptoms was reported by Parvu (2004). Several patients with cystic mastosis and breast cancer appeared to do well. In a 3-year randomized, double-blind, placebo-controlled pilot trial of healthy women aged 35–70 years with a family history of breast cancer, treatment with red clover isoflavones did not adversely affect breast density, skeletal strength or cardiovascular status (Powles et al. 2008). In postmenopausal women, endometrial status was not adversely affected. The adverse event profile was similar between red clover isoflavones, and placebo and endocrine status did not differ. Treatment with red clover isoflavones was found to be safe and well tolerated in healthy women. The principal isoflavones genistein and daidzein contained in red clover extracts acted as weak oestrogenic compounds when administered alone in ER positive breast cancer cells (Mannella et al. 2012). However, when provided in association with physiological amounts of estradiol, red clover extract acted as oestrogen antagonist on remodelling of actin cytoskeleton. The results indicated that isoflavones contained in red clover acted as natural selective oestrogen receptor modulators in the presence of physiological amounts of oestrogens.

The 95 % ethyl alcohol extract of one of red clover significantly inhibited the metabolism of [3H]benzo(a)pyrene [B(a)P] and decreased the level of binding of B(a)P to DNA by 30–40 % (Cassady et al. 1988). Its active isoflavone

component, biochanin A, also decreased the metabolism of B(a)P by 54 % in comparison to control cultures and decreased B(a)P-DNA binding by 37–50 % at a dose of 25 μg/ml indicating its potential as a chemopreventive agent. A separate study showed that biochanin A was able to decrease dimethylbenz[a]anthracene (DMBA)-induced DNA damage in MCF-7 cells by curbing cytochrome P450 (CYP) 1 enzymes through the interference of XRE-dependent transactivation (Chan et al. 2003). Enzyme kinetic studies also indicated that biochanin A inhibited both CYP1A1 and CYP1B1 enzymes. The study illustrated that the red clover isoflavone could protect against polycylic aromatic hydrocarbon-induced DNA damage.

Red clover isoflavones, namely, daidzein, genistein, formononetin and biochanin, were found to inhibit COX enzyme activity in both the murine macrophage cell line RAW 264.7 and human monocytes (Lam et al. 2004). Within the range of 1–40 μM in RAW 264.7 cells and 10–100 μM in human monocytes, isoflavones were able to reduce significantly the synthesis of prostaglandin E2 and/or thromboxane B2 indicating COX inhibition. They concluded that it was possible that the lower rates of some cancers in populations with a high intake of dietary isoflavones could be linked to their inhibition of COX activity. Another study found that biochanin A and/or formononetin, predominant isoflavones from red clover, may exert anticarcinogenic effects directly by acting as competitive substrates for human cytochrome CYP1B1 or indirectly through their metabolites daidzein and genistein, which inhibited CYP1B1(Roberts et al. 2004). Three of the biochanin A metabolites (5,7,3′-trihydroxy-4′-methoxyisoflavone, 5,7,8-trihydroxy-4′-methoxyisoflavone and 5,6,7-trihydroxy-4′-methoxyisoflavone) were characterized. Daidzein (Ki = 3.7 μM) exhibited competitive inhibition of CYP1B1 7-ethoxyresorufin *O*-deethylase activity, and genistein (Ki = 1.9 μM) exhibited mixed inhibition. In-vitro studies in MCF-7 breast carcinoma cells showed that biochanin A, the red clover isoflavone, may act as a antagonist/agonist to bind on the aryl hydrocarbon receptor that mediates the carcinogen activation pathway (Han et al. 2006). Treating the cells with biochanin A alone caused the accumulation of CYP1A1 mRNA and an increase in CYP1A1-specific 7-ethoxyresorufin *O*-deethylase (EROD) activity in a dose-dependent manner. A concomitant treatment with 7,12-dimethylbenz[a]anthracene (DMBA) and biochanin A markedly reduced the DMBA-inducible EROD activity and CYP1A1 mRNA level. Biochanin A competitively inhibited the metabolic activation of DMBA, as measured by the formation of the DMBA-DNA adducts. In MCF-7 breast cancer cells stably transfected with CYP19, biochanin A inhibited aromatase activity and hampered cell growth attributing to the enzyme activity (Wang et al. 2008). Additionally, biochanin A significantly reduced CYP19 mRNA abundance in the oestrogen receptor-negative breast cancer cells SK-BR-3. Luciferase reporter gene assays also revealed that biochanin A could repress the transcriptional control dictated by the promoter regulation. The present study illustrated that biochanin A inhibited CYP19 and aromatase activities and gene expression.

Estrogenic Activity/Menopause Management

In-Vitro Studies

Methanol extracts of red clover and hops showed significant competitive binding to oestrogen receptors alpha (ER alpha) and beta (ER beta) (Liu et al. 2001). With cultured Ishikawa (endometrial) cells, red clover and hops exhibited oestrogenic activity as indicated by induction of alkaline phosphatase (AP) activity and upregulation of progesterone receptor (PR) mRNA. Genistein was the most active component of red clover and was found to be the most effective of four red clover isoflavones tested in the above in-vitro assays. Another study showed that a preformulated (i.e. no excipients present) red clover extracts an EC_{50} of 2.0–2.2 μg/ml in the AP (alkaline phosphatase) oestrogenicity assay and IC_{50}s of 18.4–32.6 μg/ml and 1.9–3.4 μg/ml in the recombinant human oestrogen receptors ERα and ERβ binding assays, respectively (Booth

et al. 2006). The preformulated extract was composed of 35.54 % isoflavones, 1.11 % flavonoids, 0.06 % pterocarpans, ≤0.03 % coumarins and ≤0.03 % tyramine. Daidzein, genistein, formononetin, biochanin A, coumestrol and naringenin were oestrogenic in the AP assay, and all of these, except formononetin, bound to one or both ERs. Red clover extracts were found to activate NO synthesis in endothelial cells by recruiting transcriptional pathways mediated by a recruitment of oestrogen receptor-beta but were not capable of inducing rapid NO synthesis through nongenomic mechanisms (Simoncini et al. 2005). They showed that red clover-derived isoflavones synergized with 17beta-estradiol in increasing endothelial nitric oxide synthase activity and expression, therefore being devoid of antiestrogenic effects in human endothelial cells.

Red clover extract and its active isoflavone components were found to have oestrogenic activity. The IC_{50} values for the oestrogen receptor alpha and beta binding assays were 18.0 and 2.0 µg/ml, respectively, for the red clover extract (Overk et al. 2005). The extract and genistein activated the oestrogen response element (ERE) in Ishikawa cells while the extract, biochanin A and genistein significantly induced ERE-luciferase expression in MCF-7 cells. The red clover extract upregulated progesterone receptor (PR) mRNA in the Ishikawa cell line. In the MCF-7 cell line, PR mRNA was significantly upregulated by the extracts biochanin A and genistein. The extract had an EC50 value of 1.9 µg/ml in the alkaline phosphatase induction assay. The results suggested that red clover could be attractive for the development as herbal dietary supplements to alleviate menopause-associated symptoms.

Red clover extracts were reported to contain a variety of isoflavones, with affinity towards oestrogen receptor alpha (ERalpha), oestrogen receptor beta (ERbeta), androgen receptor (AR) and progesterone receptor (PR) (Pfitscher et al. 2008). Testing of biochanin A, formononetin, genistein, daidzein, dihydrobiochanin A, dihydroformononetin, dihydrogenistein, dihydrodaidzein, 3′-hydroxygenistein, 6-hydroxydaidzein, 6-hydroxydesmethylangolensin, equol, *O*-desmethylangolensin, angolensin and p-ethylphenol for their transactivation potential towards ERalpha, AR and PR in yeast revealed that the compounds showed only weak binding affinity to AR and PR, with IC_{50} values being greater (i.e. lesser affinity) than 10^{-5} M for the respective receptor. Mueller and Jungbauer (2008) found that red clover extracts and its major components, genistein and biochanin A, and especially several main metabolites exerted significant PPAR-γ ligand binding and transactivational activity. 6-Hydroxydaidzein exerted a more than 100-fold higher binding affinity than its precursor daidzein. The maximal transactivational activity of 6-hydroxydaidzein and 3′-hydroxygenistein exceeded even that of rosiglitazone, a known PPAR-γ agonist. Equol and *O*-desmethylangolensin showed an approximately fivefold higher binding affinity and, in the case of *O*-desmethylangolensin, a fourfold higher PPAR-γ agonistic activity than the precursor. Red clover extract, which is currently used for treating menopausal disorders, could be simultaneously used for ameliorating the metabolic syndrome.

Trifolium pratense, a common herb used for the relief of menopausal symptoms, was found to possess opiate activity (Nissan et al. 2007). The extract was found to have affinity at the delta-opiate receptor. Given the essential role of the opioid system in regulating temperature, mood, and hormonal levels and actions, this may explain in part the beneficial effect of red clover in alleviating menopausal symptoms.

Animal Studies

Administration of red clover extract containing 15 % isoflavones [250, 500 and 750 mg/(kg × *d*)] to ovariectomized 50-day-old Sprague–Dawley rats, for 21 days, produced a dose-dependent increase in uterine weight and differentiated vaginal cells at the two higher doses, but it did not stimulate cell proliferation in the mammary glands (Burdette et al. 2002). Neither antiestrogenic nor additive oestrogenic properties were observed in any of the tissues studied. The results suggested red clover extract to be weakly oestrogenic in the ovariectomized rat model.

Rimoldi et al. (2007) found in rats treated with either of the 17β-estradiol E(2) or high dose of genistein (isoflavone from red clover) exhibited increased uterine weight, and histological analysis showed oestrogen-induced features in the uteri. In vaginae, either E(2) dose or genistein high dose induced hyperplastic epithelium compared with the atrophic controls. In the mammary gland, E(2) (either dose) or genistein increased proliferation and PR expression. Serum levels of luteinizing hormone were decreased by E(2) (both doses) but not by genistein.

In ovariectomized uterotrophic adult rats, Overk et al. (2008) found that *Humulus lupulus* extract and a 30 % isoflavone extract of *T. pratense* did not have an oestrogenic effect on the uterus, and none of the secondary outcome measures were positive; but 8-prenylnaringenin (8-PN) from *H. lupulus* at equivalent doses to those previously used in humans did have an effect and may therefore have a deleterious effect in women. In another study, oral administration of formononetin from red clover to ovariectomized mice increased the uterine weight of the mice significantly as well as the content of SOD, GSH-Px, CAT and reduced MDA (Mu et al. 2009). The results indicated that formononetin had obvious antioxidant effects and oestrogenic effect, and the oestrogenic effect was not dosage related. Adaikan et al. (2009) found that supplementing red clover extract daily for 12 weeks or daidzein isoflavone to rabbits with experimentally induced menopause led to significant improvements in bone density, tissue integrity and vaginal blood flow with minimal effect on uterine weight and may therefore be a viable alternative to conventional regimens using synthetic oestrogens.

Supplementation of rat chow diet with red clover elicited oestrogen-like biological effects in pregnant rats (Yatkin and Daglioglu 2011). Relative uterus, ovary weights, number of uterine glands and luminal epithelium heights in the experimental groups were increased compared to control. However, there were no statistically significant changes detected in the immunostaining intensity of ERα and PR between the groups.

Clinical Studies

In a study of 17 menopausal women, isoflavones from red clover were found to significantly improve systemic arterial compliance which diminishes with menopause, but not plasma lipids (Nestel et al. 1999). As diminished compliance leads to systolic hypertension and may increase left ventricular work, the findings indicated a potential new therapeutic approach for improved cardiovascular function after menopause.

In a three-period, randomized, double blind, placebo trial of 66 postmenopausal women with plasma cholesterol levels between 5.0 and 9.0 mmol/l, dietary supplementation of isoflavone phytoestrogens from red clover in the proportions and quantities studied did not significantly alter total plasma cholesterol, LDL cholesterol, HDL cholesterol or plasma triglyceride levels (Howes et al. 2000). However, inverse correlations were found between urinary genistein excretion and plasma triglyceride levels and between urinary *O*-DMA excretion (an isoflavone metabolite) and plasma triglyceride levels in subjects receiving one isoflavone tablet, suggesting a weak relationship between isoflavone intake and plasma triglycerides which may be influenced by individual differences in isoflavone absorption or metabolism. In another 90-day randomized, double-blind, placebo-controlled study wherein 53 postmenopausal women (88.3 %) completed the trial, red clover isoflavone supplementation significantly decreased menopausal symptoms and had a positive effect on vaginal cytology and triglyceride levels (Hidalgo et al. 2005). Mean total cholesterol, low-density lipoprotein-cholesterol and triglyceride levels also decreased; however, only the latter was significantly lower compared with placebo.

In a randomized, four-arm, double-blind clinical trial of standardized black cohosh, red clover and placebo, and 0.625 mg conjugated equine oestrogens plus 2.5 mg medroxyprogesterone acetate (CEE/MPA) of menopausal women, compared with placebo (63 %), black cohosh (34 %) and red clover (57 %), did not reduce the number of vasomotor symptoms. Only CEE/MPA (94 %) differed significantly from placebo (Geller et al. 2009). Safety monitoring

indicated that chemically and biologically standardized extracts of black cohosh and red clover were safe during daily administration for 12 months. In a double-blind, randomized, parallel study for four menstrual cycles involving 23 premenopausal women, supplementation of purified red clover isoflavone (86 mg/day) tablets elicited no effect on serum homocysteine or folate in premenopausal women (Samman et al. 2009). In a phase II randomized, double-blinded, placebo-controlled safety and efficacy trial of two botanicals, black cohosh and red clover, for the management of vasomotor symptoms in healthy perimenopausal and postmenopausal women Geller et al. (2009) found that compared with placebo, black cohosh and red clover did not reduce the number of vasomotor symptoms. Safety monitoring indicated that chemically and biologically standardized extracts of black cohosh and red clover were safe during daily administration for 12 months.

In a randomized, crossover, placebo clinical trial involving 109 postmenopausal women aged 40 or more for a total of 187 days with a 7-day washout period, treatment with isoflavones derived from red clover extracts was found to be effective in reducing depressive and anxiety symptoms among postmenopausal women (Lipovac et al. 2010). This effect was equivalent to a 76.9 % reduction in the total Hospital Anxiety and Depression Scale (HADS) score (76 % for anxiety and 78.3 % for depression) and an 80.6 % reduction in the total Zung Self-Rating Depression Scale (SDS) score. They also found that red clover isoflavone supplementation was more effective than placebo in reducing daily vasomotor frequency and overall menopausal intensity in postmenopausal women (Lipovac et al. 2012). Studies by del Giorno et al. (2010) found that a 12-month treatment of women aged 45–65 years with menopausal symptoms, with a daily dose of 40 mg *Trifolium pratense*, did not yield a significant improvement in menopausal symptoms and sexual satisfaction.

Review Studies

The report on the role of isoflavones in menopausal health by the North American Menopause Society (NAMS) (2000) found that the data were inconclusive regarding whether the observed health effects in humans were attributable to isoflavones alone or to isoflavones plus other components in whole foods. The most convincing health effects had been attributed to the actions of isoflavones on lipids as studies had associated isoflavones with statistically significant reductions in low-density lipoproteins and triglycerides as well as increases in high-density lipoproteins. Although some data appeared to support the efficacy of isoflavones in reducing the incidence and severity of hot flashes, many studies had not found any difference between the isoflavone recipients and the controls. Inadequate data existed to evaluate the effect of isoflavones on breast and other female-related cancers, bone mass and vaginal dryness.

In their review, Fugh-Berman and Kronenberg (2001) stated that studies showed that red clover extracts to date have not clearly demonstrated benefits for menopausal symptoms as the potential oestrogenic effects on breast and endometrium had not been adequately assessed. However, study examining the effect of red clover on arterial compliance found a significant beneficial effect on arterial compliance. A review of randomized, controlled trials of peri- or postmenopausal women reported that isoflavones found in soy foods and red clover appeared to have a small but positive health effect on plasma lipid concentrations, bone mass density and cognitive abilities (Geller and Studee 2006). The review and meta-analysis conducted by Coon et al. (2007) found evidence of a marginally significant effect of *T. pratense* isoflavones for treating hot flushes in menopausal women.

Antihypercholesterolaemic Antihyperlipidaemic Activity

Animal Studies

Asgary et al. (2007) found that dietary use of red clover (RC) in hyperlipidaemic rabbits significantly decreased C-reactive protein (CRP), triglyceride (TG), total cholesterol and LDL cholesterol (LDL-C) whereas, HDL cholesterol

(HDL-C) was significantly increased in those animals. Fatty streak formation was also significantly lower in aorta and left and right coronary arteries in the same animals due to use of dietary RC supplementation. The findings suggested that dietary RC may reduce cardiovascular risk factors. Treatment of red clover extract 450 mg/kg/day for 4 days to ovariectomized rats significantly reduced plasma LDL concentrations, whereas triglycerides increased and plasma HDL and total cholesterol remained unchanged (Pakalapati et al. 2009). The extract influenced the transcript levels of many novel oestrogen and non-oestrogen-responsive genes as well as other regulatory genes. Quantitative reverse transcription analysis with real-time PCR confirmed that red clover extract regulates genes involved in lipid metabolism and antioxidation mechanisms. The scientists concluded that isoflavone-rich red clover extract mediated numerous genomic and nongenomic effects, which influence besides the lipid metabolism a broad range of cellular functions, including metabolic actions, cell cycle regulation and antioxidant activity.

Red clover extract exerted a significant effect on lowering of blood glucose levels and serum triglyceride, serum total cholesterol, liver triglyceride and liver cholesterol levels of type 2 diabetic db/db mice compared to those of the untreated diabetic mice (Qiu et al. 2012a). The significant improvement in glucose and lipid homeostasis in db/db diabetic mice was partly attributed to activation of hepatic peroxisome proliferator-activated receptor (PPAR) gamma and suppression of hepatic fatty acid synthase. In another study they found that red clover extract had no significant effect on lowering the blood glucose levels of streptozotocin (STZ)-induced diabetic mice (Qiu et al. 2012c). Similarly, its constituents biochanin A and formononetin exerted no hypoglycaemic effect. However, the serum triglycerides, total cholesterols and low-density lipoprotein-cholesterol levels for STZ-diabetic mice receiving red clover extract or biochanin A or formononetin were significantly lower than that of untreated STZ-diabetic mice. The antihyperlipidaemic effects of red clover extract, biochanin A and formononetin were found to be partly due to activation of hepatic peroxisome proliferator-activated receptor (PPAR) alpha.

Clinical Studies

In a double-blind, randomized, parallel study of healthy premenopausal women, supplementation of purified isoflavones, derived from red clover, resulted in no significant effects on total cholesterol, LDL and HDL cholesterol, HDL subfractions, triacylglycerol, lipoprotein(a), glucose or insulin concentrations (Blakesmith et al. 2003). Supplementation with isoflavones resulted in a 15-fold increase in urinary isoflavone excretion. The results indicated that purified isoflavones derived from red clover had no effect on cholesterol homeostasis or insulin resistance in premenopausal women, a group with low risk of coronary heart disease.

In a 6-week, randomized, placebo-controlled, double-blind, crossover design trial of 46 middle-aged men and 34 postmenopausal women, isolated isoflavones from red clover enriched in biochanin (genistein precursor) but not in formononetin (daidzein precursor) lowered LDL-C in men (Nestel et al. 2004). No other lipid was affected and women failed to respond significantly to treatment. In another randomized, placebo-controlled crossover study with a minimum 2-month washout period involving healthy pre- ($n=16$) and postmenopausal ($n=7$) women, 1-month supplementation with red clover isoflavones was found to have a positive effect on HDL cholesterol, but at most a small effect on insulin-like growth factor status in premenopausal and no effect in postmenopausal subjects (Campbell et al. 2004). In another randomized double-blind, placebo-controlled study of 177 perimenopausal 49–65 year-old women, supplementation of red clover-derived isoflavones gave no differences between treatments for changes from baseline to 12 months in total cholesterol, LDL cholesterol, triglycerides, HDL cholesterol, systolic and diastolic blood pressures, fibrinogen and plasminogen activator inhibitor type 1 (PAI-1) (Atkinson et al. 2004). Interactions between treatment and menopausal status were significant for changes in triglycerides and PAI-1, and changes were significant among perimenopausal women. Interactions between apolipoprotein E (apoE)

genotype and treatment tended to be significant for changes in total and LDL cholesterol, and differences between treatments were significant in E2/E3 women. This study suggested that isoflavones alone were not responsible for the well-documented effects.

In a 90-day crossover, randomized placebo study of equal design wherein 53 postmenopausal women with increased body mass index (88.3 %) completed the trial, *Trifolium pratense*-derived isoflavone supplementation had a positive effect on the lipid profile as evidenced by a significant decrease in TC, LDL-C and lipoprotein A levels (Chedraui et al. 2008). In another clinical study of 40 healthy postmenopausal women with an average age of 56 years, red clover phytoestrogen supplementation was found to have favourable metabolic effects on serum lipids (Tercic et al. 2009). Both total serum cholesterol and low-density lipoprotein (LDL) cholesterol levels, as well as triglyceride levels, were decreased significantly in the group receiving phytoestrogens. However, high-density lipoprotein (HDL) cholesterol showed a significant increase. Furthermore, red clover phytoestrogens had no side effects and could be considered safe.

Antimicrobial Activity

Both clover extracts and its isoflanoid component biochanin A inhibited the growth of *Clostridium sticklandii* in broth culture, but formononetin had no effect (Flythe and Kagan 2010). This Gram-positive, hyperammonia-producing bacterium (HAB) is largely responsible for amino acid deamination in the rumen. Ruminal proteolysis and subsequent amino acid degradation represent considerable economic loss in ruminant production. Biochanin A inhibited the HAB bacterium growth at a very low concentration of 8 nmol. (Kagan and Flythe 2012).

Neuroprotective Activity

Studies showed that five isoflavones (formononetin, daidzein, pratensein, calycosin and irilone) from *Trifolium pratense* attenuated lipopolysaccharide (LPS)-induced decrease in dopamine uptake and the number of dopaminergic neurons in a dose-dependent manner in rat mesencephalic neuron–glia cultures (Chen et al. 2008). They also significantly inhibited LPS-induced activation of microglia and production of tumour necrosis factor-alpha, nitric oxide and superoxide in mesencephalic neuron-glia cultures and microglia-enriched cultures. The protective potency of five isoflavones ranked as follows: pratensein > daidzein > calycosin > formononetin > irilone. Another study showed that pretreatment of human cortical cell line HCN 1-A with 0.5, 1 and 2 μg/ml isoflavone-enriched fraction from red clover prevented the morphological disruption caused by glutamate toxicity (Occhiuto et al. 2008). In contrast exposure of HCN 1-A cell cultures to glutamate resulted in concentration-dependent damage in neuronal membrane damage and decreases in neuron viability. The results indicated that the isoflavone fraction had a neuroprotective effect in human cortical neurons and that this effect might had resulted from antioxidant and oestrogenic actions. In another study, they reported that a 24-hour pretreatment of HCN 1-A with 0.5, 1 and 2 μg/ml isoflavones (genistein, daidzein, biochanin A and formononetin from *Trifolium pratense*) extract significantly increased cell survival and significantly prevented the morphological disruption caused by hydrogen peroxide (Occhiuto et al. 2009). Exposure of HCN 1-A cell cultures to hydrogen peroxide resulted in a concentration-dependent decrease in neuron viability. The neuroprotective effect of isoflavones extract was partly attributed to theirs antioxidant activity. Further, the results indicated that although isoflavones extract exerted a neuroprotective effect, they did not promote cortical neuron process outgrowth.

A recent study found that exposure of neuronal PC12 cells to 10 mM L glutamate significantly increased cell viability loss and apoptosis, whereas pretreatment with various concentrations of biochanin A, from *T. pratense*, attenuated the cytotoxic effects of L-glutamate (Tan et al. 2013). The pretreatment elicited not only decreases in the release of lactate dehydrogenase, the number of apoptotic cells, and the activity of caspase-3

but also an increase in the total glutathione level in the L-glutamate-treated PC12 cells. These results indicated that biochanin A may be able to exert neuroprotective effects against L-glutamate-induced cytotoxicity. Pretreatment of primary-cultured cortical neurons with formononetin (10 μM) for 12 hours significantly attenuated the cell loss induced by N-methyl-D-asparate (NMDA) exposure (Tian et al. 2013). It was found that treatment of formononetin attenuated the number of apoptotic cells, especially the early phase apoptotic cells, induced by NMDA exposure. Formononetin regulated the expression of apoptosis-related proteins by increasing the levels of Bcl-2 and pro-caspase-3 and decreasing the levels of Bax and caspase-3. The findings demonstrated that formononetin was capable of protecting neurons from NMDA-evoked excitotoxic injury and may have potential to be used in the clinical treatment of neurodegenerative disorders in central nervous system.

Antiinflammatory Activity

Yang et al. (2008) found that red clover extract exhibited potent antiinflammatory effects on mice by inhibiting the activation and proliferation of mouse lymphocytes and by inhibiting the excessive production of inflammatory mediators (NO, CD69, CD25, CD71) by mouse macrophages in a dose-dependent manner. Studies showed that red clover extracts acted as antiinflammatory and antiatherogenic agents on human endothelial cells by reducing the expression of the leukocyte adhesion molecules ICAM-1 and VCAM-1 induced bacterial lipopolysaccharide (Simoncini et al. 2008). It was concluded that red clover extracts may induce beneficial actions on human vessels. Qiu et al. (2012b) showed that a total amount of 10 μmol/l of biochanin A or genistein significantly suppressed the secretion of tumour necrosis factor α (TNFα) and interleukin-6 (IL-6) in LPS-induced RAW264.7 cells, whereas another two isoflavones, formononetin and daidzein, only significantly suppressed the secretion of interleukin IL-6. Their antiinflammatory efficiencies were not in correspondence with their peroxisome proliferator-activated receptors PPARα/γ agonist activities.

Red clover extract was found to be a source for substances that activated peroxisome proliferator-activated receptor (PPAR) alpha and ameliorated the cytokine secretion profile of lipopolysaccharide-stimulated macrophages (Mueller et al. 2010). Red clover extract and its isoflavones genistein and biochanin A were found to be moderate PPARα activators. Daidzein only slightly activated PPARα, but its metabolite 6-hydroxydaidzein exerted a much higher PPARα activity. Similarly, the metabolite 3′-hydroxygenistein afforded higher activation efficiency than its precursor, genistein. In lipopolysaccharide-stimulated macrophages, red clover extract and its isoflavone compounds reduced the secretion of proinflammatory cytokines, interleukin-6 and tumour necrosis factor-alpha, increased the secretion of the antiinflammatory interleukin-10 and/or reduced the expression of nuclear factor-kappaB, inducible nitric oxide synthase and/or cyclooxygenase 2. Tumour necrosis factor alpha production was most efficiently reduced by biochanin A and genistein. Interleukin-6 levels were most markedly reduced by genistein and equol. The results suggested red clover extract to be a putative candidate for preventing atherosclerosis and, thus, cardiovascular disease.

Spasmolytic Activity

Crude red clover extract (Trinovin) inhibited electrical field stimulation induced contractions of the rat prostate across a range of frequencies with an IC_{50} of approximately 68 μg/ml (Brandli et al. 2010). The following isoflavones, daidzein, calycosin, formononetin, prunetin, pratensin, biochanin A and genistein, were isolated. Genistein, formononetin and biochanin A (100 μM) from either commercial sources or isolated from red clover extract inhibited electrical field stimulation induced contractions of the isolated rat prostate. It was concluded that isoflavones contained in red clover were able to inhibit prostatic smooth muscle contractions in addition to their antiproliferative effects.

Photoprotective Activity

Studies showed that whereas the primary red clover isoflavones, daidzein, biochanin A and formononetin were inactive, 20 μM lotions of genistein and the metabolites equol, isoequol and the related derivative dehydroequol had powerful potential to reduce the inflammatory oedema reaction and the suppression of contact hypersensitivity induced by moderate doses of solar-simulated UV radiation in hairless mice (Widyarini et al. 2001). For equol the protection was concentration dependent and 5 μM equol markedly reduced the UV-induced inflammation but abrogated the UV-induced immunosuppression. Equol protected similarly from immunosuppression induced by the putative epidermal mediator, *cis*-urocanic acid (UCA), indicating a potential mechanism of action involving inactivation of this UV photoproduct. They also found that lotions containing equol, unlike topical UV sunscreens, more readily protected the immune system from photosuppression than from the inflammation of the sunburn reaction, even when applied after exposure, and thus such compounds may have a future role as sun-protective cosmetic ingredients.

Antiosteoporotic Activity

Wende et al. (2004) found that while butanol and methanol red clover extracts had no influence on either alkaline phosphatase or cellular protein production, enzyme activity was increased significantly on incubation with chloroform red clover extracts. The results suggested a role for red clover isoflavonoids in the stimulation of osteoblastic osteosarcoma HOS58 cell differentiation and thus may have potential as a bone-inducing agent. Animal study showed that treatment of ovariectomized Wistar rats with isoflavones significantly increased bone mineral content, mechanical strength of the tibia, femoral weight, femoral density and prevented the rise of serum alkaline phosphatase levels (Occhiuto et al. 2007). In contrast ovariectomy reduced bone mineral content, femoral weight, femoral density and mechanical strength of the tibia and increased the levels of bone specific alkaline phosphatase in the serum and the number of osteoclasts in the femur sections compared with sham-operated controls. In addition, the treatment with isoflavones significantly reduced the number of osteoclasts compared with the ovariectomized control rats. The findings suggested that red clover isoflavones were effective in reducing bone loss induced by ovariectomy, probably by reducing of the bone turnover via inhibition of bone resorption. Recent studies showed that daily oral administration for 4 weeks of both *Trifolium medium* and *T. pratense* extracts significantly increased the strength of the femoral diaphysis and calcium and phosphorus content in the bone mineral of ovariectomized rats (Cegieła et al. 2012). However, only *T. pratense* extract increased the strength of the tibial metaphysis. The effects of both *Trifolium* extracts differed from those of estradiol which also counteracted the worsening of the tibial strength and increases in bone turnover markers.

Antiangiogenic Activity

In-vivo studies showed that at a dosage of 250 μg/pellet red clover extract showed excellent inhibition of angiogenesis in the chorioallantoic membrane assay of fertilized hen's eggs (Krenn and Paper 2009). The antiangiogenic activity of the non-methylated isoflavones daidzein and genistein was higher than that of the methylated compounds formononetin and biochanin A. The results demonstrated that red clover extract was not only suitable for menopausal complaints but might also be a powerful chemopreventive agent against chronic diseases especially in elderly females.

Skin-Whitening Activity

The methanol extract from *Trifolium pratense* exerted potent inhibitory activity on melanogenesis in mouse B16 melanoma cells, and the active compound was isolated and identified as

biochanin A (Lin et al. 2011). Biochanin A dose-dependently was found to inhibit both melanogenesis and cellular tyrosinase activity in B16 cells and in zebra fish embryos. Application of a cream containing 2 % biochanin A twice daily to the skin of mice also increased the skin-whitening index value after 1 week of treatment, and the increase continued for another 2 weeks. Biochanin A was confirmed as a good candidate for use as a skin-whitening agent in the treatment of skin hyperpigmentation disorders.

Anti-skin Aging Activity

Studies found that the skin of the ovariectomized rats treated with red clover isoflavones (20 and 40 mg of total isoflavones daily for 14 weeks) appeared well organized with a normal epidermis with uniform thickness and regular keratinization; vascularity, collagen and elastic fibres were well developed (Circosta et al. 2006). In contrast, in untreated ovariectomized rats, the thickness and keratinization of the epidermis were reduced; glands were less in number and vascularity was poor; the distribution and morphology of the collagen bundles and elastic fibres were altered. The amount of collagen significantly increased in the isoflavone treated group in comparison with the control group. The findings suggested that red clover isoflavones were effective in reducing skin aging induced by oestrogen deprivation.

Nociceptive Activity

Studies using tail flicking and formalin tests showed that the pain threshold in ovariectomized rats was reduced due to oestrogen deprivation, whereas the pain threshold levels in ovariectomized rats treated with isoflavones methanol extract from red clover were similar to the control animals (Vishali et al. 2011). The study demonstrated the influence of phytoestrogen on long-term ovariectomized rats in pain perception in the absence of ovarian oestrogen and without toxic side effects.

Pharmacokinetic Studies

Metabolites of the isoflavones were identified in their urine samples of seven women who ingested four red clover dietary supplements (Heinonen et al. 2004). New reduced metabolites of formononetin (dihydroformononetin and angolensin) and biochanin A (dihydrobiochanin A and 6′-hydroxyangolensin) were identified in the urine samples. Studies found intestinal bacteria may influence bioavailability and physiological activity of dietary red clover isoflavones (Braune et al. 2010). In contrast to genistein, irilone was largely resistant to transformation by faecal slurries of ten human subjects. The faecal microbiota converted genistein to dihydrogenistein, 6′-hydroxy-*O*-desmethylangolensin and 2-(4-hydroxyphenyl)-propionic acid. Only one metabolite, namely, dihydroirilone, was formed from irilone in minor amounts. In further experiment, it was found that in contrast to genistein, irilone was not converted by *Eubacterium ramulus*.

In a pilot study of seven volunteers ingesting a single dose of a commercial red clover dietary supplement, the metabolism and bioavailability of the main isoflavones from red clover were monitored (Maul and Kulling 2010). A single intake of an amount of as low as 3.8 mg irilone (out of 38.8 mg total isoflavones) resulted in an irilone plasma concentration of 0.35 μm at 6.5 hours post-ingestion. Compared to the plasma concentrations found for daidzein (0.39 μm) and genistein (0.06 μm), the present findings indicated that irilone might possess a relatively high bioavailability. Additionally, prunetin and pseudobaptigenin were detected in human plasma for the first time.

Proteinase Inhibitory Activity

Maliar et al. (2011) found that *Trifolium pratense* accession POLKIE99-3 expressed the highest relative trypsin inhibition activity (80.0 %) compared to standards. They also found that *Trifolium pratense* genetic resources SVKZAH98-40 possessed relatively high antioxidant properties.

Toxic Red Clover Hay

The mycotoxin slaframine (1-acetoxy-6-amino-octahydroindolizine) was isolated from toxic red clover hay diseased by *Rhizoctonia leguminicola* (Hagler and Behlow 1981). Toxic hay caused extreme salivation, piloerection, lacrimation and respiratory distress and increased defecation when fed to guinea pigs. Similar effects were elicited with purified toxic red clover hay and pure slaframine.

Traditional Medicinal Uses

Red clover is commonly used to treat skin conditions (especially eczema and psoriasis), normally in combination with other purifying herbs, as a folk remedy for breast cancer, menopausal complaint, chronic degenerative diseases, gout, whooping cough and dry coughs (Bown 1995; Chevallier 1996). The flowering heads are alterative, antiscrofulous, antispasmodic, aperient, detergent, diuretic, expectorant, sedative and tonic (Grieve 1971; Duke and Ayensu 1985; Bown 1995).

In Turkish folk medicine, some *Trifolium* species including *T. pratense* and *T. repens* are used for their expectorant, analgesic, antiseptic properties and also to treat rheumatic aches (Sabudak and Guler 2009). *Trifolium pratense* has also gained popularity due to research into its use for the treatment for menopausal symptoms. Traditionally, red clover has been administered to help restore irregular menses and to balance the acid–alkaline level of the vagina to promote conception (Geller et al. 2009). Because the aerial parts of red clover are rich in oestrogenic isoflavones, women have also been using red clover products for the management of vasomotor symptoms related to menopause.

Other Uses

Red clover is one of the richest sources of isoflavones. Red clover is widely grown as a pasture/fodder crop. It is also used as a green manure crop as it enhances soil fertility by fixing nitrogen. It forms fairly deep tap roots and is useful for remediation of compacted soils especially when grown with grass mixtures. Red clover is also good for weed suppression. The flowers yield a yellow dye.

Comments

Refer also to notes under *Trifolium repens,* white clover, which share numerous similar bioactive phytochemicals and pharmacological properties.

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Trifolium repens

Scientific Name

***Trifolium repens* L.**

Synonyms

Lotodes repens Kuntze, *Trifolium limonium* Phil., *Trifolium repens* f. *riparia* Hauman, *Trifolium repens* L. ssp. *giganteum* (Lagr.-Fossat) Ponert, *Trifolium repens* L. var. *giganteum* Lagr.-Fossat, *Trifolium stipitatum* Clos

Family

Fabaceae, also placed in Papilionaceae

Common/English Names

Honeysuckle Clover, Ladino Clover, Lodi Clover, Dutch Clover, Dutch White Clover, White Clover, White Sweet Clover

Vernacular Names

Brazil: Trevo Branco (Portuguese)
Chinese: Bai Che Zhou Cao, Bai Hua San Ye Cao, Bai San Ye Cao, San Xiao Cao
Czech: Jetel Plazivý, Jetel Plazivý Bílý, Jetelovec Plazivý
Danish: Hvid Kløver
Dutch: Schapebloem, Witte Klaver
Eastonian: Valge Ristik
Esperanto: Trifolio Blanka
Finnish: Valkoapila
French: Trèfle Blanc, Trèfle De Hollande, Trèfle Rampant
Gaelic: Seamair Bhán
German: Kriech-Klee, Kriechender Klee, Kriechender Weiss-Klee, Lämmer-Klee, Weiss-Klee, Weisser Wiesen-Klee
Hebrew: Tiltan Zochel
Hungarian: Fehér Here, Kúszó Here
Icelandic: Hvítsmári
India: Safed Tipatiya Ghaas (Hindi)
Indonesia: Semanggi Landi (Java)
Italian: Trifoglio Bianco, Trifoglio Ladino, Trifoglio Rampicante
Japanese: Oranda Genge, Shiro Kurooba, Shiro Tsume Kusa
Norwegian: Hvitkløver, Kvitkløver, Okseblom, Smære, Småkløver
Polish: Koniczyna Biała
Portuguese: Trevo-Branco, Trevo-Coroa-De-Rei, Trevo-Da-Holanda, Trevo-Ladino, Trevo-Rasteiro
Russian: Klever Belyj, Klever Polzuchii
Slovaščina: Bela Detelja, Detelja Plazeča, Plazeča Detelja
Slovencina: Ďatelina Plazivá
Spanish: Trébol Amargo, Trébol Blanco, Trébol Rastrero
Swedish: Hvitklöfver, Krypklöver, Vitklöver, Vitväppling
Taiwan: Shu Cao
Thai: Thua Clover

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Turkish: Aküçgül, Yonca, Yonca Beyaz
Vietnamese: Chẻ Ba, Cỏ Ba Lá Hà Lan, Cỏ Ba Lá Hoa Trắng
Welsh: Meillion Gwyn

Origin/Distribution

White clover is native to Mediterranean Europe, North Africa and West Asia and has been used as a pasture legume in both Europe and the British Isles for centuries. It is also cultivated as a pasture crop in many cool temperate and subtropical parts of the world such as North America, southern Latin America, South Africa, Australasia, China and Japan. It has naturalized in many of these areas.

Agroecology

White clover grows in turfgrass, crops and landscapes. It is also found in a wide range of different soil type environments but less vigorously on acid, poorly drained or shallow, drought-prone soils especially soils with toxic levels of exchangeable aluminium and manganese. It thrives on moisture-retentive but free-draining soils with adequate soil pH, 5.8–6.0 on mineral soils and 5.5–5.8 on peaty soils. Optimum temperature for growth is 20–25 °C. It tolerates moderate but not severe drought.

Edible Plant Parts and Uses

Young leaves and flower heads are eaten (Cribb and Cribb 1976; Launert 1981; Facciola 1990; Schofield 2003). Clovers are a valuable survival food: they are high in protein, are widespread, are abundant and are eaten boiled or cooked as potherb, in soups and also used in salads. The dried leaves impart a vanilla flavour to cakes and other confectionery. Young flower heads can be used in salads. Dried flower heads and seedpods can also be ground into nutritious flour and mixed with other foods such as rice. Dried flower heads also can be steeped in hot water for a healthy, tasty tea-like infusion. Roots are also edible cooked (Kunkel 1984; Schofield 2003). The high quercetin concentration and soyasaponin occurrence make the seeds of some *Trifolium* species (*T. repens, T. pratense*) a potential source of health beneficial phytochemicals for use in human nutrition (Sabudak and Guler 2009).

Botany

Glabrous perennial, low growing, herbaceous plant, rooting at nodes with trifoliate leaves arranged alternately. Leaflets broadly ovate or circular, rounded or retuse at the tip and usually with whitish leaf markings on the upper mid surface (Plates 1 and 2). Stipules pale and translucent with a short point and broad at the base. Leaf sizes vary from very small in the prostrate, short-

Plate 1 White Clover pasture crop

Plate 2 Close view of leaves and inflorescence

petiolate types to large in the longer-petiolate, more erect cultivar types. Stolons initiated from leaf axils form a branched network radiating from an initially tap-rooted seedling. Inflorescences are globular racemes, 15–25 mm across, with 20–40 florets at the end of long peduncles originating from leaf axils on the stolons (Plates 1 and 2). Flowers scented; calyx 2–6 mm, 10-nerved with unequal teeth; corolla white often tinged pink, becoming deflexed with age with 8–13 mm long vexillum. Fruit linear, 3–4-seeded legume. Seeds cordate with a smooth surface, bright yellow to yellowish brown, becoming darker with age.

Nutritive/Medicinal Properties

Plant/Shoot Phytochemicals

White clover had been reported to be high in protein and minerals (Anonymous 2005; Frame and Newbould 1986; Frame et al. 1998), containing 22–28 % crude protein, 2.7–3.3 % crude fat, 9.4–11.9 % ash, 6.6–7 % lignin and a crude fibre content of 15.7–21.1 % (Anonymous 2005). White clover was reported to contain per kg dry matter: 26.6–5.3 g N, 1.9–4.7 g P, 15.4–38.0 g K, 12.0–23.1 g Ca, 1.4–2.9 g Mg, 2.4–3.6 g S, 0.5–4.6 g Na, 3.4–25.6 g Cl, 102–448gm Fe, 40–87 mg Mn, 22–32 mg Zn, 5.4–9.7 mg Cu, 0.10–0.38 mg Co, 0.14–0.44 mg I, 1.3–14.2 mg Mo, 0.005–153 mg Se and 26–50 mg B (Frame and Newbould 1986). As animal forage, white clover contributes optimally as a 10–20 % component when grown in conjunction with other grasses (Anonymous 2005). It was found to be more digestible than other temperate forage legumes and therefore the ingested nutrients could be utilized more efficiently.

Healthy and stressed white clover plants contained many types of secondary metabolite such as flavonols, flavones, condensed tannins, isoflavones, isoflavanones, pterocarpans, coumestans, cyanogenic glucosides and saponins in various plant tissues (Carlsen and Fomsgaard 2008). Many of these bioactive compounds from white clover could be exploited for suppressing weeds and soil-borne diseases. The oil yield for *T. repens* was small 0.021 % (weight/fresh weight basis) (Tava et al. 2009). Several classes of compounds were found in the oil, including alcohols, aldehydes, ketones, terpenes, esters, hydrocarbons, phenolics and acids.

HE strains of white clover in New Zealand were reported to contain the cyanogenetic glucosides lotaustralin and linamarin, the glucosides of methylethylketone cyanhydrin and acetone cyanohydrin, respectively (Butler and Butler 1960). The isoflavones genistein, biochanin A and formononetin were found in glycosidic forms in white clover and insignificant amount of coumestrol (Francis et al. 1967). The cyanogenic glucosides linamarin and lotaustralin were isolated as a mixture from *Trifolium repens* (Maher and Hughes 1971). α-Hydroxy-methylbutyronitrile-β-D-glucoside was found in white clover (Hughes and Conn 1976). Linamarin and lotaustralin were identified in *T. repens* cv. Armena in concentrations of 1.29 and 3.13 mg/g of dry matter, respectively (Stochmal and Oleszek 1994). The linamarin/lotaustralin ratio ranged from 0.4 to 0.8 and was inversely correlated with the total cyanogen content; cultivars with higher cyanogen level had a lower linamarin/lotaustralin ratio (Stochmal and Oleszek 1997). At temperatures below 15 °C all varieties contained the highest cyanogen content; an increase in temperature during the summer time resulted in a drastic decrease in cyanogen synthesis.

In leaves, petioles, roots and nodules of white clover, pinitol (3-*O*-methyl-chiro-inositol) was found to be the predominant sugar, with sucrose present in lower amount (Davis and Nordin 1983). Significant amounts of α-methyl glucoside and β-methyl glucoside, linamarin, glucose and fructose were found in the leaves and petioles. In the nodules, glucose was rarely present at detectable levels. Malonic acid did not appear to be present in unusually high concentrations in either leaves or nodules.

From white clover plant, sapogenins soyasapogenols A, B and C were isolated (Walter et al. 1955). From the whole plant of white clover, five triterpenoid saponins, designated cloversaponins I–V, were isolated together with four known

saponins, β-D-glucuronopyranosylsoyasapogenol B, soyasaponin I, soyasaponin II, azukisaponin II as their methyl esters and astragaloside VIII (Sakamoto et al. 1992).

Phytoestrogens isolated from ladino clover included genistein, biochanin A, formononetin and most significantly coumestrol (Bickoff et al. 1957, 1958, 1960, 1962; Guggolz et al. 1961). Sachse (1974) reported five estrogenic isoflavones—biochanin A, formononetin, pratensein, genistein, daidzein—and the estrogenic coumarin derivate coumestrol in 32 white clover varieties. Other phenolic compounds isolated from ladino clover included 3′,4′,7-trihydroxyflavone (Livingston and Bickoff 1964), daphnoretin (2-hydroxy-6-methoxy-3-(2-oxochromen-7-yl)oxychromen-7-one) (Livingston et al. 1964a), trifoliol (3,7-dihydroxy-9-methoxy-6H-benzofuro(3,2,-c)-1-benzopyran-6-one) (Livingston et al. 1964b; Bickhoff et al. 1965a) and 7,4′-dihydryoxyflavone (Bickhoff et al. 1965b). An acetylated isoflavone, genistein 7-(2″-*p*-coumaroylglucoside), genistein (Saxena and Jain 1986), 2″-*O*-acetylated formononetin and formononetin (Saxena and Jain 1989) were identified in *Trifolium repens*. Saloniemi et al. (1993) found the following isoflavones daidzein, formononetin, genistein and biochanin A in white clover varieties.

Flavones 4′,5,6,7,8-pentahydroxy-3-methoxyflavone and 5,6,7,8-tetrahydroxy-3-methoxyflavone, as well as two flavones 3,7-dihydroxy-4′-methoxyflavone and 5,6,7,8-tetrahydroxy-4′-methoxyflavone, were isolated from white clover shoots (Ponce et al. 2004). The known quercetin, rhamnetin, acacetin, 7-hydroxy-4′-methoxyflavonol; 3,5,6,7,8-pentahydroxy-4′-methoxyflavone; 2′,3′,4′,5′,6′-pentahydroxychalcone; 6-hydroxykaempferol; 4′,5,6,7,8-pentahydroxyflavone; and 3,4′-dimethoxykaempferol were also obtained.

Two bicoumarins, named repensin A and B, were isolated from *Trifolium repens* and their structures established as 7-methoxy-7′,8′-dihydroxy-8,6′-bicoumarinyl and 7,5′-dihydroxy-3,6′-bicoumarinyl, respectively (Zhan et al. 2003). Shoots of *T. repens* were found to contain cyanogenic glycosides, mostly linamarin (α-hydroxyisobutyronitrile-β-D-glucopyranoside) and a smaller proportion of lotaustralin (2-hydroxy-2-methylbutyronitrile-β-D-glucopyranoside) that breaks down to release toxic hydrogen cyanide when damaged (Gleadow et al. 2009).

In all tissues of clover seedlings not infected by the stem nematode, *Ditylenchus dipsaci*, isoflavonoids occurred predominantly as their glycosidic conjugates, in the order roots > meristems > leaves with formononetin-7-0-glucoside-6″-*O*-malonate (FGM) and medicarpin-3-*O*-glucoside-6″-*O*-malonate (MGM) as the major metabolites (Cook et al. 1995). The conjugates accumulated with age in all tissues and no differences were observed between the isoflavonoid content of healthy susceptible and resistant plants. Infection with either *D. dipsaci* race (oat and clover) elicited the accumulation of medicarpin, MGM and FGM in the meristems to a similar degree in resistant and susceptible seedlings. However, formononetin accumulated only in the infected meristems of the resistant plants. Johnson et al. (2005) found that different flavonoids increased in concentration in plants without rhizobial nodules than in plants with active or inactive nodules. The concentration of 4′,7-dihydroxyflavone was higher in plants without rhizobial nodules than in plants with active or inactive nodules. The content of formononetin was higher in roots with active rhizobial nodules than in inactive nodules and roots alone. Flavonol contents of white clover seeds (2.8–2,000 mg/g), leaves (<2–1,700 mg/g) and total above-ground material (20–2,210 mg/g) were higher than in roots (n.d.–208 mg/g) and flowers (66–481 mg/g) (Carlsen et al. 2008).

Leaf Phytochemicals

L-pipecolinic acid (piperidine-2-carboxylic acid) was isolated from the leaves (Morrison 1953) and a leaf protease (Brady 1961). Four coumestans detected in white clover infected with various foliar pathogens and were identified as coumestrol, 12-*O*-methylcoumestrol, trifoliol and 7,10,12-trihydroxycoumestan (repensol) (Wong and Latch 1971a; 1971b); other phenolic compounds found in diseased white clover included isorhamnetin; 4′,7-dihydroxyflavonol;

kaempferol; quercetin; 4′,7-dihydroxyflavone; 3′ 4″,7-trihydroxyflavone; geraldone; luteolin; formononetin; daphnoretin; and a trihydroxy-coumestan (Wong and Latch 1971b). White clover contained the phytoalexin medicarpin (Gustine 1981). Isoflavonoids medicarpin and demethylmedicarpin were detected in the droplet of white clover leaflets inoculated with *Monilia fructicola*; several minor isoflavonoids detected in the extracts were identified as formononetin (7-hydroxy-4′-methoxyisoflavone), 2′-hydroxy-formononetin and vestitone (7,2′-dihydroxy-4′-methoxyisoflavanone) (Woodward 1981). The following isoflavonoid phytoalexins were detected in fungus-inoculated leaflets: 7,2′,4′-trihydroxyi-soflavanone, vestitone, medicarpin, demethyl-medicarpin, variabilin, sativan, vestitol, genistein, formononetin, glycitein and daidzein (Ingham 1978, 1982).

In white clover, decreased foliar protein coincided with an increased number of protease isoforms (Kingston-Smith et al. 2003). Major flavonoids in the leaves were found to be derivatives of quercetin and kaempferol (Hofmann et al. 2000). Total leaf flavonoids in *Trifolium repens* were found to be low only 1 mg/g compared to 50–65 mg/g for *T. dubium* and *Lotus corniculatus* and up to 15 mg/g for *T. pratense* (de Rijke et al. 2004) In *T. pratense* and *T. repens*, the main constituents were flavonoid glucoside-(di)malonates, while *T. dubium* and *L. corniculatus* mainly contained flavonoid (di)glycosides.

Leaf and Flower Phytochemicals

A total of 12 flavonoids, pterocarpan and methyl caffeate were isolated from leaves and flowers and identified as quercetin 3-*O*-(6″-α-rhamnopyranosyl-2″-β-xylopyranosyl)-β-galactopyranoside (1), kaempferol 3-*O*-(6″-α-rhamnopyranosyl-2″-β-xylopyranosyl)-β-galactopyranoside (2), kaempferol 3-*O*-(2″,6″-α-dirhamnopyranosyl)-β-galactopyranoside, mauritianin(3),quercetin3-*O*-(2″-β-xylopyranosyl)-β-galactopyranoside (4), kaempferol 3-*O*-(2″-β-xylopyranosyl)-β-galactopyranoside (5), kaempferol 3-*O*-β-(6″-*O*-acetyl)-galactopyranoside (6), quercetin 3-*O*-β-(6″-*O*-acetyl)-galactopyranoside (7), trifolin (8), hyperoside (9), myricetin 3-*O*-β-galactopyranoside (10), quercetin (11), ononin (12), medicarpin 3-*O*-β-glucopyranoside (13) and methyl caffeate (14) (Kicel and Wolbiś 2012b).

Flower Phytochemicals

More than 50 compounds were identified in the essential oil samples of red and white Austrian clover flowers (Buchbauer et al. 1996). The main constituents (concentration >2 %) were maltol (8.2 %), linalool (4.2 %), 1-phenylethyl alcohol (3.2 %), phenol (2.9 %), phenylethyl acetate (2.7 %), acetophenone (2.4 %) and (*Z*)-3-hexenyl acetate (2.2 %) for red clover flowers and maltol (5.3 %), linalool (3.8 %), phenol (3.6 %), phenyl-ethyl acetate (3.3 %) and 2-phenylethyl alcohol (2.8 %) for white clover flowers.

Major flavonoids in white clover flowers were identified as glycosidic derivatives of quercetin and myricetin (Foo et al. 2000; Schittko et al. 1999). Three main flavonoid components of flower extracts, quercetin-3-*O*-galactoside, its 6″-*O*-acetyl derivative and myricetin-3-*O*-galactoside, were isolated from the flowers (Schittko et al. 1999). White clover flowers were found to contain an abundance of phenolics, namely, quercetin myricetin, *cis*-*p*-coumaric acid 4-*O*-β-D-glucopyranoside; *trans*-*p*-coumaric acid 4-*O*-β-D-glucopyranoside; the 3-*O*-β-D-galactopyranosides of myricetin, quercetin and kaempferol together with two new derivatives, namely, myricetin 3-*O*-(6″-acetyl)-β-D-galactopyranoside and kaempferol 3-*O*-(6″-acetyl)-β-D-galactopyranoside (Foo et al. 2000). Gallocatechin, epigallocatechin, gallocatechin-(4α-8)-epigallocatechin and their corresponding prodelphinidin polymers were also present. The following coumarins umbelliferone, scopoletin, repensin B, daphnoretin and daphnorin (daphnoretin 7-*O*-β-D-glucoside) were isolated from the flowers (Kicel and Wolbiś 2012a). Coumarins, bicoumol (7,7′-dihydroxy-6,8′-bicuomarinyl) and umbelliferone (7-hydroxycoumarin) were found in ladino clover (Spencer et al. 1967). Floral tissues in white clover plants were found to produce both proanthocyanidins and antho-

cyanins (Abeynayake et al. 2012). The white clover floral prodelphinidins were found to consist of terminal units with nearly equal proportions of epigallocatechin (52 %) and gallocatechin (48 %) and extender units showing epigallocatechin (56 %) and gallocatechin (39 %) (Sivakumaran et al. 2004). Tannins were found to accumulate in the flowers of white clover but not in the leaves or stolons (Anonymous 2005).

Seed Phytochemicals

Aqueous extracts of white clover seeds were found to contain myricetin, which was not toxic to *Rhizobium trifolii*, and condensed tannins (prodelphinidins) which were separated into three fractions each of which was toxic to *R. trifolii* (Young and Paterson 1980). The three tannin fractions, one of which had molecular weight of 6,000–12,000 and the other 2,6000–18,000, produced delphinidin on hydrolysis. A natural substance, 2,3-dihydroxy-2,4-cyclopentadien-1-one, was isolated from the seeds along with kaempferol, quercetin and myricetin (Nakatani et al. 1989). The flavonol quercetin and saponins astragaloside VIII, soyasaponin I 22-*O*-glucoside and soyasaponin I 22-*O*-diglucoside were found in the seeds (Oleszek and Stochmal 2002). Main flavonoids found in the seeds were quercetin, myricetin and kaempferol (Prati et al. 2007).

Germinated white clover seeds were found to contain oligosaccharides and galactomannans and enzymes, 5 α-galactosidases I–V (Williams et al. 1978), galactomannans, manno-oligosaccharides and 2 β-mannanases I and II (Villarroya et al. 1978).

Root Phytochemicals

Quercetin, acacetin and rhamnetin accumulated in roots of arbuscular mycorrhizal fungus *Glomus intraradices*-inoculated plants, whereas they were not detected in non-inoculated plants. Two isoflavonoids isolated from clover roots grown under phosphate stress were characterized as formononetin (7-hydroxy,4′-methoxy isoflavone) and biochanin A (5,7-dihydroxy,4′-methoxy isoflavone) (Nair et al. 1991). At 5 ppm, both compounds stimulated hyphal growth in-vitro and root colonization of an undescribed vesicular-arbuscular mycorrhiza, a *Glomus* sp. The following flavonoids were found in white clover root exudates which acted as signal compounds for nodulation by *Rhizobium* bacteria: 7,4′-dihydroxyflavone, geraldone and 4′-hydroxy-7-methoxyflavone (Redmond et al. 1968). Quercetin, acacetin and rhamnetin accumulated in roots of mycorrhizal inoculated plants, whereas they were not detected in non-inoculated plants (Ponce et al. 2004). Eight flavonoids kaempferol, medicarpin, demethylmedicarpin coumestrol, daidzein, formononetin, genistein and biochanin A were found in the roots (Carlsen et al. 2008). Only plants colonized with the arbuscular mycorrhizal fungus, *Glomus claroideum,* showed detectable concentrations of either coumestrol or kaempferol (cultivar dependant). Only the concentrations of formononetin and daidzein increased in clover roots in response to infection with *Pythium ultimum*. White clover contained the flavonoid aglycones, formononetin, medicarpin and kaempferol and glycosides kaempferol-Rha-Xyl-Gal and quercetin-Xyl-Gal which it released into the soil (Carlsen et al. 2012).

Antioxidant Activity

T. repens flower and leaf extracts showed antioxidant activity towards DPPH radical with EC_{50} values ranging from 72.3 to 179.3 μg/ml, respectively (Kicel and Wolbiś 2013) Significant linear correlations were found between antioxidant potentials of flowers and leaves and total phenolic and flavonoid contents determined (R^2 in the range of 0.97–0.99). The flowers were the richest source of phenolics ranging from 28.7 to 38.8 mg GAE/g and flavonoids, calculated for hyperoside, up to 20 mg HP/g, which hydrolyzed mainly to flavonols (the quercetin level greater than 6 mg/g). *T. repens* was found to be poor in isoflavones; similar quantities of Ca 0.2 mg/g were detected in the flowers and leaves.

Phenolic compounds from leaves and flowers, quercetin 3-*O*-(2″-β-xylopyranosyl)-β-galactopyranoside (4), quercetin 3-*O*-β-(6″-*O*-acetyl)-galactopyranoside (7), hyperoside (9), myricetin 3-*O*-β-galactopyranoside (10) and quercetin (11), were found to have potent antioxidant effect against DPPH, but the most effective were compounds 9, 10 and 11 (EC_{50} values in the range 7.51–9.52 μM) (Kicel and Wolbiś 2012b).

Estrogenic Activity

Estrogenic compound coumestrol together with other related compounds, coumestans, had been found in white clover (Bickoff et al. 1969; Wong and Latch 1971a); however their normal levels in plants were very low and estrogenically insignificant. Wong et al. (1971) demonstrated estrogenic activity in diseased white clover samples when fed to mice and sheep. Potencies were in parallel to concentration of coumestans. Phytoestrogens can cause infertility in sheep and cattle (Adams 1995). Cows and ewes fed estrogenic forage may suffer impaired ovarian function, often accompanied by reduced conception rates and increased embryonic loss. In cows, clinical signs resembled those associated with cystic ovaries. The infertility was found to be temporary, reverting to normal within 1 month after abstinence from the oestrogenic feed. However, ewes exposed to oestrogen for prolonged periods may suffer a second form of infertility that was permanent, caused by developmental actions of oestrogen during adult life. There have been sporadic reports of estrogenic problems in animals grazed on white clover (*Trifolium repens).* If affected by foliar disease, white clover may produce higher levels of oestrogenic coumestans including coumestrol, 9-*O*-methyl-coumestrol, trifoliol and repensol (Wong and Latch 1971a; Wong et al. 1971). The estrogenic isoflavone contents in white clover varieties were generally low, consisting mainly of formononetin (90–95 %) and genistein (5–10 %), and their contents did not differ between varieties (Nykänen-Kurki et al. 1993). Saloniemi et al. (1993) also reported that white clover varieties contained very small quantities of estrogenic isoflavones and coumestrol, and they did not explain the increased weight of the immature rat uterus observed in the biological studies. Some coumestrol was found in the autumn. The oestrogenic effect of white clover on rat uterus was found to be positive, the uterine weight of control rats averaged 21 mg, in test groups from 29 to 66 mg. Bickoff et al. (1969) showed coumestrol to be active in mice and sheep, while some poly-hydroxycoumestans were active in mice. Most growth studies indicated that coumestrol had no effect on the rate of growth of either cattle or sheep. However, some evidence existed which suggested that coumestrol may have beneficial effects on carcass quality in lambs.

Traditional Medicinal Uses

The plant is regarded as antirheumatic, antiscrophulatic, depurative, detergent and tonic and a tincture of the leaves is applied as an ointment for gout (Duke and Ayensu 1985). An infusion of the plant has been used in the treatment of coughs, colds, fevers and leucorrhoea, and flower infusion has been used as an eyewash (Moerman 1998). In Turkish folk medicine, for example, some *Trifolium* species including *T. pratense* and *T. repens* are used for their expectorant, analgesic, antiseptic properties and also to treat rheumatic aches (Sabudak and Guler 2009).

Other Uses

White clover is highly important in the dairy, meat and wool industries, significantly improving yields of these products. It is one of the best quality forage legume and the most important one in grazed pastures of moist temperate regions. White clover is suited to both continuous stocking and rotational grazing systems. It provides highly acceptable and nutritious forage to livestock whether as silage, hay or when grazed at a leafy stage. White clover is protein and mineral rich and retains a high digestibility for animals. Physical, chemical and anatomical features contribute to superior intake of white clover compared with grass.

White clover makes a good green manure crop especially with mixture of *Lolium perenne* as well as a good ground cover in sunny locations. It is also an important honey crop for beekeeping.

The isoflavonoids, formononetin and biochanin A, identified from clover roots, stimulated colonization and growth of white clover, while several other flavonoid compounds were inactive when tested at concentrations of 5 mg/l (Siqueira et al. 1991). The stimulatory effects of these isoflavonoids on plant growth were mediated by vesicular-arbuscular mycorrhizal fungi.

Comments

Refer also to notes under *Trifolium pratense*, red clover, which share numerous similar bioactive phytochemicals imparting many pharmacological effects.

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Author's Blurb

TK Lim (Tong Kwee Lim) obtained his Bachelor and Masters in Agricultural Science from the University of Malaya and his PHD (Botanical Sciences) from the University of Hawaii. He worked in the University of Agriculture Malaysia for 20 years as a lecturer and Associate Professor; as Principal Horticulturist for 9 years for the Department of Primary Industries and Fisheries, Darwin, Northern Territory; 6 years as Manager of the Asia and Middle East Team in Plant Biosecurity Australia, Department of Agriculture, Fisheries and Forestry, Australia; and 4 years as Research Program Manager with the Australian Centre for International Agriculture Research (ACIAR), Department of Foreign Affairs and Trade, Australia before he retired from public service. He has published over a hundred scientific papers including several books: "Guava in Malaysia: Production, Pest and Diseases", "Durian Diseases and Disorders", "Diseases of Mango in Malaysia", chapters in books, international refereed journals, conference proceedings (as editor) and technical bulletins in the areas of plant pathology, crop protection, horticulture, agronomy and quarantine science. He was also a reviewer of scientific papers for several international scientific journals. As Principal Horticulturist in Darwin, he and his team were instrumental in establishing the horticultural industry in the Northern Territory, Australia, especially on tropical fruits, vegetables, culinary herbs, spices/medicinal herbs and tropical flowers. During his tenure with Plant Biosecurity, he led a team responsible for conducting pest risk analyses and quarantine policy issues dealing with the import and export of plants and plant products into and out of Australia for the Middle East and Asian region. During his time with ACIAR, he oversaw and managed international research and development programs in plant protection and horticulture covering a wide array of crops that included fruits, plantation crops, vegetables, culinary and medicinal herbs and spices mainly in southeast Asia and the Pacific. In the course of his four decades of working career he has travelled extensively worldwide to many countries in South Asia, East Asia, southeast Asia, Middle East, Europe, the Pacific Islands, USA and England, and also throughout Malaysia and Australia. Since his tertiary education days he always had a strong passion for crops and took an avid interest in edible and medicinal plants. Over the four decades, he has taken several thousands of photographs of common, known and lesser known edible, medicinal and non-medicinal plants, amassed local literature, local indigenous knowledge, books, and has developed and established close rapport with many local researchers, scientists, growers and farmers during the course of his work and travels. All relevant available and up-to-date information collated on more than a thousand species of edible, medicinal and non-medicinal plants will be provided in a comprehensive reference series fully illustrated with coloured images to help in plant identification. This work will cover scientific names, synonyms, common and vernacular names, origin and distribution, agro-ecology, edible plant parts and uses, plant habit/description, nutritive and medicinal value, other uses and selected current references. Additional information is provided on the medicinal uses

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and pharmacological properties of the plants. This work will be of significant interest to scientists, researchers, practitioners (medical practitioners, pharmacologists, ethnobotanists, horticulturists, food nutritionists, agriculturists, botanists, herbalogists, herbologists, naturalists, conservationists, extension scientists, teachers, lecturers), students and the general public.

Medical Glossary

AAD Allergic airway disease. An inflammatory disorder of the airways caused by allergens.

AAPH 2,2′-Azobis(2-amidinopropane) dihydrochloride. A water-soluble azo compound used extensively as a free radical generator, often in the study of lipid peroxidation and the characterization of antioxidants.

Abeta Aggregation Amyloid beta protein (Abeta) aggregation is associated with Alzheimer's disease (AD); it is a major component of the extracellular plaque found in AD brains.

Abdominal Distension Referring to generalized distension of most or all of the abdomen. Also referred to as stomach bl oating often caused by a sudden increase in fibre from consumption of vegetables, fruits and beans.

Ablation Therapy The destruction of small areas of myocardial tissue, usually by application of electrical or chemical energy, in the treatment of some tachyarrhythmias.

Abortifacient A substance that causes or induces abortion.

Abortivum A substance inducing abortion.

Abscess A swollen infected, inflamed area filled with pus in body tissues.

ABTS 2.2 Azinobis-3-ethylhenthiazoline-6-sulfonic acid. A type of mediator in chemical reaction kinetics of specific enzymes.

ACAT Acyl-CoA: cholesterol acyltransferase.

ACE See Angiotensin-Converting Enzyme.

Acetogenins Natural products from the plants of the family Annonaceae and are very potent inhibitors of the NADH-ubiquinone reductase (Complex I) activity of mammalian mitochondria.

Acetyl-CoA Carboxylase (ACC) Enzyme that catalyzes the biotin-dependent carboxylation of acetyl-CoA to produce malonyl-CoA.

Acetylcholinesterase (AChE) Is an enzyme that degrades (through its hydrolytic activity) the neurotransmitter acetylcholine, producing choline.

Acne Vulgaris Also known as chronic acne, usually occurring in adolescence, with comedones (blackheads), papules (red pimples), nodules (inflamed acne spots) and pustules (small inflamed pus-filled lesions) on the face, neck and upper part of the trunk.

Acidosis Increased acidity, an excessively acid condition of the body fluids.

Acquired Immunodeficiency Syndrome (AIDS) An epidemic disease caused by an infection by human immunodeficiency virus (HIV-1, HIV-2), retrovirus that causes immune system failure and debilitation and is often accompanied by infections such as tuberculosis.

Acridone An organic compound based on the acridine skeleton, with a carbonyl group at the 9 position.

ACTH Adrenocorticotropic hormone (or corticotropin). A polypeptide tropic hormone produced and secreted by the anterior pituitary gland. It plays a role in the synthesis and secretion of gluco- and mineralocorticosteroids and androgenic steroids.

Activating Transcription Factor (ATF) A protein (gene) that binds to specific DNA sequences regulating the transfer or transcription of information from DNA to mRNA.

Activator Protein-1 (AP-1) A heterodimeric protein transcription factor that regulates gene

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expression in response to a variety of stimuli, including cytokines, growth factors, stress and bacterial and viral infections. AP-1 in turn regulates a number of cellular processes including differentiation, proliferation and apoptosis.

Actoprotective Increasing the body's physical performance.

Actoprotectors Preparations that increase the mental performance and enhance body stability against physical loads without increasing oxygen consumption. Actoprotectors are regarded as a subclass of adaptogens that hold a significant capacity to increase physical performance.

Acute Otitis Media (AOM) See Otitis Media.

Acyl-CoA Dehydrogenases A group of enzymes that catalyzes the initial step in each cycle of fatty acid β-oxidation in the mitochondria of cells.

Adaptogen A term used by herbalists to refer to a natural herb product that increases the body's resistance to stresses such as trauma, stress and fatigue.

Adaptogenic Increasing the resistance of the body to stress.

Addison's Disease Is a rare endocrine disorder. It occurs when the adrenal glands cannot produce sufficient hormones (corticosteroids). It is also known as chronic adrenal insufficiency, hypocortisolism or hypocorticism.

Adenocarcinoma A cancer originating in glandular tissue.

Adenoma A benign tumour from a glandular origin.

Adenopathy Abnormal enlargement or swelling of the lymph node.

Adenosine Receptors A class of purinergic, G-protein-coupled receptors with adenosine as endogenous ligand. In humans, there are four adenosine receptors. A_1 and A_{2A} receptors play roles in the heart, regulating myocardial oxygen consumption and coronary blood flow, while the A_{2A} receptor also has broader antiinflammatory effects throughout the body. These two receptors also have important roles in the brain, regulating the release of other neurotransmitters such as dopamine and glutamate, while the A_{2B} and A_3 receptors are located mainly peripherally and are involved in inflammation and immune responses.

ADH See Alcohol Dehydrogenase.

Adipocyte A fat cell involved in the synthesis and storage of fats.

Adipocytokine Bioactive cytokines produced by adipose tissues.

Adiponectin A protein in humans that modulates several physiological processes, such as metabolism of glucose and fatty acids, and immune responses.

Adipose Tissues Body fat, loose connective tissue composed of adipocytes (fat cells).

Adaptogen Containing smooth pro-stressors which reduce reactivity of host defense systems and decrease damaging effects of various stressors due to increased basal level of mediators involved in the stress response.

Adrenal Glands Star-shaped endocrine glands that sit on top of the kidneys.

Adrenalectomized Having had the adrenal glands surgically removed.

Adrenergic Having to do with adrenaline (epinephrine) and/or noradrenaline (norepinephrine).

Adrenergic Receptors A class of G protein-coupled receptors that are targets of the noradrenaline (norepinephrine) and adrenaline (epinephrine).

Adulterant An impure ingredient added into a preparation.

Advanced Glycation End Products (AGEs) Resultant products of a chain of chemical reactions after an initial glycation reaction. AGEs may play an important adverse role in process of atherosclerosis, diabetes, aging and chronic renal failure.

Aegilops An ulcer or fistula in the inner corner of the eye.

Afferent Something that so conducts or carries towards, such as a blood vessel, fibre or nerve.

Agammaglobulinaemia An inherited disorder in which there are very low levels of protective immune proteins called immunoglobulins. Cf. X-linked agammaglobulinaemia.

Agalactia Lack of milk after parturition (birth).

Age-Related Macular Degeneration (AMD) A medical condition of elderly adults that results in a loss of vision in the centre of the visual field (the macula) because of damage to the retina.

Agglutinin A protein substance, such as an antibody, that is capable of causing agglutination (clumping) of a particular antigen.

Agglutination Clumping of particles.

Agonist A drug that binds to a receptor of a cell and triggers a response by the cell.

Ague A fever (such as from malaria) that is marked by paroxysms of chills, fever and sweating that recurs with regular intervals.

AhR Aryl hydrocarbon receptor. A cytosolic protein transcription factor.

AIDS See Acquired Immunodeficiency Syndrome.

Akathisia A movement disorder in which there is an urge or need to move the legs to stop unpleasant sensations. Also called restless leg syndrome, the disorder is often caused by long-term use of antipsychotic medications.

AKT Serine/threonine kinase (also known as protein kinase B or PKB) plays a critical regulatory role in diverse cellular processes, including cancer progression and insulin metabolism.

Akt Signalling Pathway Akt are protein kinases involved in mammalian cellular signalling and inhibit apoptotic processes.

Akt/FoxO Pathway Cellular processes involving Akt and FoxO transcription factors that play a role in angiogenesis and vasculogenesis.

Alanine Transaminase (ALT) Also called serum glutamic pyruvate transaminase (SGPT) or alanine aminotransferase (ALAT), an enzyme present in hepatocytes (liver cells). When a cell is damaged, it leaks this enzyme into the blood.

ALAT (Alanine Aminotransferase) See Alanine Transaminase.

Albumin Water-soluble proteins found in egg white, blood serum, milk, various animal tissues and plant juices and tissues.

Albuminuria Excessive amount of albumin in the urine, a symptom of severe kidney disease.

Aldose Reductase, **Aldehyde Reductase** An enzyme in carbohydrate metabolism that converts glucose to sorbitol.

Alexipharmic An antidote, remedy for poison.

Alexiteric A preservative against contagious and infectious diseases and the effects of poisons.

Alcohol Dehydrogenase (ADH) An enzyme involved in the breakdown of alcohol.

Algesic Endogenous substances involved in the production of pain that is associated with inflammation, e.g. serotonin, bradykinin and prostaglandins.

Alkaline Phosphatase (ALP) An enzyme in the cells lining the biliary ducts of the liver. ALP levels in plasma will rise with large bile duct obstruction, intrahepatic cholestasis or infiltrative diseases of the liver. ALP is also present in bone and placental tissues.

Allergenic Having the properties of an antigen (allergen), immunogenic.

Allergic Pertaining to, caused, affected with or the nature of the allergy.

Allergic Conjunctivitis Inflammation of the tissue lining the eyelids (conjunctiva) due to allergy.

Allergy A hypersensitivity state induced by exposure to a particular antigen (allergen) resulting in harmful immunologic reactions on subsequent exposures. The term is usually used to refer to hypersensitivity to an environmental antigen (atopic allergy or contact dermatitis) or to drug allergy.

Allogeneic Cells or tissues which are genetically different because they are derived from separate individuals of the same species. Also refers to a type of immunological reaction that occurs when cells are transplanted into a genetically different recipient.

Allografts Or homografts, a graft between individuals of the same species but of different genotypes.

Alloknesis Itch produced by innocuous mechanical stimulation.

Allostasis The process of achieving stability, or homeostasis, through physiological or behavioural change.

Alopecia Is the loss of hair on the body.

Alopecia Areata Is a particular disorder affecting hair growth (loss of hair) in the scalp and elsewhere.

ALP See Alkaline Phosphatase.

Alpha-Adrenoceptor Receptors postulated to exist on nerve cell membranes of the sympathetic nervous system in order to explain the specificity of certain agents that affect only some sympathetic activities (such as vasoconstriction and relaxation of intestinal muscles and contraction of smooth muscles).

Alpha Amylase (α-Amylase) A major form of amylase found in humans and other mammals that cleaves alpha-bonds of large sugar molecules.

ALT See Alanine Transaminase.

Alterative A medication or treatment which gradually induces a change and restores healthy functions without sensible evacuations.

Alveolar Macrophage A vigorously phagocytic macrophage on the epithelial surface of lung alveoli that ingests carbon and other inhaled particulate matter. Also called coniophage or dust cell.

Alzheimer's Disease A degenerative, organic, mental disease characterized by progressive brain deterioration and dementia, usually occurring after the age of 50.

Amastigote Refers to a cell that does not have any flagella, used mainly to describe a certain phase in the life cycle of trypanosome protozoans.

Amenorrhoea The condition when a woman fails to have menstrual periods.

Amidolytic Cleavage of the amide structure.

Amoebiasis State of being infected by amoeba such as *Entamoeba histolytica*.

Amoebicidal Lethal to amoeba.

AMPK (5′ AMP-Activated Protein Kinase) Or 5′ adenosine monophosphate-activated protein kinase, enzyme that plays a role in cellular energy homeostasis.

Amygdalitis Inflammation of one or both tonsils, tonsillitis.

Amyloid Beta (Aβ or Abeta) A peptide of 39–43 amino acids that appear to be the main constituent of amyloid plaques in the brains of Alzheimer's disease patients.

Amyloidosis A disorder that results from abnormal deposition of the protein, amyloid, in various tissues of the body.

Amyotrophic Lateral Sclerosis Or ALS, is a disease of the motor neurons in the brain and spinal cord that control voluntary muscle movement.

Amyotrophy Progressive wasting of muscle tissues. *Adj.* amyotrophic.

Anaemia A blood disorder in which the blood is deficient in red blood cells and in haemoglobin.

Anaesthesia Condition of having sensation temporarily suppressed.

Anaesthetic A substance that decreases partially or totally nerve the sense of pain.

Analeptic A central nervous system (CNS) stimulant medication.

Analgesia Term describing relief, reduction or suppression of pain. *Adj.* analgetic.

Analgesic A substance that relieves or reduces pain.

Anaphoretic An antiperspirant.

Anaphrodisiac Or antiaphrodisiac is something that reduces or blunts the libido.

Anaphylaxis A severe, life-threatening allergic response that may be characterized by symptoms such as reduced blood pressure, wheezing, vomiting or diarrhoea.

Anaphylactic *Adj.* see Anaphylaxis.

Anaphylatoxins Are fragments (C3a, C4a or C5a) that are produced during the pathways of the complement system. They can trigger release of substances of endothelial cells, mast cells or phagocytes, which produce a local inflammatory response.

Anaplasia A reversion of differentiation in cells and is characteristic of malignant neoplasms (tumours).

Anaplastic *Adj.* see Anaplasia.

Anasarca Accumulation of great quantity of fluid in body tissues.

Androgen Male sex hormone in vertebrates. Androgens may be used in patients with breast cancer to treat recurrence of the disease.

Android Adiposity Centric fat distribution patterns with increased disposition towards the abdominal area, visceral fat—apple shaped. Cf. gynoid adiposity.

Andrology Branch of medicine concerned with the reproductive diseases in men.

Anencephaly A cephalic disorder that results from a neural tube defect that occurs when the cephalic (head) end of the neural tube fails to close, resulting in the absence of a major portion of the brain, skull and scalp.

Aneugen An agent that affects cell division and the mitotic spindle apparatus, causing the loss or gain of whole chromosomes, thereby inducing aneuploidy. *Adj.* aneugenic.

Angina Pectoris, Angina Chest pain or chest discomfort that occurs when the heart muscle does not get enough blood.

Angioedema Rapid swelling of the dermis, subcutaneous tissues and mucosa and submucosal tissues caused by small blood vessels leaking fluid into these tissues.

Angiogenic *Adj.* see Angiogenesis.

Angiogenesis A physiological process involving the growth of new blood vessels from pre-existing vessels.

Angiotensin An oligopeptide hormone in the blood that causes blood vessels to constrict and drives blood pressure up. It is part of the renin-angiotensin system.

Angiotensin-Converting Enzyme (ACE) An exopeptidase, a circulating enzyme that participates in the body's renin-angiotensin system (RAS) which mediates extracellular volume (i.e. that of the blood plasma, lymph and interstitial fluid) and arterial vasoconstriction.

Angioplasty Medical procedure used to open obstructed or narrowed blood vessel resulting usually from atherosclerosis.

Anguillulosis A parasitosis caused by the intestinal nematode *Strongyloides stercoralis* (round worm).

Anisakiasis A human parasitic infection of the gastrointestinal tract caused by the consumption of raw or undercooked seafood containing larvae of the nematode *Anisakis simplex*.

Anisonucleosis A morphological manifestation of nuclear injury characterized by variation in the size of the cell nuclei.

Ankylosing Spondylitis (AS) Is a type of inflammatory arthritis that targets the joints of the spine.

Annexin V Or Annexin A5 is a member of the annexin family of intracellular proteins that binds to phosphatidylserine (PS) in a calcium-dependent manner.

Annexitis Also called adnexitis, a pelvic inflammatory disease involving the inflammation of the ovaries or fallopian tubes.

Anodyne A substance that relieves or soothes pain by lessening the sensitivity of the brain or nervous system. Also called an analgesic.

Anoikis Apoptosis that is induced by inadequate or inappropriate cell-matrix interactions.

Anorectal Relating to the rectum and anus.

Anorectics Appetite suppressants, substances which reduce the desire to eat. Used on a short-term basis clinically to treat obesity. Also called anorexigenics.

Anorexia Lack or loss of desire to eat.

Anorexic Having no appetite to eat.

Anorexigenics See Anorectics.

Anoxia Absence of oxygen supply.

Antagonist A substance that acts against and blocks an action.

Antalgic A substance used to relive a painful condition.

Antecubital Vein This vein is located in the antecubital fossa—the area of the arm in front of the elbow.

Anterior Uveitis Is the most common form of ocular inflammation that often causes a painful red eye.

Anthelmintic An agent or substance that is destructive to worms and used for expulsion of internal parasitic worms in animals and humans.

Anthocyanins A subgroup of antioxidant flavonoids, are glucosides of anthocyanidins which are beneficial to health. They occur as water-soluble vacuolar pigments that may appear red, purple or blue according to pH in plants.

Anthrax A bacterial disease of cattle and ship that can be transmitted to man though unprocessed wool.

Anthropometric Pertaining to the study of human body measurements.

Antiamoebic A substance that destroys or suppresses parasitic amoebae.

Antiamyloidogenic Compounds that inhibit the formation of Alzheimer's β-amyloid fibrils (fAβ) from amyloid β-peptide (Aβ) and destabilize fAβ.

Antianaphylactic Agent that can prevent the occurrence of anaphylaxis (life-threatening allergic response).

Antiangiogenic A drug or substance used to stop the growth of tumours and progression of cancers by limiting the pathologic formation of new blood vessels (angiogenesis).

Antiarrhythmic A substance to correct irregular heartbeats and restore the normal rhythm.

Antiasthmatic Drug that treats or ameliorates asthma.

Antiatherogenic That protects against atherogenesis, the formation of atheromas (plaques) in arteries.

Antibacterial Substance that kills or inhibits bacteria.

Antibilious An agent or substance which helps remove excess bile from the body.

Antibiotic A chemical substance produced by a microorganism which has the capacity to inhibit the growth of or to kill other microorganisms.

Antiblennorrhagic A substance that treats blennorrhagia a conjunctival inflammation resulting in mucus discharge.

Antibody A gamma globulin protein produced by a kind of white blood cell called the plasma cell in the blood used by the immune system to identify and neutralize foreign objects (antigen).

Anticarcinomic A substance that kills or inhibits carcinomas (any cancer that arises in epithelium/tissue cells).

Anticephalalgic Headache-relieving or preventing.

Anticestodal A chemical destructive to tapeworms.

Anticholesterolemic A substance that can prevent the buildup of cholesterol.

Anticlastogenic Having a suppressing effect of chromosomal aberrations.

Anticoagulant A substance that thins the blood and acts to inhibit blood platelets from sticking together.

Antidepressant A substance that suppresses depression or sadness.

Antidiabetic A substance that prevents or alleviates diabetes. Also called antidiabetogenic.

Antidiarrhoeal Having the property of stopping or correcting diarrhoea, an agent having such action.

Antidote A remedy for counteracting a poison.

Antidopaminergic A term for a chemical that prevents or counteracts the effects of dopamine.

Antidrepanocytary Anti-sickle-cell anaemia.

Antidysenteric An agent used to reduce or treat dysentery and diarrhoea.

Antidyslipidaemic Agent that will reduce the abnormal amount of lipids and lipoproteins in the blood.

Anti-oedematous Reduces or suppresses oedema.

Antiemetic An agent that stops vomiting and nausea.

Antiepileptic A drug used to treat or prevent convulsions, anticonvulsant.

Antifebrile A substance that reduces fever. Also called antipyretic.

Antifeedant Preventing something from being eaten.

Antifertility Agent that inhibits formation of ova and sperm and disrupts the process of fertilization (antizygotic).

Antifibrosis Preventing/retarding the development of fibrosis, i.e. excessive growth and activity of fibroblasts.

Antifilarial Effective against human filarial worms.

Antifungal An agent that kills or inhibits the growth of fungi.

Antigen A substance that prompts the production of antibodies and can cause an immune response. *Adj.* antigenic.

Antigenotoxic An agent that inhibits DNA adduct formation, stimulates DNA repair mechanisms and possesses antioxidant functions.

Antiganacratia Anti-menstruation.

Antigastralgic Preventing or alleviating gastric colic.

Antihematic Agent that stops vomiting.

Antihaemorrhagic An agent which stops or prevents bleeding.

Antihepatotoxic Counteracting injuries to the liver.

Antiherpetic Having activity against herpes simplex virus (HSV).

Antihistamine An agent used to counteract the effects of histamine production in allergic reactions.

Antihyperalgesia The ability to block enhanced sensitivity to pain, usually produced by nerve injury or inflammation, to nociceptive stimuli. *Adj.* antihyperalgesic.

Antihypercholesterolaemia Term to describe lowering of cholesterol level in the blood or blood serum.

Antihypercholesterolemic Agent that lowers cholesterol level in the blood or blood serum.

AntihyperlidemicPromoting a reduction of lipid levels in the blood or an agent that has this action.

Antihypersensitive A substance used to treat excessive reactivity to any stimuli.

Antihypertensive A drug used in medicine and pharmacology to treat hypertension (high blood pressure).

Antiinflammatory A substance used to reduce or prevent inflammation.

Antileishmanial Inhibiting the growth and proliferation of *Leishmania*, a genus of flagellate protozoans that are parasitic in the tissues of vertebrates.

Antileprotic Therapeutically effective against leprosy.

Antilithiatic An agent that reduces or suppresses urinary calculi (stones) and acts to dissolve those already present.

Antileukaemic Anticancer drugs that are used to treat leukaemia.

Antilithogenic Inhibiting the formation of calculi (stones).

Antimalarial An agent used to treat malaria and/or kill the malaria-causing organism, *Plasmodium* spp.

Antimelanogenesis Obstructs production of melanin.

Antimicrobial A substance that destroys or inhibits growth of disease-causing bacteria, viruses, fungi and other microorganisms.

Antimitotic Inhibiting or preventing mitosis.

Antimutagenic An agent that inhibits mutations.

Antimycotic Antifungal.

Antineoplastic Said of a drug intended to inhibit or prevent the maturation and proliferation of neoplasms that may become malignant by targeting the DNA.

Antineuralgic A substance that stops intense intermittent pain, usually of the head or face, caused by neuralgia.

Antinociception Reduction in pain: a reduction in pain sensitivity produced within neurons when an endorphin or similar opium-containing substance opioid combines with a receptor.

Antinociceptive Having an analgesic effect.

AntioxytocicInhibiting premature labour. Cf. tocolytic.

Antinutrient Are natural or synthetic compounds that interfere with the absorption of nutrients and are commonly found in food sources and beverages.

Antioestrogen A substance that inhibits the biological effects of female sex hormones.

Antiophidian Antivenoms of snake.

Antiosteoporotic Substance that can prevent osteoporosis.

Antiovulatory Substance suppressing ovulation.

Antioxidant A chemical compound or substance that inhibits oxidation and protects against free radical activity and lipid oxidation such as vitamin E, vitamin C or beta-carotene (converted to vitamin B), carotenoids and flavonoids which are thought to protect body cells from the damaging effects of oxidation. Many foods including fruit and vegetables contain compounds with antioxidant properties. Antioxidants may also reduce the risks of cancer and age-related macular degeneration (AMD).

Antipaludic Antimalarial.

Antiperiodic Substance that prevents the recurrence of symptoms of a disease, e.g. malaria.

Antiperspirant A substance that inhibits sweating. Also called antisudorific, anaphoretic.

Antiphlogistic A traditional term for a substance used against inflammation, an antiinflammatory.

Antiplatelet Agent Drug that decreases platelet aggregation and inhibits thrombus formation.

Antiplasmodial Suppressing or destroying plasmodia.

Antiproliferative Preventing or inhibiting the reproduction of similar cells.

Antiprostatic Drug to treat the prostate.

Antiprotozoal Suppressing the growth or reproduction of protozoa.

Antipruritic Alleviating or preventing itching.

Antipyretic A substance that reduces fever or quells it. Also known as antithermic.

Antirheumatic Relieving or preventing rheumatism.

Antiscorbutic A substance or plant rich in vitamin C that is used to counteract scurvy.

Antisecretory Inhibiting or diminishing secretion.

Antisense Refers to antisense RNA strand because its sequence of nucleotides is the complement of message sense. When mRNA forms a duplex with a complementary antisense RNA sequence, translation of the mRNA into the protein is blocked. This may slow or halt the growth of cancer cells.

Antiseptic Preventing decay or putrefaction, a substance inhibiting the growth and development of microorganisms.

Anti-sickling Agent An agent used to prevent or reverse the pathological events leading to sickling of erythrocytes in sickle-cell conditions.

Antispasmodic A substance that relieves spasms or inhibits the contraction of smooth muscles; smooth muscle relaxant, muscle relaxer.

Antispermatogenic Preventing or suppressing the production of semen or spermatozoa.

Antisudorific See Antiperspirant.

Antisyphilitic A drug (or other chemical agent) that is effective against syphilis.

Antithermic A substance that reduces fever and temperature. Also known as antipyretic.

Antithrombotic Preventing or interfering with the formation of thrombi.

Antitoxin An antibody with the ability to neutralize a specific toxin.

Antitumoural Substance that acts against the growth, development or spread of a tumour.

Antitussive A substance that depresses coughing.

Antiulcerogenic An agent used to protect against the formation of ulcers or is used for the treatment of ulcers.

Antivenin An agent used against the venom of a snake, spider or other venomous animal or insect.

Antivinous An agent or substance that treats addiction to alcohol.

Antiviral Substance that destroys or inhibits the growth and viability of infectious viruses.

Antivomitive A substance that reduces or suppresses vomiting.

Antizygotic See Antifertility.

Anuria Absence of urine production and excretion. *Adj.* anuric.

Anxiogenic Substance that causes anxiety.

Anxiolytic A drug prescribed for the treatment of symptoms of anxiety.

APAF-1 Apoptotic protease-activating factor 1.

Apelin Also known as APLN, a peptide which in humans is encoded by the APLN gene.

Aperient A substance that acts as a mild laxative by increasing fluids in the bowel.

Aperitif An appetite stimulant.

Aphonia Loss of the voice resulting from disease, injury to the vocal cords or various psychological causes, such as hysteria.

Aphrodisiac An agent that increases sexual activity and libido and/or improves sexual performance.

Aphthae White, painful oral ulcer of unknown cause.

Aphthous ulcer Also known as a canker sore, is a type of oral ulcer, which presents as a painful open sore inside the mouth or upper throat.

Aphthous stomatitis A canker sore, a type of painful oral ulcer or sore inside the mouth or upper throat, caused by a break in the mucous membrane. Also called aphthous ulcer.

Apnea Suspension of external breathing.

Apoliprotein B (APOB) Primary apolipoprotein of low-density lipoproteins which is responsible for carrying cholesterol to tissues.

Apoplexy A condition in which the brain's function stops with loss of voluntary motion and sense.

Apoprotein The protein moiety of a molecule or complex, as of a lipoprotein.

Appendicitis Is a condition characterized by inflammation of the appendix. Also called epityphlitis.

Appetite Stimulant A substance to increase or stimulate the appetite. Also called aperitif.

APPT (Activated Partial Thromboplastin Time) A blood test, a measure of the part of the blood clotting pathway.

Apolipoprotein A-I (APOA1) A major protein component of high-density lipoprotein (HDL) in plasma. The protein promotes cholesterol efflux from tissues to the liver for excretion.

Apolipoprotein B (APOB) Is the primary apolipoprotein of low-density lipoproteins (LDL or 'bad cholesterol'), which is responsible for carrying cholesterol to tissues.

Apolipoprotein E (APOE) The apolipoprotein found on intermediate density lipoprotein and chylomicron that binds to a specific receptor on liver and peripheral cells.

Apoplexy Bleeding within internal organs.

Apoptogenic Ability to cause death of cells.

Apoptosis Death of cells.

Apurinic Lyase A DNA enzyme that catalyzes a chemical reaction.

Arachidonate Cascade Includes the cyclooxygenase (COX) pathway to form prostanoids and the lipoxygenase (LOX) pathway to generate several oxygenated fatty acids, collectively called eicosanoids.

ARE Antioxidant response element is a transcriptional control element that mediates expression of a set of antioxidant proteins.

Ariboflavinosis A condition caused by the dietary deficiency of riboflavin that is characterized by mouth lesions, seborrhoea and vascularization.

Aromatase An enzyme involved in the production of oestrogen that acts by catalyzing the conversion of testosterone (an androgen) to estradiol (an oestrogen). Aromatase is located in oestrogen-producing cells in the adrenal glands, ovaries, placenta, testicles, adipose (fat) tissue and brain.

Aromatic Having a pleasant, fragrant odour.

Aromatherapy A form of alternative medicine that uses volatile liquid plant materials, such as essential oils and other scented compounds from plants for the purpose of affecting a person's mood or health.

ARPE-19 Cells A human retinal pigment epithelial cell line with differentiated properties.

Arrhythmias Abnormal heart rhythms that can cause the heart to pump less effectively. Also called dysrhythmias.

Arsenicosis See Arsenism.

Arsenism An incommunicable disease resulting from the ingestion of groundwater containing unsafe levels of arsenic, also known as arsenicosis.

Arteriogenic Erectile Dysfunction A penis dysfunction caused by the narrowing of the arteries in the penis, decreasing blood inflow to it, thus making erection impossible.

Arteriosclerosis Imprecise term for various disorders of arteries, particularly hardening due to fibrosis or calcium deposition, often used as a synonym for atherosclerosis.

Arthralgia Is pain in the joints from many possible causes.

Arthritis Inflammation of the joints of the body.

Aryl Hydrocarbon Receptor (AhR) A ligand-activated transcription factor best known for mediating the toxicity of dioxin and other exogenous contaminants and is responsible for their toxic effects, including immunosuppression.

ASAT or AST Aspartate aminotransferase; see Aspartate Transaminase.

ASBT Apical sodium-dependent bile acid transporter, belongs to the solute carrier family (SLC), of transporters and is an important carrier protein expressed in the small intestine.

Ascaris A genus of parasitic intestinal round worms.

Ascites Abnormal accumulation of fluid within the abdominal or peritoneal cavity.

Ascorbic Acid See Vitamin C.

Aspartate Transaminase (AST) Also called serum glutamic oxaloacetic transaminase (SGOT) or aspartate aminotransferase (ASAT) and is similar to ALT in that it is another enzyme associated with liver parenchymal cells. It is increased in acute liver damage, but is also present in red blood cells, and cardiac and skeletal muscle and is therefore not specific to the liver.

Asphyxia Failure or suppression of the respiratory process due to obstruction of air flow to the lungs or to the lack of oxygen in inspired air.

Asphyxiation The process of undergoing asphyxia.

Asthenia A nonspecific symptom characterized by loss of energy and strength and feeling of weakness.

Asthenopia Weakness or fatigue of the eyes, usually accompanied by headache and dimming of vision. *Adj.* Asthenopic.

Asthma A chronic illness involving the respiratory system in which the airway occasionally constricts, becomes inflamed and is lined with excessive amounts of mucus, often in response to one or more triggers.

Astringent A substance that contracts blood vessels and certain body tissues (such as mucous membranes) with the effect of reducing secretion and excretion of fluids and/or has a drying effect.

Astrocytes Collectively called astroglia, are characteristic star-shaped glial cells in the brain and spinal cord.

Ataxia (Loss of coordination) results from the degeneration of nerve tissue in the spinal cord and of nerves that control muscle movement in the arms and legs.

Ataxia Telangiectasia and Rad3-Related Protein (ATR) Also known as serine/threonine-protein kinase ATR and FRAP-related protein 1 (FRP1), and is an enzyme encoded by the ATR gene. It is involved in sensing DNA damage and activating the DNA damage checkpoint, leading to cell cycle arrest.

Atelectasis The collapse or closure of the lung resulting in reduced or absent gas exchange.

ATF-2 Activating transcription factor 2.

Athlete's Foot A contagious skin disease caused by parasitic fungi affecting the foot and hands, causing itching, blisters and cracking. Also called dermatophytosis.

Atherogenic Having the capacity to start or accelerate the process of atherogenesis.

Atherogenesis The formation of lipid deposits in the arteries.

Atheroma A deposit or degenerative accumulation of lipid-containing plaques on the innermost layer of the wall of an artery.

Atherosclerosis The condition in which an artery wall thickens as the result of a buildup of fatty materials such as cholesterol.

Atherothrombosis Medical condition characterized by an unpredictable, sudden disruption (rupture or erosion/fissure) of an atherosclerotic plaque, which leads to platelet activation and thrombus formation.

Athymic Mice Laboratory mice lacking a thymus gland.

Atonic Lacking normal tone or strength.

Atony Insufficient muscular tone.

Atopic Dermatitis An inflammatory, noncontagious, pruritic skin disorder of unknown aetiology; often called eczema.

Atresia A congenital medical condition in which a body orifice or passage in the body is abnormally closed or absent.

Atretic Follicle Follicular atresia is the breakdown of the ovarian follicles.

Atretic Ovarian Follicles An involuted or closed ovarian follicle.

Atrial Fibrillation Is the most common cardiac arrhythmia (abnormal heart rhythm) and involves the two upper chambers (atria) of the heart.

Attention-Deficit Hyperactivity Disorder (ADHD, ADD or AD/HD) Is a neurobehavioural developmental disorder, primarily characterized by the coexistence of attentional problems and hyperactivity.

Auditory Brainstem Response (ABR) Also called brainstem evoked response (BSER) is an electrical signal evoked from the brainstem of a human by the presentation of a sound such as a click.

Augmerosen A drug that may kill cancer cells by blocking the production of a protein that makes cancer cells live longer. Also called bcl-2 antisense oligonucleotide.

Auricular Of or relating to the auricle or the ear in general.

Aurones [2-Benzylidenebenzofuran-3(2H)-ones] are the secondary plant metabolites and is a subgroup of flavonoids. See Flavonoids.

Autoantibodies Antibodies manufactured by the immune system that mistakenly target and

damage specific tissues and organs of the body.

Autolysin An enzyme that hydrolyzes and destroys the components of a biological cell or a tissue in which it is produced.

Autonomic Disorder A neurological disease in which the autonomic nervous system ceases to function properly.

Autophagy Digestion of the cell contents by enzymes in the same cell.

Autopsy Examination of a cadaver to determine or confirm the cause of death.

Avenanthramides Low molecular weight, soluble phenolic compounds found in oats.

Avidity Index Describes the collective interactions between antibodies and a multivalent antigen.

Avulsed Teeth Is tooth that has been knocked out.

Ayurvedic Traditional Hindu system of medicine based largely on homeopathy and naturopathy.

Azoospermia Is the medical condition of a male not having any measurable level of sperm in his semen.

Azotaemia A higher than normal blood level of urea or other nitrogen containing compounds in the blood.

B Cell-Activating Factor (BAFF) Also called tumour necrosis factor ligand superfamily member 13B. It plays an important role in the proliferation and differentiation of B cells.

Babesia A protozoan parasite (malaria-like) of the blood that causes a haemolytic disease known as Babesiosis.

Babesiosis Malaria-like parasitic disease caused by Babesia, a genus of protozoal piroplasms.

Back Tonus Normal state of balanced tension in the tissues of the back.

Bactericidal Lethal to bacteria.

Balanitis Is an inflammation of the glans (head) of the penis.

BALB/c Mice Balb/c mouse was developed in 1923 by McDowell. It is a popular strain and is used in many different research disciplines, but most often in the production of monoclonal antibodies.

Balm Aromatic oily resin from certain trees and shrubs used in medicine.

Baroreceptor A type of interoceptor that is stimulated by pressure changes, as those in blood vessel wall.

Barrett's Oesophagus (Barrett's Oesophagitis) A disorder in which the lining of the oesophagus is damaged by stomach acid.

Basophil A type of white blood cell with coarse granules within the cytoplasm and a bilobate (two-lobed) nucleus.

Bax/Bad Proapoptotic proteins.

BCL-2 A family of apoptosis regulator proteins in humans encoded by the B cell lymphoma 2 (BCL-2) gene.

BCL-2 Antisense Oligonucleotide See Augmereson.

BCR/ABL A chimeric oncogene, from fusion of BCR and ABL cancer genes associated with chronic myelogenous leukaemia.

Bechic A remedy or treatment of cough.

Bed Nucleus of the Stria Terminalis (BNST) Acts as a relay site within the hypothalamic-pituitary-adrenal axis and regulate its activity in response to acute stress.

Belching or **Burping** Refers to the noisy release of air or gas from the stomach through the mouth.

Beri-BeriIs a disease caused by a deficiency of thiamine (vitamin B1) that affects many systems of the body, including the muscles, heart, nerves and digestive system.

Beta-Carotene Naturally occurring retinol (vitamin A) precursor obtained from certain fruits and vegetables with potential antineoplastic and chemopreventive activities. As an antioxidant, beta-carotene inhibits free radical damage to DNA. This agent also induces cell differentiation and apoptosis of some tumour cell types, particularly in early stages of tumorigenesis, and enhances immune system activity by stimulating the release of natural killer cells, lymphocytes and monocytes.

Beta-CateninIs a multifunctional oncogenic protein that contributes fundamentally to cell development and biology; it has been implicated as an integral component in the Wnt signalling pathway.

Beta Cells A type of cell in the pancreas in areas called the islets of Langerhans.

Beta-Glucans Polysaccharides of D-glucose monomers linked by β-glycosidic bonds, (1→3), (1→4)-β-D-glucan, soluble, viscous component of fibres found in cereals like oats.

Beta-Lactamase Enzymes produced by some bacteria that are responsible for their resistance to beta-lactam antibiotics like penicillins.

Beta-Thalassaemia An inherited blood disorder that reduces the production of haemoglobin.

BHT Butylated hydroxytoluene (phenolic compound), an antioxidant used in foods, cosmetics, pharmaceuticals and petroleum products.

Bifidobacterium Is a genus of Gram-positive, nonmotile, often branched anaerobic bacteria. Bifidobacteria are one of the major genera of bacteria that make up the gut flora. Bifidobacteria aid in digestion, are associated with a lower incidence of allergies, and also prevent some forms of tumour growth. Some bifidobacteria are being used as probiotics.

Bifidogenic Promoting the growth of (beneficial) bifidobacteria in the intestinal tract.

Bile Fluid secreted by the liver and discharged into the duodenum where it is integral in the digestion and absorption of fats.

Bilharzia, Bilharziasis See Schistosomiasis.

Biliary Relating to the bile or the organs in which the bile is contained or transported.

Biliary Infections Infection of organ(s) associated with bile and comprises (a) acute cholecystitis, an acute inflammation of the gallbladder wall, and (b) cholangitis, inflammation of the bile ducts.

Biliousness Old term used in the eighteenth and nineteenth centuries pertaining to bad digestion, stomach pains, constipation and excessive flatulence.

Bilirubin A breakdown product of heme (a part of haemoglobin in red blood cells) produced by the liver that is excreted in bile which causes a yellow discoloration of the skin and eyes when it accumulates in those organs.

Biotin Also known as vitamin B7. See Vitamin B7.

Bitter A medicinal agent with a bitter taste and used as a tonic, alterative or appetizer.

Blackhead See Comedone.

Blackwater Fever Dangerous complication of malarial whereby the red blood cells burst in the bloodstream (haemolysis) releasing haemoglobin directly into the blood.

Blain See Chilblain.

Blastocyst Blastocyst is an embryonic structure formed in the early embryogenesis of mammals, after the formation of the morula, but before implantation.

Blastocystotoxic Agent that suppresses further development of the blastocyst through to the ovum stage.

Blebbing Bulging, e.g. membrane blebbing also called membrane bulging or ballooning.

Bleeding Diathesis Is an unusual susceptibility to bleeding (haemorrhage) due to a defect in the system of coagulation.

Blennorrhagia Gonorrhoea.

Blennorrhoea Inordinate discharge of mucus, especially a gonorrhoeal discharge from the urethra or vagina.

Blepharitis Inflammation of the eyelids.

Blister Thin vesicle on the skin containing serum and caused by rubbing, friction or burn.

Blood–Brain Barrier (BBB) Is a separation of circulating blood and cerebrospinal fluid (CSF) in the central nervous system (CNS). It allows essential metabolites, such as oxygen and glucose, to pass from the blood to the brain and central nervous system (CNS) but blocks most molecules that are more massive than about 500 Da.

Boil Localized pyrogenic, painful infection, originating in a hair follicle.

Borborygmus Rumbling noise caused by the muscular contractions of peristalsis, the process that moves the contents of the stomach and intestines downward.

Bowman–Birk Inhibitors Type of serine proteinase inhibitor.

Bouillon A broth in French cuisine.

Bradycardia As applied to adult medicine, is defined as a resting heart rate of under 60 beats per minute.

Bradyphrenia Referring to the slowness of thought common to many disorders of the brain.

Brain-Derived Neurotrophic Factor (BDNF) A protein member of the neurotrophin family that plays an important role in the growth, maintenance, function and survival of neurons. The protein molecule is involved in the modulation of cognitive and emotional functions and in the treatment of a variety of mental disorders.

Bright's Disease Chronic nephritis.

Bronchial Inflammation See Bronchitis.

Bronchiectasis A condition in which the airways within the lungs (bronchial tubes) become damaged and widened.

Bronchitis Is an inflammation of the main air passages (bronchi) to the lungs.

Bronchoalveolar Lavage (BAL) A medical procedure in which a bronchoscope is passed through the mouth or nose into the lungs and fluid is squirted into a small part of the lung and then recollected for examination.

Bronchopneumonia Or bronchial pneumonia; inflammation of the lungs beginning in the terminal bronchioles.

Bronchopulmonary Relating to the bronchi and lungs.

Bronchospasm Is a difficulty in breathing caused by a sudden constriction of the muscles in the walls of the bronchioles as occurs in asthma.

Brown Fat Brown adipose tissue (BAT) in mammals; its primary function is to generate body heat in animals or newborns that do not shiver.

Bubo Inflamed, swollen lymph node in the neck or groin.

Buccal Of or relating to the cheeks or the mouth cavity.

Bullae Blisters; circumscribed, fluid-containing, elevated lesions of the skin, usually more than 5 mm in diameter.

Bursa A fluid-filled sac or saclike cavity situated in areas subjected to friction.

Bursitis Condition characterized by inflammation of one or more bursae (small sacs) of synovial fluid in the body.

C Fibres Afferent fibres found in the nerve of the somatic sensory system.

c-FOS A cellular proto-oncogene belonging to the immediate early gene family of transcription factors.

c-Jun I (Ser 73) Substrate of JNK-1 activated by phosphorylation at Ser73.

c-Jun II (Ser 63) Substrate of JNK-1 activated by phosphorylation at Ser63.

c-Jun NH(2)-Terminal Kinase Enzymes that belong to the family of the MAPK superfamily of protein kinases. These kinases mediate a plethora of cellular responses to such stressful stimuli, including apoptosis and production of inflammatory and immunoregulatory cytokines in diverse cell systems. *Cf.* MAPK.

C-Reactive Protein A protein found in the blood, the levels of which rise in response to inflammation.

c-Src A cellular non-receptor tyrosine kinase.

CAAT Element-Binding Proteins-Alpha (c/EBP-akpha) Regulates gene expression in adipocytes in the liver.

Cachexia Physical wasting with loss of weight, muscle atrophy, fatigue and weakness caused by disease.

Caco-2 Cell Line A continuous line of heterogeneous human epithelial colorectal adenocarcinoma cells.

Cadaver A dead body, corpse.

Ca^{2+} ATPase (PMCA) Is a transport protein in the plasma membrane of cells that serves to remove calcium (Ca^{2+}) from the cell.

Calcitonin Gene-Related Peptide (CGRP) Is a 37-amino acid neuropeptide that is abundant in the sensory neurons which innervate bone.

Calcium (Ca) Is the most abundant mineral in the body found mainly in bones and teeth. It is required for muscle contraction, blood vessel expansion and contraction, secretion of hormones and enzymes and transmission of impulses throughout the nervous system. Dietary sources include milk, yogurt, cheese, Chinese cabbage, kale, broccoli, some green leafy vegetables, fortified cereals, beverages and soybean products.

Calcium ATPase Is a form of P-ATPase which transfers calcium after a muscle has contracted.

Calcium Channel Blockers (CCBs) A class of drugs and natural substances that disrupt the calcium (Ca^{2+}) conduction of calcium channels.

Calciuria Abnormal presence of calcium in the urine.

Calculosis The tendency or deposition to form calculi or stones.

Calculus (Calculi) Hardened, mineral deposits that can form a blockage in the urinary system.

Calculi Infection Most calculi arise in the kidney when urine becomes supersaturated with a salt that is capable of forming solid crystals. Symptoms arise as these calculi become impacted within the ureter as they pass towards the urinary bladder.

Caligo Dimness or obscurity of sight, dependent upon a speck on the cornea.

Calmodulin Is a calcium-modulated protein that can bind to and regulate a multitude of different protein targets, thereby affecting many different cellular functions.

cAMP-Dependent Pathway Cyclic adenosine monophosphate is a G protein-coupled receptor triggered signalling cascade used in cell communication in living organisms.

CAMP Factor Diffusible, heat-stable, extracellular protein produced by Group B *Streptococcus* that enhances the haemolysis of sheep erythrocytes by *Staphylococcus aureus.* It is named after Christie, Atkins and Munch-Peterson, who described it in 1944.

Campylobacteriosis Is a gastrointestinal disease (gastroenteritis) caused by bacteria called *Campylobacter* which is frequently associated with the consumption of contaminated poultry.

Cancer A malignant neoplasm or tumour in any part of the body.

Candidiasis Infections caused by members of the fungus genus *Candida* that range from superficial, such as oral thrush and vaginitis, to systemic and potentially life-threatening diseases.

Canker See Chancre.

Cannabinoid Receptor Family Includes CB1 cannabinoid receptors found predominantly in the brain and nervous system and CB2 cannabinoid receptors mainly associated with immune tissues and expressed at low levels in the brain.

Cannabinoid Receptor Type 2 (CB 2 Receptor) A G protein-coupled receptor from the cannabinoid receptor family that are mainly expressed on T cells of the immune system, on macrophages and B cells and in haematopoietic cells.

Carboxypeptidase An enzyme that hydrolyzes the carboxy-terminal (C-terminal) end of a peptide bond. It is synthesized in the pancreas and secreted into the small intestine.

Carbuncle Is an abscess larger than a boil, usually with one or more openings draining pus onto the skin.

Carcinogenesis Production of carcinomas. *Adj.* carcinogenic.

Carcinoma Any malignant cancer that arises from epithelial cells.

Carcinosarcoma A rare tumour containing carcinomatous and sarcomatous components.

Cardiac Relating to, situated near or affecting the heart.

Cardiac Asthma Acute attack of dyspnoea with wheezing resulting from a cardiac disorder.

Cardiac Hypertrophy Is a thickening of the heart muscle (myocardium) resulting in a decrease chamber size, including the left and right ventricles. Common causes of cardiac hypertrophy include high blood pressure (hypertension) and heart valve stenosis.

Cardialgia Heartburn.

Cardinolides Cardiac glycosides with a 5-membered lactone ring in the side chain of the steroid aglycone.

Cardinolide Glycoside Cardenolides that contain structural groups derived from sugars.

Cardioactive Having an effect on the heart.

Cardiogenic Shock Is characterized by a decreased pumping ability of the heart that causes a shock like state associated with an inadequate circulation of blood due to primary failure of the ventricles of the heart to function effectively.

Cardiomyocytes Cardiac muscle cells.

Cardiomyopathy Heart muscle disease.

Cardiopathy Disease or disorder of the heart.

Cardioplegia Stopping the heart so that surgical procedures can proceed in a still and bloodless field.

Cardiotonic Something which strengthens, tones or regulates heart functions without overt stimulation or depression.

Cardiovascular Pertaining to the heart and blood vessels.

Caries Tooth decay, commonly called cavities.

Cariogenic Leading to the production of caries.

Carminative Substance that stops the formation of intestinal gas and helps expel gas that has already formed, relieving flatulence: relieving flatulence or colic by expelling gas.

Carnitine Palmitoyltransferase I (CPT1) Also known as carnitine acyltransferase I or CAT1 is a mitochondrial enzyme, involved in converting long chain fatty acid into energy.

Carotenes Are a large group of intense red and yellow pigments found in all plants; these are hydrocarbon carotenoids (subclass of tetraterpenes) and the principal carotene is beta-carotene which is a precursor of vitamin A.

Carotenoids A class of natural fat-soluble pigments found principally in plants, belonging to a subgroup of terpenoids containing eight isoprene units forming a C40 polyene chain. Carotenoids play an important potential role in human health by acting as biological antioxidants. See also Carotenes.

Carotenodermia Yellow skin discoloration caused by excess blood carotene.

Carpopedal Spasm Spasm of the hand or foot or of the thumbs and great toes.

Capases Cysteine-aspartic acid proteases, are a family of cysteine proteases, which play essential roles in apoptosis (programmed cell death), necrosis and inflammation.

Catalase (CAT) Enzyme in living organism that catalyzes the decomposition of hydrogen peroxide to water and oxygen.

Catalepsy Indefinitely prolonged maintenance of a fixed body posture; seen in severe cases of catatonic schizophrenia.

Catamenia Menstruation.

Cataplasia Degenerative reversion of cells or tissue to a less differentiated form.

Cataplasm A medicated poultice or plaster. A soft moist mass, often warm and medicated, that is spread over the skin to treat an inflamed, aching or painful area, to improve the circulation.

Cataractogenesis Formation of cataracts.

Catarrh, Catarrhal Inflammation of the mucous membranes especially of the nose and throat.

Catechins Are polyphenolic antioxidant plant metabolites. They belong to the family of flavonoids; tea is a rich source of catechins. See Flavonoids.

Catecholamines Hormones that are released by the adrenal glands in response to stress.

Cathartic Is a substance which accelerates defecation.

Caustic Having a corrosive or burning effect.

Cauterization A medical term describing the burning of the body to remove or close a part of it.

Caveolae Tiny (50–100 nm) invaginations of the plasma membrane of the cell.

CB-1 Receptor Cannabinoid receptor type 1 held to be one of the most widely expressed G protein-coupled receptors in the brain.

cdc2 Kinase A member of the cyclin-dependent protein kinases (CDKs).

CDKs Cyclin-dependent protein kinases, a family of serine/threonine kinases that mediate many stages in mitosis.

CD4T cell Helper T cell with CD4 receptor that recognizes antigens on the surface of a virus-infected cell and secretes lymphokines that stimulate B cells and killer T cells.

CD28 Is one of the molecules expressed on T cells that provide co-stimulatory signals, which are required for T cell (lymphocytes) activation.

CD31 Also known as PECAM-1 (platelet endothelial cell adhesion molecule-1), a member of the immunoglobulin superfamily, that mediates cell-to-cell adhesion.

CD36 An integral membrane protein found on the surface of many cell types in vertebrate animals.

CD40 An integral membrane protein found on the surface of B lymphocytes, dendritic cells, follicular dendritic cells, haematopoietic progenitor cells, epithelial cells and carcinomas.

CD68 A glycoprotein expressed on monocytes/macrophages which binds to low-density lipoprotein.

Cecal Ligation tying up the caecum.

Celiac Disease An autoimmune disorder of the small intestine, triggered in genetically susceptible individuals by ingested gluten from

wheat, rye, barley and other closely related cereal grains. Peptides resulting from partially digested gluten of wheat, barley or rye cause inflammation of the small intestinal mucosa.

Cell Adhesion Molecules (CAM) Glycoproteins located on the surface of cell membranes involved with binding of other cells or with the extracellular matrix.

Cellular Respiration Is the set of the metabolic reactions and processes that take place in organisms' cells to convert biochemical energy from nutrients into adenosine triphosphate (ATP) and then release waste products. The reactions involved in respiration are catabolic reactions that involve the oxidation of one molecule and the reduction of another.

Cellulitis A bacterial infection of the skin that tends to occur in areas that have been damaged or inflamed.

Central Nervous System Part of the vertebrate nervous system comprising the brain and spinal cord.

Central Venous Catheter A catheter placed into the large vein in the neck, chest or groin.

Cephalalgia Pain in the head, a headache.

Cephalic Relating to the head.

Ceramide Oligosides Oligosides with an N-acetyl-sphingosine moiety.

Cercariae A free-swimming larva of the parasitic schistosome worm that has a tail and suckers on its head for penetration into a host.

Cerebral Embolism A blockage of blood flow through a vessel in the brain by a blood clot that formed elsewhere in the body and travelled to the brain.

Cerebral Ischaemia Is the localized reduction of blood flow to the brain or parts of the brain due to arterial obstruction or systematic hyperfusion.

Cerebral Infarction Is the ischemic kind of stroke due to a disturbance in the blood vessels supplying blood to the brain.

Cerebral Tonic Substance that can alleviate poor concentration and memory, restlessness, uneasiness and insomnia.

Cerebrosides Are glycosphingolipids which are important components in animal muscle and nerve cell membranes.

Cerebrovascular Disease Is a group of brain dysfunctions related to disease of the blood vessels supplying the brain.

Cerumen Ear wax, a yellowish waxy substance secreted in the ear canal of humans and other mammals.

cFLIP Cellular FLICE-inhibitory protein, an inhibitor of death ligand-induced apoptosis.

cGMP Cyclic guanosine monophosphate is a cyclic nucleotide derived from guanosine triphosphate (GTP). cGMP is a common regulator of ion channel conductance, glycogenolysis and cellular apoptosis. It also relaxes smooth muscle tissues.

CGRP Calcitonin Gene-Related Peptide A vasodilator neuropeptide that is expressed in a subgroup of small neurons in the dorsal root, trigeminal and vagal ganglia. This neuropeptide has been postulated to play a role in the pathophysiology of migraine.

Chalcones A subgroup of flavonoids.

Chancre A painless lesion formed during the primary stage of syphilis.

Chemoembolization A procedure in which the blood supply to the tumour is blocked surgically or mechanically and anticancer drugs are administered directly into the tumour.

Chemokines Are chemotactic cytokines, which stimulate migration of inflammatory cells towards tissue sites of inflammation.

Chemonociceptors Nociceptors or sensory peripheral neurons that are sensitive to chemical stimuli.

Chemosensitizer A drug that makes tumour cells more sensitive to the effects of chemotherapy.

Chemosis Oedema of the conjunctiva of the eye.

Chickenpox Is also known as varicella and is a highly contagious illness caused by primary infection with varicella zoster virus (VZV). The virus causes red, itchy bumps on the body.

Chilblains Small, itchy, painful lumps that develop on the skin. They develop as an abnormal response to cold. Also called perniosis or blain.

Chlorosis Iron deficiency anaemia characterized by greenish yellow colour.

Cholagogue Is a medicinal agent which promotes the discharge of bile from the system.

Cholecalciferol A form of vitamin D, also called vitamin D3. See Vitamin D.

Cholecyst Gall bladder.

Cholecystitis Inflammation of the gall bladder.

Cholecystokinin A peptide hormone that plays a key role in facilitating digestion in the small intestine.

Cholera An infectious gastroenteritis caused by enterotoxin-producing strains of the bacterium *Vibrio cholera* and characterized by severe, watery diarrhoea.

Choleretic Stimulation of the production of bile by the liver.

Cholestasis A condition caused by rapidly developing (acute) or long-term (chronic) interruption in the excretion of bile from the liver to the duodenum.

Cholesterol A soft, waxy, steroid substance found among the lipids (fats) in the bloodstream and in all our body's cells.

Cholethiasis Presence of gall stones (calculi) in the gall bladder.

Choline A water-soluble, organic compound, usually grouped within the vitamin B complex. It is an essential nutrient and is needed for physiological functions such as structural integrity and signalling roles for cell membranes, cholinergic neurotransmission (acetylcholine synthesis).

Cholinergic Activated by or capable of liberating acetylcholine, especially in the parasympathetic nervous system.

Cholinergic System A system of nerve cells that uses acetylcholine in transmitting nerve impulses.

Cholinomimetic Having an action similar to that of acetylcholine. Also called parasympathomimetic.

Chonotropic Affecting the time or rate, as the rate of contraction of the heart.

Choriocarcinoma A quick-growing malignant, trophoblastic, aggressive cancer that occurs in a woman's uterus (womb).

Chromium (Cr) Is required in trace amounts in humans for sugar and lipid metabolism. Its deficiency may cause a disease called chromium deficiency. It is found in cereals, legumes, nuts and animal sources.

Chromoblastomycosis A chronic fungal infection of the skin and the subcutaneous tissue caused by traumatic inoculation of a specific group of dematiaceous fungi (such as *Fonsecaea pedrosoi*, *Phialophora verrucosa*, *Fonsecaea compacta*) through the skin.

Chromosome Long pieces of DNA found in the centre (nucleus) of cells.

Chronic Persisting over extended periods.

Chronic Obstructive Pulmonary Disease (COPD) A progressive disease that makes it hard to breathe.

Chronic Venous Insufficiency (CVI) A medical condition where the veins cannot pump enough oxygen-poor blood back to the heart.

Chyle A milky bodily fluid consisting of lymph and emulsified fats or free fatty acids.

Chylomicrons Are large lipoprotein particles that transport dietary lipids from the intestines to other locations in the body. Chylomicrons are one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL, HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream.

Chylorus Milky (having fat emulsion).

Chyluria Also called chylous urine, is a medical condition involving the presence of chyle (emulsified fat) in the urine stream, which results in urine appearing milky.

Chymase Member of the family of serine proteases found primarily in mast cell.

Chymopapain An enzyme derived from papaya, used in medicine and to tenderize meat.

Cicatrizant The term used to describe a product that promotes healing through the formation of scar tissue.

C-Kit Receptor A protein-tyrosine kinase receptor that is specific for stem cell factor. This interaction is crucial for the development of haematopoietic, gonadal and pigment stem cells.

Cirrhosis Chronic liver disease characterized by replacement of liver tissue by fibrous scar tissue and regenerative nodules/lumps leading progressively to loss of liver function.

Clastogen Is an agent that can cause one of two types of structural changes and breaks in chromosomes that result in the gain, loss or rearrangements of chromosomal segments. *Adj.* clastogenic.

Claudication Limping, impairment in walking.

Climacterium Refers to menopause and the bodily and mental changes associated with it.

Clonic Seizures Consist of rhythmic jerking movements of the arms and legs, sometimes on both sides of the body.

Clonus A series of involuntary muscular contractions and relaxations.

Clyster Enema.

C-Myc Codes for a protein that binds to the DNA of other genes and is therefore a transcription factor.

CNS Depressant Anything that depresses, or slows, the sympathetic impulses of the central nervous system (i.e. respiratory rate, heart rate).

Coagulopathy A defect in the body's mechanism for blood clotting, causing susceptibility to bleeding.

Cobalamin Vitamin B12. See Vitamin B12.

Cocarcinogen A chemical that promotes the effects of a carcinogen in the production of cancer.

Cold An acute inflammation of the mucous membrane of the respiratory tract especially of the nose and throat caused by a virus and accompanied by sneezing and coughing.

Collagen Protein that is the major constituent of cartilage and other connective tissue; comprises the amino acids hydroxyproline, proline, glycine and hydroxylysine.

Collagenases Enzymes that break the peptide bonds in collagen.

Colic A broad term which refers to episodes of uncontrollable, extended crying in a baby who is otherwise healthy and well fed.

Colitis Inflammatory bowel disease affecting the tissue that lines the gastrointestinal system.

Collyrium A lotion or liquid wash used as a cleanser for the eyes, particularly in diseases of the eye.

Colorectal Relating to the colon or rectum.

Coma A state of unconsciousness from which a patient cannot be aroused.

Comedone A blocked, open sebaceous gland where the secretions oxidize, turning black. Also called blackhead.

Comitogen Agent that is considered not to induce cell growth alone but to promote the effect of the mitogen.

Concoction A combination of crude ingredients that is prepared or cooked together.

Condyloma, Condylomata Acuminata Genital warts, venereal warts, anal wart or anogenital wart, a highly contagious sexually transmitted infection caused by epidermotropic human papillomavirus (HPV).

Conglutination Becoming stuck together.

Conjunctival Hyperaemia Enlarged blood vessels in the eyes.

Conjunctivitis Sore, red and sticky eyes caused by eye infection.

Constipation A very common gastrointestinal disorder characterized by the passing of hard, dry bowel motions (stools) and difficulty of bowel motion.

Constitutive Androstane Receptor (CAR, NR113) Is a nuclear receptor transcription factor that regulates drug metabolism and homoeostasis.

Consumption Term used to describe wasting of tissues including but not limited to tuberculosis.

Consumptive Afflicted with or associated with pulmonary tuberculosis.

Contraceptive An agent that reduces the likelihood of or prevents conception.

Contraindication A condition which makes a particular treatment or procedure inadvisable.

Contralateral Muscle Muscle of opposite limb (leg or arm).

Contralateral Rotation Rotation occurring or originating in a corresponding part on an opposite side.

Contusion Another term for a bruise. A bruise, or contusion, is caused when blood vessels are damaged or broken as the result of a blow to the skin.

Convulsant A drug or physical disturbance that induces convulsion.

Convulsion Rapid and uncontrollable shaking of the body.

Coolant That which reduces body temperature.

Copper (Cu) Is essential in all plants and animals. It is found in a variety of enzymes, including the copper centres of cytochrome C oxidase and the enzyme superoxide dismutase (containing copper and zinc). In addition to its enzymatic roles, copper is used for biological electron transport. Because of its role in facilitating iron uptake, copper deficiency can often produce anaemia-like symptoms. Dietary sources include curry powder, mushroom, nuts, seeds, wheat germ, whole grains and animal meat.

Copulation To engage in coitus or sexual intercourse. *Adj.* copulatory.

Cordial A preparation that is stimulating to the heart.

Corn Or callus is a patch of hard, thickened skin on the foot that is formed in response to pressure or friction.

Corpora Lutea A yellow, progesterone-secreting body that forms from an ovarian follicle after the release of a mature egg.

Corticosteroids A class of steroid hormones that are produced in the adrenal cortex, used clinically for hormone replacement therapy, for suppressing ACTH secretion, for suppression of immune response and as antineoplastic, antiallergic and antiinflammatory agents.

Corticosterone A 21-carbon steroid hormone of the corticosteroid type produced in the cortex of the adrenal glands.

Cortisol Is a corticosteroid hormone made by the adrenal glands.

Cornification Is the process of forming an epidermal barrier in stratified squamous epithelial tissue.

Coryza A word describing the symptoms of a head cold. It describes the inflammation of the mucus membranes lining the nasal cavity which usually gives rise to the symptoms of nasal congestion and loss of smell, among other symptoms.

COX-1 See Cyclooxygenase-1.

COX-2 See Cyclooxygenase-2.

CpG Islands Genomic regions that contain a high frequency of CpG sites.

CpG Sites The cytosine-phosphate-guanine nucleotide that links two nucleosides together in DNA.

cPLA(2) Cytosolic phospholipases A2; these phospholipases are involved in cell signalling processes, such as inflammatory response.

CPY1B1, CPY1A1 A member of the cytochrome P450 superfamily of heme-thiolate monooxygenase enzymes.

Corticosterone A 21-carbon corticosteroid hormone produced in the cortex of the adrenal glands that functions in the metabolism of carbohydrates and proteins.

Creatine A nitrogenous organic acid that occurs naturally in vertebrates and helps to supply energy to muscle.

Creatine Hosphokinase (CPK, CK) Enzyme that catalyzes the conversion of creatine and consumes adenosine triphosphate (ATP) to create phosphocreatine and adenosine diphosphate (ADP).

CREB cAMP response element binding, a protein that is a transcription factor that binds to certain DNA sequences called cAMP response elements.

Crohn's Disease An inflammatory disease of the intestines that affect any part of the gastrointestinal tract.

Crossover Study A longitudinal, balance study in which participants receive a sequence of different treatments or exposures.

Croup Is an infection of the throat (larynx) and windpipe (trachea) that is caused by a virus. Also called laryngotracheobronchitis.

Cryptococcal Meningitis A fungal infection of the membranes covering the brain and spinal cord (meninges).

Crytorchidism (Cryptorchism) A developmental defect characterized by the failure of one or both testes to move into the scrotum as the male foetus develops.

Curettage Surgical procedure in which a body cavity or tissue is scraped with a sharp instrument or aspirated with a cannula.

Cutaneous Pertaining to the skin.

CXC8 Also known as interleukin 8, IL-8.

Cyanogenesis Generation of cyanide. *Adj.* cyanogenetic.

Cyclooxygenase (COX) An enzyme that is responsible for the formation of prostanoids—prostaglandins, prostacyclins and thromboxanes that are each involved in the inflammatory response. Two different COX enzymes existed, now known as COX-1 and COX-2.

Cyclooxygenase-1 (COX-1) Is known to be present in most tissues. In the gastrointestinal tract, COX-1 maintains the normal lining of the stomach. The enzyme is also involved in kidney and platelet function.

Cyclooxygenase-2 (COX-2) Is primarily present at sites of inflammation.

Cysteine Proteases Are enzymes that degrade polypeptides possessing a common catalytic mechanism that involves a nucleophilic cysteine thiol in a catalytic triad. They are found in fruits like papaya, pineapple and kiwifruit.

Cystitis A common urinary tract infection that occurs when bacteria travel up the urethra, infect the urine and inflame the bladder lining.

Cystorrhoea Discharge of mucus from the bladder.

Cytochrome bc-1 Complex Ubihydroquinone: cytochrome c oxidoreductase.

Cytochrome P450 3A CYP3A A very large and diverse superfamily of heme-thiolate proteins found in all domains of life. This group of enzymes catalyzes many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids.

Cytokine Non-antibody proteins secreted by certain cells of the immune system which carry signals locally between cells. They are a category of signalling molecules that are used extensively in cellular communication.

Cytopathic Any detectable, degenerative changes in the host cell due to infection.

Cytoprotective Protecting cells from noxious chemicals or other stimuli.

Cytosolic Relates to the fluid of the cytoplasm in cells.

Cytostatic Preventing the growth and proliferation of cells.

Cytotoxic Of or relating to substances that are toxic to cells, cell-killing.

D-Galactosamine An amino sugar with unique hepatotoxic properties in animals.

Dandruff Scurf, dead, scaly skin among the hair.

Dartre Condition of dry, scaly skin.

Debility Weakness, relaxation of muscular fibre.

Debridement Is the process of removing non-living tissue from pressure ulcers, burns and other wounds.

Debriding Agent Substance that cleans and treats certain types of wounds, burns and ulcers.

Deciduogenic Relating to the uterus lining that is shed off at childbirth.

Deciduoma Decidual tissue induced in the uterus (as by trauma) in the absence of pregnancy.

Deciduomata Plural of deciduoma.

Decidual Stromal Cells Like endometrial glands and endothelium, express integrins that bind basement components.

Decoction A medical preparation made by boiling the ingredients.

Decongestant A substance that relieves or reduces nasal or bronchial congestion.

Deep Venous Thrombosis Is a blood clot that forms in a vein deep inside a part of the body.

Defibrinated Plasma Blood whose plasma component has had fibrinogen and fibrin removed.

Degranulation Cellular process that releases antimicrobial cytotoxic molecules from secretory vesicles called granules found inside some cells.

DelayedAfterdepolarizations(DADs) Abnormal depolarization that begins during phase 4, after repolarization is completed but before another action potential would normally occur.

Delirium Is common, sudden severe confusion and rapid changes in brain function that occur with physical or mental illness; it is reversible and temporary.

Demulcent An agent that soothes internal membranes. Also called emollient.

Dendritic Cells Are immune cells and form part of the mammalian immune system, functioning as antigen presenting cells.

Dentition A term that describes all of the upper and lower teeth collectively.

Deobstruent A medicine which removes obstructions. Also called an aperient.

Deoxypyridinoline (DPD) A cross-link product of collagen molecules found in bone and excreted in urine during bone degradation.

Depilatory An agent for removing or destroying hair.

Depressant A substance that diminish functional activity, usually by depressing the nervous system.

Depurative An agent used to cleanse or purify the blood; it eliminates toxins and purifies the system.

Dermatitis Inflammation of the skin causing discomfort such as eczema.

Dermatitis Herpetiformis An autoimmune chronic blistering skin disorder characterized by blisters filled with a watery fluid.

Dermatophyte A fungus parasitic on the skin.

Dermatosis Is a broad term that refers to any disease of the skin, especially one that is not accompanied by inflammation.

Dermonecrotic Pertaining to or causing necrosis of the skin.

Desquamation The shedding of the outer layers of the skin.

Desquamative Gingivitis Red, painful, glazed and friable gingivae which may be a manifestation of some mucocutaneous conditions such as lichen planus or the vesiculobullous disorders.

Detoxifier A substance that promotes the removal of toxins from a system or organ.

Diabetes A metabolic disorder associated with inadequate secretion or utilization of insulin and characterized by frequent urination and persistent thirst. See Diabetes mellitus.

Diabetes Mellitus (DM) Sometimes called 'sugar diabetes' is a set of chronic, metabolic disease conditions characterized by high blood sugar (glucose) levels that result from defects in insulin secretion, or action, or both. Diabetes mellitus appears in two forms.

Diabetes Mellitus Type I Formerly known as juvenile onset diabetes, it is caused by deficiency of the pancreatic hormone insulin as a result of destruction of insulin-producing beta cells of the pancreas. Lack of insulin causes an increase of fasting blood glucose that begins to appear in the urine above the renal threshold.

Diabetes Mellitus Type II Formerly called non-insulin-dependent diabetes mellitus or adult-onset diabetes, the disorder is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency in which insulin is available but cannot be properly utilized.

Diabetic Neuropathy A neuropathic disorder that is associated with diabetes mellitus. It affects all peripheral nerves including pain fibres, motor neurons and the autonomic nervous system.

Diabetic Retinopathy Damage to the retina caused by complications of diabetes mellitus, which can eventually lead to blindness.

Dialysis Is a method of removing toxic substances (impurities or wastes) from the blood when the kidneys are unable to do so.

Diaphoresis Is profuse sweating commonly associated with shock and other medical emergency conditions.

Diaphoretic A substance that induces perspiration. Also called sudorific.

Diaphyseal Pertaining to or affecting the shaft of a long bone (diaphysis).

Diaphysis The main or midsection (shaft) of a long bone.

Diarrhoea A profuse, frequent and loose discharge from the bowels.

Diastolic Referring to the time when the heart is in a period of relaxation and dilatation (expansion). *Cf*. systolic.

Dieresis Surgical separation of parts.

Dietary Fibre Is a term that refers to a group of food components that pass through the stomach and small intestine undigested and reach the large intestine virtually unchanged. Scientific evidence suggests that a diet high in dietary fibre can be of value for treating or preventing such disorders as constipation, irritable bowel syndrome, diverticular disease, hiatus hernia and haemorrhoids. Some components of dietary fibre may also be of value in reducing the level of cholesterol in blood and thereby decreasing a risk factor for coronary heart disease and the development of gallstones. Dietary fibre is beneficial in the treatment of some diabetics.

Digalactosyl Diglycerides Are the major lipid components of chloroplasts.

Diosgenin A steroid-like substance that is involved in the production of the hormone progesterone, extracted from roots of *Dioscorea* yam.

Dipsia Sensation of dryness in the mouth and throat related to a desire to drink.

Dipsomania Pathological use of alcohol.

Discutient An agent (as a medicinal application) which serves to disperse morbid matter.

Disinfectant An agent that prevents the spread of infection, bacteria or communicable disease.

Distal Sensory Polyneuropathy (DSPN) Or peripheral neuropathy is the most common neurological problem in HIV disease. DSPN also represents a complex symptom that occurs because of peripheral nerve damage related to advanced HIV disease.

Diuresis Increased urination.

Diuretic A substance that increases urination (diuresis).

Diverticular Disease Is a condition affecting the large bowel or colon and is thought to be caused by eating too little fibre.

DMBA 7,12-Dimethylbenzanthracene. A polycyclic aromatic hydrocarbon found in tobacco smoke that is a potent carcinogen.

DNA Deoxyribonucleic acid. A nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms.

DOCA Deoxycorticosterone acetate. A steroid chemical used as replacement therapy in Addison's disease.

Dopamine A catecholamine neurotransmitter that occurs in a wide variety of animals, including both vertebrates and invertebrates.

Dopaminergic Relating to or activated by the neurotransmitter, dopamine.

Double Blind Refer to a clinical trial or experiment in which neither the subject nor the researcher knows which treatment any particular subject is receiving.

Douche A localized spray of liquid directed into a body cavity or onto a part.

DPPH 2,2-Diphenyl-1-picryl-hydrazyl. A crystalline, stable free radical used as an inhibitor of free radical reactions.

Dracunculiasis Also called guinea worm disease (GWD), is a parasitic infection caused by the nematode, *Dracunculus medinensis*.

Dropsy An old term for the swelling of soft tissues due to the accumulation of excess water. *Adj.* dropsical.

Drug-Metabolizing Enzymes Play central roles in the biotransformation, metabolism and/or detoxification of xenobiotics or foreign compounds that are introduced to the human body.

Drusen Tiny yellow or white deposits of extracellular materials in the retina of the eye or on the optic nerve head.

DT-Diaphorase Also called DTD or NAD(P)H:quinone oxidoreductase, is an obligate two-electron reductase which bioactivates chemotherapeutic quinones.

Dyads Two adjacent structural units in a polymer molecule.

Dysaesthesia An unpleasant abnormal sensation produced by normal stimuli.

Dysentery Formerly known as flux or the bloody flux, is a disorder of the digestive system that results in severe diarrhoea containing mucus and blood in the faeces. It is caused usually by a bacterium called *Shigella*.

Dysgeusia Distortion of the sense of taste.

Dyshomeostasis An imbalance or other breakdown of a homeostasis system.

Dyskinesia The impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. *Adj.* dyskinetic.

Dyslipidaemia Abnormality in or abnormal amount of lipids and lipoproteins in the blood.

Dysmenorrhoea Is a menstrual condition characterized by severe and frequent menstrual cramps and pain associated with menstruation.

Dysmotility Syndrome A vague, descriptive term used to describe diseases of the muscles of the gastrointestinal tract (oesophagus, stomach, small and large intestines).

Dyspareunia Painful sexual intercourse.

Dyspedia Indigestion followed by nausea.

Dyspepsia Refers to a symptom complex of epigastric pain or discomfort. It is often defined as chronic or recurrent discomfort centred in the upper abdomen and can be caused by a variety of conditions. *Cf.* functional dyspepsia.

Dysphagia Swallowing disorder.

Dysphonia A voice disorder and an impairment in the ability to produce voice sounds using the vocal organs.

Dysplasia Refers to abnormality in development.

Dyspnoea Shortness of breath; difficulty in breathing.

Dysrhythmias See Arrhythmias.

Dystocia Abnormal or difficult childbirth or labour.

Dystonia A neurological movement disorder characterized by prolonged, repetitive muscle contractions that may cause twisting or jerking movements of muscles.

Dysuria Refers to difficult and painful urination.

E-Selectin Also known as endothelial leukocyte adhesion molecule-1 (ELAM-1), CD62E, a member of the selectin family. It is transiently expressed on vascular endothelial cells in response to IL-1 beta and TNF-alpha.

EC 50 Median effective concentration that produces desired effects in 50 % of the test population.

Ecbolic A drug (as an ergot alkaloid) that tends to increase uterine contractions and that is used especially to facilitate delivery.

Ecchymosis Skin discoloration caused by the escape of blood into the tissues from ruptured blood vessels.

ECG See Electrocardiography.

EC–SOD Extracellular superoxide dismutase. A tissue enzyme mainly found in the extracellular matrix of tissues. It participates in the detoxification of reactive oxygen species by catalyzing the dismutation of superoxide radicals.

Ectopic Heartbeats Small changes in an otherwise normal heartbeat that lead to extra or skipped heartbeats.

Ectrodactyly Involves the absence of one or more central digits of the hand or foot.

Eczema Is broadly applied to a range of persistent skin conditions. These include dryness and recurring skin rashes which are characterized by one or more of these symptoms: redness, skin oedema, itching and dryness, crusting, flaking, blistering, cracking, oozing or bleeding.

Eczematous Rash Dry, scaly, itchy rash.

ED 50 Is defined as the dose producing a response that is 50 % of the maximum obtainable.

EGFR Proteins Epidermal growth factor receptor (EGFR) proteins. Protein kinases are enzymes that transfer a phosphate group from a phosphate donor onto an acceptor amino acid in a substrate protein.

EGR-1 Early growth response 1, a human gene.

Eicosanoids Are signalling molecules made by oxygenation of arachidonic acid, a 20-carbon essential fatty acid, includes prostaglandins and related compounds.

Elastase A serine protease that also hydrolyzes amides and esters.

Electrocardiography Or ECG is a transthoracic interpretation of the electrical activity of the heart over time captured and externally recorded by skin electrodes.

Electromyogram (EMG) A test used to record the electrical activity of muscles. An electromyogram (EMG) is also called a myogram.

Electuary A medicinal paste composed of powders, or other medical ingredients, incorporated with sweeteners to hide the taste, suitable for oral administration.

Elephantiasis A disorder characterized by chronic thickened and oedematous tissue on the genitals and legs due to various causes.

Embrocation Lotion or liniment that relieves muscle or joint pains.

Embryonation Formation of embryo in the egg.

Embryotoxic Term that describes any chemical which is harmful to an embryo.

Emesis Vomiting, throwing up.

Emetic An agent that induces vomiting. *Cf.* antiemetic.

Emetocathartic Causing vomiting and purging.

Emmenagogue A substance that stimulates, initiates and/or promotes menstrual flow. Emmenagogues are used in herbal medicine to balance and restore the normal function of the female reproductive system.

Emollient An agent that has a protective and soothing action on the surfaces of the skin and membranes.

Emphysema A long-term, progressive disease of the lungs that primarily causes shortness of breath.

Emulsion A preparation formed by the suspension of very finely divided oily or resinous liquid in another liquid.

Encephalitis Inflammation of the brain.

Encephalocele Protrusion of brain tissue through a congenital fissure in the skull.

Encephalomalacia Cerebral softening, a localized softening of the brain substance, due to haemorrhage or inflammation.

Encephalopathy A disorder or disease of the brain.

Endocrine *Adj.* of or relating to endocrine glands or the hormones secreted by them.

Endocytosis Is the process by which cells absorb material (molecules such as proteins) from outside the cell by engulfing it with their cell membrane.

Endometrial Cancer Cancer that arises in the endometrium, the lining of the uterus (womb).

Endometriosis Is a common and often painful disorder of the female reproductive system in which the endometrium, the tissue that normally lines the womb (uterus), grows outside the uterus. The two most common symptoms of endometriosis are pain and infertility.

Endometritis Refers to inflammation of the endometrium, the inner lining of the uterus.

Endometrium The inner lining of the uterus.

Endoplasmic Reticulum Is a network of tubules, vesicles and sacs around the nucleus that are interconnected.

Endostatin A naturally occurring 20-kDa C-terminal protein fragment derived from type XVIII collagen. It is reported to serve as an anti-angiogenic agent that inhibits the formation of the blood vessels that feed cancer tumours.

Endosteum The thin layer of cells lining the medullary cavity of a bone.

Endosteal Pertaining to the endosteum.

Endothelial Progenitor Cells Population of rare cells that circulate in the blood with the ability to differentiate into endothelial cells, the cells that make up the lining of blood vessels.

Endothelin Any of a group of vasoconstrictive peptides produced by endothelial cells that constrict blood vessels and raise blood pressure.

Endotoxemia The presence of endotoxins in the blood, which may result in shock. *Adj.* endotoxemic.

Endotoxin Toxins associated with certain bacteria, unlike an 'exotoxin' that is not secreted in soluble form by live bacteria, but is a structural component in the bacteria which is released mainly when bacteria are lysed.

Enema Liquid injected into the rectum either as a purgative or medicine. Also called clyster.

Enophthalmos A condition in which the eye falls back into the socket and inhibits proper eyelid function.

Enteral Term used to describe the intestines or other parts of the digestive tract.

Enteralgia Pain in the intestines; intestinal colic.

Enteral Administration Involves the oesophagus, stomach and small and large intestines (i.e. the gastrointestinal tract).

Enteritis Refers to inflammation of the small intestine.

Enterocolic Disorder Inflamed bowel disease.

Enterocytes Tall columnar cells in the small intestinal mucosa that are responsible for the final digestion and absorption of nutrients.

Enterohaemorrhagic Causing bloody diarrhoea and colitis, said of pathogenic microorganisms.

Enterohepatonephropathy Hepatorenal lesions accompanied by renal failure.

Enterolactone A lignin formed by the action of intestinal bacteria on lignan precursors found in plants; acts as a phytoestrogen.

Enteropooling Increased fluids and electrolytes within the lumen of the intestines due to increased levels of prostaglandins.

Enterotoxigenic Of or being an organism containing or producing an enterotoxin.

Enterotoxin Is a protein toxin released by a microorganism in the intestine.

Entheogen A substance taken to induce a spiritual experience.

Enuresis Bed-wetting, a disorder of elimination that involves the voluntary or involuntary

release of urine into bedding, clothing or other inappropriate places.

Envenomation Is the entry of venom into a person's body, and it may cause localized or systemic poisoning.

Eosinophilia The state of having a high concentration of eosinophils (eosinophil granulocytes) in the blood.

Eosinophils Or, less commonly, acidophils, are white blood cells that are one of the immune system components.

Epidermal Growth Factor Receptor (EGFR) Belongs to the ErbB family of receptor tyrosine kinases (RTK). EGFR are involved in the pathogenesis and progression of different carcinoma types.

Epididymis A structure within the scrotum attached to the backside of the testis and whose coiled duct provides storage, transit and maturation of spermatozoa.

Epididymitis A medical condition in which there is inflammation of the epididymis.

Epigastralgia Pain in the epigastric region.

Epigastric Discomfort Bloated abdomen, swelling of abdomen and abdominal distension.

Epilepsy A common chronic neurological disorder that is characterized by recurrent unprovoked seizures.

Epileptiform Resembling epilepsy or its manifestations. *Adj.* epileptiformic.

Epileptogenesis A process by which a normal brain develops epilepsy, a chronic condition in which seizures occur. *Adj.* epileptogenic.

Episiotomy A surgical incision through the perineum made to enlarge the vagina and assist childbirth.

Epithelioma A usually benign skin disease most commonly occurring on the face, around the eyelids and on the scalp.

Epitope A single antigenic site on a protein against which an antibody reacts.

Epitrochlearis The superficial-most muscle of the arm anterior surface.

Epistaxis Acute haemorrhage from the nostril, nasal cavity or nasopharynx (nosebleed).

Epstein–Barr Virus Herpes virus that is the causative agent of infectious mononucleosis. It is also associated with various types of human cancers.

ERbeta Oestrogen receptor beta. A nuclear receptor which is activated by the sex hormone, oestrogen.

Ergocalciferol A form of vitamin D. Also called vitamin D2. See Vitamin D.

Ergonic Increasing capacity for bodily or mental labour, especially by eliminating fatigue symptoms.

ERK (Extracellular Signal-Regulated Kinases) Widely expressed protein kinase intracellular signalling molecules which are involved in functions including the regulation of meiosis, mitosis and postmitotic functions in differentiated cells.

Eructation The act of belching or of casting up wind from the stomach through the mouth.

Eruption A visible rash or cutaneous disruption.

Erysipelas Is an intensely red *Streptococcus* bacterial infection that occurs on the face and lower extremities.

Erythema Abnormal redness and inflammation of the skin, due to vasodilation.

Erythema Multiforme Is a skin disorder due to an allergic reaction or infection; it is characterized by fever, general ill feeling, skin itching, joint aches and multiple skin lesions.

Erythematous Characterized by erythema.

Erythroleukoplakia An abnormal patch of red and white tissue that forms on mucous membranes in the mouth and may become cancer. Tobacco (smoking and chewing) and alcohol may increase the risk of erythroleukoplakia.

Erythropoietin (EPO) A hormone produced by the kidney that promotes the formation of red blood cells (erythrocytes) in the bone marrow.

Eschar A slough or piece of dead tissue that is cast off from the surface of the skin.

Escharotic Capable of producing an eschar; a caustic or corrosive agent.

Estradiol Is the predominant sex hormone present in females. Also called oestradiol.

Euglycaemia Normal blood glucose concentration.

Eupeptic Conducive to digestion.

Exanthematous Characterized by or of the nature of an eruption or rash.

Excitotoxicity Is the pathological process by which neurons are damaged and killed by glutamate and similar substances.

Excipient A pharmacologically inert substance used as a diluent or vehicle for the active ingredients of a medication.

Exfoliative Cheilitis Is a reactive process, in which upper, lower or both lips become chronically inflamed, crusted and sometimes fissured.

Exocytosis The cellular process by which cells excrete waste products or chemical transmitters.

Exophthalmos or Exophthalmia or Proptosis Is a bulging of the eye anteriorly out of the orbit. *Adj.* exophthalmic.

Exotoxin A toxin secreted by a microorganism and released into the medium in which it grows.

Expectorant An agent that increases bronchial mucous secretion by promoting liquefaction of the sticky mucous and expelling it from the body.

Exteroceptive Responsiveness to stimuli that are external to an organism.

Extrapyramidal Side Effects Are a group of symptoms (tremor, slurred speech, akathisia, dystonia, anxiety, paranoia and bradyphrenia) that can occur in persons taking antipsychotic medications.

Extravasation Discharge or escape, as of blood from the vein into the surrounding tissues; discharge or escape from a vessel or channel.

Fabry Disease Is a rare X-linked (inherited) lysosomal storage disease caused by alpha-galactosidase A deficiency, which can cause a wide range of systemic symptoms such as pain in the extremities, papules on the lower body parts, cornea clouding, fatigue, neuropathy and renal and cardiac complications.

FAC Chemotherapy Fluorouracil, doxorubicin (adriamycin) and cyclophosphamide chemotherapy.

FADD Fas-associated protein with death domain, the protein encoded by this gene is an adaptor molecule which interacts with other death cell surface receptors and mediates apoptotic signals.

Familial Adenomatous Polyposis (FAP) Is an inherited condition in which numerous polyps form mainly in the epithelium of the large intestine.

Familial Amyloid Polyneuropathy (FAP) Also called Corino de Andrade's disease, a neurodegenerative autosomal dominant genetically transmitted, fatal, incurable disease.

Familial Dysautonomia A genetic disorder that affects the development and survival of autonomic and sensory nerve cells.

Fanconi Syndrome Is a disease of the proximal renal tubes which certain substances normally absorbed into the bloodstream by the kidneys are released into the urine instead.

FasL or CD95L Fas ligand is a type-II transmembrane protein that belongs to the tumour necrosis factor (TNF) family.

FAS Fatty Acid Synthase (FAS) A multienzyme that plays a key role in fatty acid synthesis.

Fas Molecule A member of the tumour necrosis factor receptors that mediates apoptotic signal in many cell types.

Fauces The passage leading from the back of the mouth into the pharynx.

Favus A chronic skin infection, usually of the scalp, caused by the fungus, *Trichophyton schoenleinii*, and characterized by the development of thick, yellow crusts over the hair follicles. Also termed tinea favosa.

Febrifuge An agent that reduces fever. Also called an antipyretic.

Febrile Pertaining to or characterized by fever.

Febrile Neutropenia The development of fever, often with other signs of infection, in an individual with neutropenia, an abnormally low number of neutrophil granulocytes in the blood.

Felon A purulent infection in the bulbous distal end of a finger.

Fetotoxic Toxic to the foetus.

Fibrates Hypolipidemic agents primarily used for decreasing serum triglycerides while increasing high-density lipoprotein (HDL).

Fibril A small slender fibre or filament.

Fibrin Insoluble protein that forms the essential portion of the blood clot.

Fibrinolysis A normal ongoing process that dissolves fibrin and results in the removal of small blood clots.

Fibrinolytic Causing the dissolution of fibrin by enzymatic action.

Fibroblast Type of cell that synthesizes the extracellular matrix and collagen, the structural framework (stroma) for animal tissues, and plays a critical role in wound healing.

Fibrogenic Promoting the development of fibres.

Fibromyalgia A common and complex chronic, body-wide pain disorder that affects people physically, mentally and socially. Symptoms include debilitating fatigue, sleep disturbance, and joint stiffness. Also referred to as FM or FMS.

Fibronectin A high molecular weight (~440 kDa) glycoprotein of the extracellular matrix (ECM) that adheres to membrane-spanning receptor proteins called integrins.

Fibrosarcoma A malignant tumour derived from fibrous connective tissue and characterized by immature proliferating fibroblasts or undifferentiated anaplastic spindle cells.

Fibrosis The formation of fibrous tissue as a reparative or reactive process.

Filarial Pertaining to a threadlike nematode worm.

Filariasis A parasitic and infectious tropical disease that is caused by threadlike filarial nematode worms in the superfamily Filarioidea.

Fistula An abnormal connection between two organs inside of the body.

Fistula-in-Ano A track connecting the internal anal canal to the skin surrounding the anal orifice.

5′-Nucleotidase 5′-Ribonucleotide phosphohydrolase. An intrinsic membrane glycoprotein present as an ectoenzyme in a wide variety of mammalian cells, hydrolyzes 5′-nucleotides to their corresponding nucleosides.

Flatulence Is the presence of a mixture of gases known as flatus in the digestive tract of mammals expelled from the rectum. Excessive flatulence can be caused by lactose intolerance, certain foods or a sudden switch to a high fibre.

Flavans A subgroup of flavonoids. See Flavonoids.

Flavanols A subgroup of flavonoids and are a class of flavonoids that use the 2-phenyl-3,4-dihydro-2H-chromen-3-ol skeleton. These compounds include the catechins and the catechin gallates. They are found in chocolate, fruits and vegetables. See Flavonoids.

Flavanones A subgroup of flavonoids and constitutes >90 % of total flavonoids in citrus. The major dietary flavanones are hesperetin, naringenin and eriodictyol.

Flavivirus A family of viruses transmitted by mosquitoes and ticks that cause some important diseases, including dengue, yellow fever, tick-borne encephalitis and West Nile fever.

Flavones A subgroup of flavonoids based on the backbone of 2-phenylchromen-4-one (2-phenyl-1-benzopyran-4-one). Flavones are mainly found in cereals and herbs.

Flavonoids Or bioflavonoids are a group of polyphenolic antioxidant compounds in that occur in plant as secondary metabolites. They are responsible for the colour of fruit and vegetables. Twelve basic classes (chemical types) of flavonoids have been recognized: flavones, isoflavones, flavans, flavanones, flavanols, flavanolols, anthocyanidins, catechins (including proanthocyanidins), leukoanthocyanidins, chalcones, dihydrochalcones and aurones. Apart from their antioxidant activity, flavonoids are known for their ability to strengthen capillary walls, thus assisting circulation and helping to prevent and treat bruising, varicose veins, bleeding gums and nosebleeds and heavy menstrual bleeding and are also antiinflammatory.

Fluorine F is an essential chemical element that is required for maintenance of healthy bones and teeth and to reduce tooth decay. It is found in sea weeds, tea, water, seafood and dairy products.

Fluorosis A dental health condition caused by a child receiving too much fluoride during tooth development.

Flux An excessive discharge of fluid.

FMD (Flow-Mediated Dilation) A measure of endothelial dysfunction which is used to evaluate cardiovascular risk. Also called FMVD (flow-mediated vasodilation).

Focal Adhesion Kinase (FAK) Is a protein tyrosine kinase which is recruited at an early stage to focal adhesions and which mediates many of the downstream regulatory responses.

Follicle-Stimulating Hormone (FSH) A hormone produced by the pituitary gland. In women, it helps control the menstrual cycle and the production of eggs by the ovaries.

Follicular Atresia The breakdown of the ovarian follicles.

Fomentation Treatment by the application of war, moist substance.

Fontanelle Soft spot on an infant's skull.

Forkhead Box-O Transcription Factors (FOXOs) Are a family of transcription factors that play important roles in regulating the expression of genes involved in cell growth, proliferation, differentiation and longevity. It also plays an important role in tumour suppression by regulating the expression of genes involved in stress resistance, DNA damage repair, cell cycle arrest and apoptosis.

Framboesia See Yaws.

FRAP Ferric reducing ability of plasma. An assay used to assess antioxidant property.

Friedreich's Ataxia Is a genetic inherited disorder that causes progressive damage to the nervous system resulting in symptoms ranging from muscle weakness and speech problems to heart disease. *Cf.* ataxia.

Fulminant Hepatitis Acute liver failure.

Functional Dyspepsia A non-ulcer condition that causes an upset stomach or pain or discomfort in the upper belly, near the ribs.

Functional Food Is any fresh or processed food claimed to have a health-promoting or disease-preventing property beyond the basic function of supplying nutrients. Also called medicinal food.

Furuncle Is a skin disease caused by the infection of hair follicles usually caused by *Staphylococcus aureus,* resulting in the localized accumulation of pus and dead tissue.

Furunculosis Skin condition characterized by persistent, recurring boils.

GABA Gamma aminobutyric acid, required as an inhibitory neurotransmitter to block the transmission of an impulse from one cell to another in the central nervous system, which prevents over-firing of the nerve cells. It is used to treat both epilepsy and hypertension.

GADD 152 A pro-apoptotic gene.

Galctifuge Or lactifuge, causing the arrest of milk secretion.

Galactagogue A substance that promotes the flow of milk.

Galactophoritis Inflammation of the milk ducts.

Galactopoietic Increasing the flow of milk; milk producing.

Gall Bladder A small, pear-shaped muscular sac, located under the right lobe of the liver, in which bile secreted by the liver is stored until needed by the body for digestion. Also called cholecyst, cholecystitis.

Gallic Acid Equivalent (GAE) Measures the total phenol content in terms of the standard Gallic acid by the Folin–Ciocalteau assay.

Galphai Proteins or G Alpha I Proteins Are heterotrimeric guanine nucleotide-regulatory (G) proteins associated with a variety of intracellular membranes and specific plasma membrane domains.

Gamma GT (GGT) Gamma-glutamyl transpeptidase, a liver enzyme.

Gastralgia (Heartburn) Pain in the stomach or abdominal region. It is caused by excess of acid, or an accumulation of gas, in the stomach.

Gastric Pertaining to or affecting the stomach.

Gastric Emptying Refers to the speed at which food and drink leave the stomach.

Gastritis Inflammation of the stomach.

Gastrocnemius Muscle The big calf muscle at the rear of the lower leg.

Gastroprokinetic See Prokinetic.

Gastrotonic (Gastroprotective) Substance that strengthens, tones or regulates gastric functions (or protects from injury) without overt stimulation or depression.

Gavage Forced feeding.

Gene Silencing Suppression of the expression of a gene.

Genotoxic Describes a poisonous substance which harms an organism by damaging its DNA, thereby capable of causing mutations or cancer.

Genotoxin A chemical or other agent that damages cellular DNA, resulting in mutations or cancer.

Geriatrics Is a subspecialty of internal medicine that focuses on healthcare of elderly people.

Gestational Hypertension Development of arterial hypertension in a pregnant woman after 20 weeks gestation.

Ghrelin A gastrointestinal peptide hormone secreted by epithelial cells in the stomach lining; it stimulates appetite and gastric emptying and increases cardiac output.

Gingival Index An index describing the clinical severity of gingival inflammation as well as its location.

Gingivitis Refers to gingival inflammation induced by bacterial biofilms (also called plaque) adherent to tooth surfaces.

Gin-nan Sitotoxism Toxicity caused by ingestion of ginkgotoxin and characterized mainly by epileptic convulsions, paralysis of the legs and loss of consciousness.

GIP Gastric inhibitory polypeptide also known as the glucose-dependent insulinotropic peptide, a member of the secretin family of hormones.

Glaucoma A group of eye diseases in which the optic nerve at the back of the eye is slowly destroyed, leading to impaired vision and blindness.

Gleet A chronic inflammation (as gonorrhoea) of a bodily orifice usually accompanied by an abnormal discharge.

Glial Cells Support, non-neuronal cells in the central nervous system that maintain homeostasis, form myelin and provide protection for the brain's neurons.

Glioma Is a type of tumour that starts in the brain or spine. It is called a glioma because it arises from glial cells.

Glioblastoma Common and most lethal form of brain tumour.

Glioblastoma Multiforme Most common and most aggressive type of primary brain tumour in humans, involving glial cells.

Glomerulonephritis (GN) A renal disease characterized by inflammation of the glomeruli or small blood vessels in the kidneys. Also known as glomerular nephritis. *Adj.* glomerulonephritic.

Glomerulosclerosis A hardening (fibrosis) of the glomerulus in the kidney.

Glossal Pertaining to the tongue.

GLP-1 Glucagon-like peptide-1.

Glucagon-Like Peptide-1 (GLP-1) Is derived from the transcription product of the proglucagon gene, reduces insulin requirement in diabetes mellitus and promotes satiety.

Gluconeogenesis A metabolic pathway that results in the generation of glucose from non-carbohydrate carbon substrates such as lactate. *Adj.* gluconeogenic.

Glucose-6-phosphate Dehydrogenase (G6PD or G6PDH) Is a cytosolic enzyme in the pentose phosphate metabolic pathway.

Glucose Transporter Type 4 (GLUT 4) Insulin-regulated glucose transporter found in adipose tissues and striated muscles that modulates insulin-related translocation into the cell.

Glucose Transporters GLUT or SLC2A family, are a family of membrane proteins found in most mammalian cells.

Glucosuria or Glycosuria Is the excretion of glucose into the urine.

Glucosyltransferase An enzyme that enables the transfer of glucose.

Glucuronidation A phase II detoxification pathway occurring in the liver in which glucuronic acid is conjugated with toxins.

Glutamic Oxaloacetate Transaminase (GOT) Catalyzes the transfer of an amino group from an amino acid (Glu) to a 2-keto-acid to generate a new amino acid and the residual 2-keto-acid of the donor amino acid.

Glutamic Pyruvate Transaminase (GPT) See Alanine Aminotransferase.

Glutathione (GSH) A tripeptide produced in the human liver and plays a key role in intermediary metabolism, immune response and health. It plays an important role in scavenging free radicals and protects cells against several toxic oxygen-derived chemical species.

Glutathione Peroxidase (GPX) The general name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage.

Glutathione S-Transferase (GST) A major group of detoxification enzymes that participate in the detoxification of reactive electrophilic compounds by catalyzing their conjugation to glutathione.

Glycaemic Index (GI) Measures carbohydrates according to how quickly they are absorbed and raise the glucose level of the blood.

Glycaemic Load (GL) Is a ranking system for carbohydrate content in food portions based on their glycaemic index and the amount of available carbohydrate, i.e. GI x available carbohydrate divided by 100. Glycaemic load combines both the quality and quantity of carbohydrate in one 'number'. It is the best way to predict blood glucose values of different types and amounts of food.

Glycation or Glycosylation A chemical reaction in which glycosyl groups are added to a protein to produce a glycoprotein.

Glycogenolysis Is the catabolism of glycogen by removal of a glucose monomer through cleavage with inorganic phosphate to produce glucose-1-phosphate.

Glycometabolism Metabolism (oxidation) of glucose to produce energy.

Glycosuria Or glucosuria is an abnormal condition of osmotic diuresis due to excretion of glucose by the kidneys into the urine.

Glycosylases A family of enzymes involved in base excision repair.

Goitre An enlargement of the thyroid gland leading to swelling of the neck or larynx.

Goitrogen Substance that suppresses the function of the thyroid gland by interfering with iodine uptake, causing enlargement of the thyroid, i.e. goitre.

Goitrogenic *Adj.* causing goitre.

Gonadotroph A basophilic cell of the anterior pituitary specialized to secrete follicle-stimulating hormone or luteinizing hormone.

Gonadotropins Protein hormones secreted by gonadotrope cells of the pituitary gland of vertebrates.

Gonorrhoea A common sexually transmitted bacterial infection caused by the bacterium *Neisseria gonorrhoeae*.

Gout A disorder caused by a buildup of a waste product, uric acid, in the bloodstream. Excess uric acid settles in joints causing inflammation, pain and swelling.

G-Protein-Coupled Receptors (GPCRs) Constitute the largest family of cell surface molecules involved in signal transmission. These receptors play key physiological roles and their dysfunction results in several diseases.

Granulation The condition or appearance of being granulated (becoming grain-like).

Gravel Sand-like concretions of uric acid, calcium oxalate and mineral salts formed in the passages of the biliary and urinary tracts.

Gripe Water Is a home remedy for babies with colic, gas, teething pain or other stomach ailments. Its ingredients vary and may include alcohol, bicarbonate, ginger, dill, fennel and chamomile.

Grippe An epidemic catarrh; older term for influenza.

GSH See Glutathione.

GSH-PxGlutathione peroxidase. General name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage.

GSSG Glutathione disulphides are biologically important intracellular thiols, and alterations in the GSH/GSSG ratio are often used to assess exposure of cells to oxidative stress.

GSTM Glutathione S-transferase M1. A major group of detoxification enzymes.

GSTM 2 Glutathione S-transferase M2. A major group of detoxification enzymes.

G2-M Cell Cycle The phase where the cell prepares for mitosis and where chromatids and daughter cells separate.

Guillain–Barre Syndrome Is a serious disorder that occurs when the body's defense (immune) system mistakenly attacks part of the nervous system, leading to nerve inflammation, muscle weakness and other symptoms.

Gynecopathy Any or various diseases specific to women.

Gynoid Adiposity Fat distribution mainly to the hips and thighs, pear shaped.

Haemagogic Promoting a flow of blood.

Haematemesis, Hematemesis Is the vomiting of blood.

Haematinic Improving the quality of the blood, its haemoglobin level and the number of erythrocytes.

Haematochezia Passage of stools containing blood.

Haematochyluria, Hematochyluria The discharge of blood and chyle (emulsified fat) in the urine; see also Chyluria.

Haematoma, Hematoma A localized accumulation of blood in a tissue or space composed of clotted blood.

Haematometra, Hematometra A medical condition involving bleeding of or near the uterus.

Haematopoiesis, Hematopoiesis Formation of blood cellular components from the haematopoietic stem cells.

Haematopoietic *Adj.* relating to the formation and development of blood cells.

Haematuria, Hematuria Is the presence of blood in the urine. Haematuria is a sign that something is causing abnormal bleeding in a person's genitourinary tract.

Haeme Oxygenase HO-1, encoded by Hmox1, is an inducible protein activated in systemic inflammatory conditions by oxidant stress; an enzyme that catalyzes degradation of heme.

Haemochromatosis Iron overload in the body with a hereditary or primary cause.

Haemodialysis, Hemodialysis A method for removing waste products such as potassium and urea, as well as free water from the blood when the kidneys are in renal failure.

Haemolysis Lysis of red blood cells and the release of haemoglobin into the surrounding fluid (plasma). *Adj.* haemolytic.

Haemoptysis, Hemoptysis Is the coughing up of blood from the respiratory tract. The blood can come from the nose, mouth, throat and the airway passages leading to the lungs.

Haemorrhage, Hemorrhage Bleeding, discharge of blood from blood vessels.

Haemorrhoids, Hemorrhoids A painful condition in which the veins around the anus or lower rectum are enlarged, swollen and inflamed. Also called piles.

Haemostasis, Hemostasis A complex process which causes the bleeding process to stop.

Haemostatic, Hemostatic Something that stops bleeding.

Halitosis Bad breath, a common condition caused by sulphur-producing bacteria that live within the surface of the tongue and in the throat.

Hallucinogen Drug that produces hallucinogen.

Hallucinogenic Inducing hallucinations.

Hallux Abducto Valgus Commonly called bunion is an abnormal bending of the big toe towards the other toes of the foot.

Haplotype A set of alleles of closely linked loci on a chromosome that tend to be inherited together.

Hapten A small molecule that can elicit an immune response only when attached to a large carrier such as a protein.

HATs Histone acetyl transferases. Enzymes that regulate the acetylation of histones and transcription factors, playing a major role in the growth and differentiation of cells.

HbA1c Glycosylated haemoglobin.

HBeAg Hepatitis B e antigen.

HBsAg Hepatitis B s antigen.

Heartburn Burning sensation in the stomach and oesophagus caused by excessive acidity of the stomach fluids.

Heat Rash Any condition aggravated by heat or hot weather such as intertrigo.

Heat-Shock Chaperones (HSC) Ubiquitous molecules involved in the modulation of protein conformational and complexation states, associated with heat stress or other cellular stress response.

Heat-Shock Proteins (HSP) A group of functionally related proteins, the expression of which is increased when the cells are exposed to elevated temperatures or other cellular stresses.

Helminthiasis A disease in which a part of the body is infested with worms such as pinworm, roundworm or tapeworm.

Hemagglutination A specific form of agglutination that involves red blood cells.

Haemagglutination–Inhibition Test Measures of the ability of soluble antigen to inhibit the

agglutination of antigen-coated red blood cells by antibodies.

Hemagglutinin Refers to a substance that causes red blood cells to agglutinate.

Haemangioma Blood vessel.

Haematocrit Is a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells.

Haematopoietic Pertaining to the formation of blood or blood cells.

Haematopoietic Stem Cell Is a cell isolated from the blood or bone marrow that can renew itself and can differentiate to a variety of specialized cells.

Heme Oxygenase-1 (HO-1) An enzyme that catalyzes the degradation of heme; an inducible stress protein, confers cytoprotection against oxidative stress in vitro and in vivo.

Haemoglobinopathies Genetic defects that produce abnormal haemoglobins and anaemia.

Haemolytic Anaemia Anaemia due to haemolysis; the breakdown of red blood cells in the blood vessels or elsewhere in the body.

Haemorheology Study of blood flow and its elements in the circulatory system. *Adj.* haemorheological.

Haemorrhagic Colitis An acute gastroenteritis characterized by overtly bloody diarrhoea that is caused by *Escherichia coli* infection.

Haemolytic-Uremic Syndrome Is a disease characterized by haemolytic anaemia, acute renal failure (uraemia) and a low platelet count.

Hepa-1c1c7 A type of hepatoma cells.

Hepatalgia Pain or discomfort in the liver area.

Hepatomegaly Condition of enlarged liver.

Hepatectomy The surgical removal of part or all of the liver.

Hepatic Relating to the liver.

Hepatic Cirrhosis Affecting the liver and characterized by hepatic fibrosis and regenerative nodules.

Hepatic Fibrosis Is overly profuse wound healing in which excessive connective tissue builds up in the liver.

Hepatitis Inflammation of the liver.

Hepatitis A Formerly known as infectious hepatitis, is an acute infectious disease of the liver caused by the hepatovirus hepatitis A virus.

Hepatocarcinogenesis Represents a linear and progressive cancerous process in the liver in which successively more aberrant monoclonal populations of hepatocytes evolve.

Hepatocellular Carcinoma (HCC) Also called malignant hepatoma, is a primary malignancy (cancer) of the liver.

Hepatocytolysis Cytotoxicity (dissolution) of liver cells.

Hepatoma Cancer of the liver.

Hepatopathy A disease or disorder of the liver.

Hepatoprotective Liver protector, a substance that helps protect the liver from damage by toxins, chemicals or other disease processes.

Hepatoregenerative A compound that promotes hepatocellular regeneration and repairs and restores liver function to optimum performance.

Hepatotonic Liver tonic, a substance that is tonic to the liver—usually employed to normalize liver enzymes and function.

Hernia Occurs when part of an internal organ bulges through a weak area of muscle.

HER-2 Human epidermal growth factor receptor 2. A protein giving higher aggressiveness in breast cancer, also known as ErbB-2, ERBB2.

Herpes A chronic inflammation of the skin or mucous membrane characterized by the development of vesicles on an inflammatory base.

Herpes Circinatus Dermatitis herpetiformis (resembling herpes).

Herpes Simplex Virus 1 and 2 (HSV-1 and HSV-2) Are two species of the herpes virus family which cause a variety of illnesses/infections in humans such cold sores, chickenpox or varicella, shingles or herpes zoster (VZV), cytomegalovirus (CMV) and various cancers and can cause brain inflammation (encephalitis). HSV-1 is commonly associated with herpes outbreaks of the face known as cold sores or fever blisters, whereas HSV-2 is more often associated with genital herpes. They are also called human herpes virus 1 and 2 (HHV-1 and HHV-2) and are neurotropic and neuroinvasive viruses; they enter and hide in the human nervous system, accounting for their durability in the human body.

Herpes Zoster Or simply zoster, commonly known as shingles and also known as zona, is

a viral disease characterized by a painful skin rash with blisters.

Herpes Zoster Ophthalmicus (HZO) Is a viral ocular disease characterized by a painful skin rash in one or more dermatome distributions of the fifth cranial nerve, shared by the eye and orbit.

Heterophobia Term used to describe irrational fear of, aversion to or discrimination against heterosexuals.

HDL-C (HDL Cholesterol) High-density lipoprotein-cholesterol, also called 'good cholesterol'. See also High-Density Lipoprotein.

Hiatus Hernia Occurs when the upper part of the stomach pushes its way through a tear in the diaphragm.

High-Density Lipoprotein (HDL) Is one of the five major groups of lipoproteins which enable cholesterol and triglycerides to be transported within the water-based blood stream. HDL can remove cholesterol from atheroma within arteries and transport it back to the liver for excretion or reutilization—which is the main reason why HDL-bound cholesterol is sometimes called 'good cholesterol', or HDL-C. A high level of HDL-C seems to protect against cardiovascular diseases. Cf. LDL.

HGPRT, HPRT (Hypoxanthine-Guanine Phosphoribosyl Transferase) An enzyme that catalyzes the conversion of 5-phosphoribosyl-1-pyrophosphate and hypoxanthine, guanine or 6-mercaptopurine to the corresponding 5′ mononucleotides and pyrophosphate. The enzyme is important in purine biosynthesis as well as central nervous system functions.

Hippocampus A ridge in the floor of each lateral ventricle of the brain that consists mainly of grey matter.

Hippocampal Pertaining to the hippocampus.

Hirsutism A condition where women have excess facial and body hair that is dark and coarse.

Histaminergic Liberated or activated by histamine, relating to the effects of histamine at histamine receptors of target tissues.

Histaminergic Receptors Are types of G-protein-coupled receptors with histamine as their endogenous ligand.

Histone Acetyltransferases (HAT) Are enzymes that acetylate conserved lysine amino acids on histone proteins by transferring an acetyl group from acetyl-CoA to form e-N-acetyl lysine. HATs act as transcriptional coactivators.

Histone Lysine Demethylases (KDMs) Enzymes that play a key role in the amplification of hypoxia-inducible-factor signalling and expression of pro-angiogenic genes in cancer and neurological disorders.

HIV See Human Immunodeficiency Virus.

Hives Urticaria, is a skin rash characterized by circular wheals of reddened and itching skin.

HLA Human leukocyte antigen system. Name of the major histocompatibility complex (MHC) in humans.

HLA-DQB1 Human leukocyte antigen beta chain.

HLA-DR A major histocompatibility complex (MHC) class II cell surface receptor encoded by the human leukocyte antigen complex on chromosome 6 region 6p21.31.

HMG-CoAr 3-Hydroxy-3-methyl-glutaryl-CoA reductase or (HMGCR) is the rate-controlling enzyme (EC 1.1.1.88) of the mevalonate pathway.

HMG-CoA 3-Hydroxy-3-methylglutaryl-coenzyme A. An intermediate in the mevalonate pathway.

Hodgkin's Disease Disease characterized by enlargement of the lymph glands, spleen and anaemia.

Homeodomain Transcription Factor A protein domain encoded by a homeobox. Homeobox genes encode transcription factors which typically switch on cascades of other genes.

Homeostasis The maintenance of a constant internal environment of a cell or an organism, despite fluctuations in the external.

Homeotherapy Treatment or prevention of disease with a substance similar but not identical to the causative agent of the disease.

Homocysteine An amino acid in the blood.

Homograft See Allograft.

Hormesis A term used by toxicologists to refer to a biphasic dose–response to an environmental agent characterized by a low-dose stimulation or beneficial effect and a high-dose inhibitory or toxic effect.

Hormonal (Female) Substance that has a hormonelike effect similar to that of oestrogen and/or a substance used to normalize female hormone levels.

Hormonal (Male) Substance that has a hormonelike effect similar to that of testosterone and/or a substance used to normalize male hormone levels.

HRT Hormone replacement therapy. The administration of the female hormones, oestrogen and progesterone and sometimes testosterone.

HSP27 Is an ATP-independent, 27 kDa heat-shock protein chaperone that confers protection against apoptosis.

HSP90 A 90 kDa heat-shock protein chaperone that has the ability to regulate a specific subset of cellular signalling proteins that have been implicated in disease processes.

hTERT–(TERT) Telomerase reverse transcriptase is a catalytic subunit of the enzyme telomerase in humans. It exerts a novel protective function by binding to mitochondrial DNA, increasing respiratory chain activity and protecting against oxidative stress-induced damage.

HT29 Cells Are human intestinal epithelial cells which produce the secretory component of immunoglobulin A (IgA) and carcinoembryonic antigen (CEA).

Human Cytomegalovirus (HCMV) A DNA herpes virus which is the leading cause of congenital viral infection and mental retardation.

Human Factor X A coagulation factor also known by the eponym Stuart-Prower factor or as thrombokinase; it is an enzyme involved in blood coagulation. It synthesized in the liver and requires vitamin K for its synthesis.

Human Immunodeficiency Virus (HIV) A retrovirus that can lead to acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.

Humoral Immune Response (HIR) Is the aspect of immunity that is mediated by secreted antibodies (as opposed to cell-mediated immunity, which involves T lymphocytes) produced in the cells of the B lymphocyte lineage (B cell).

HUVEC Human umbilical vein endothelial cells.

Hyaluronidase Enzymes that catalyze the hydrolysis of certain complex carbohydrates like hyaluronic acid and chondroitin sulphates.

Hydatidiform A rare mass or growth that forms inside the uterus at the beginning of a pregnancy.

Hydrocele Abnormal accumulation of fluid inside the scrotum.

Hydrocholeretic An agent that stimulates an increased output of bile of low specific gravity.

Hydrogogue A purgative that causes an abundant watery discharge from the bowel.

Hydronephrosis Is distension and dilation of the renal pelvis and calyces, usually caused by obstruction of the free flow of urine from the kidney.

Hydrophobia A viral neuroinvasive disease that causes acute encephalitis (inflammation of the brain) in warm-blooded animals. Also called rabies.

Hydropsy See Dropsy.

Hydrothorax Accumulation of serous fluid in the pleural cavity.

Hyperaemia The increase of blood flow to different tissues in the body.

Hyperalgesia An increased sensitivity to pain (enhanced pricking pain), which may be caused by damage to nociceptors or peripheral nerves.

Hyperammonemia, Hyperammonaemia A metabolic disturbance characterized by an excess of ammonia in the blood.

Hypercalciuria *Idiopathic*, presence of excess calcium in the urine without obvious cause.

Hypercholesterolaemia High levels of cholesterol in the blood that increase a person's risk for cardiovascular disease leading to stroke or heart attack.

Hyperaemia Is the increased blood flow that occurs when tissue is active.

Hyperemesis Severe and persistent nausea and vomiting (morning sickness) during pregnancy.

Hyperfibrinogenaemia Excessive fibrinogen in the blood.

Hyperglycaemia hyperglycaemic High blood sugar; is a condition in which an excessive amount of glucose circulates in the blood plasma.

Hyperglycaemic A substance that raises blood sugar levels.

Hyperhomocysteinaemia Is a medical condition characterized by an abnormally large level of homocysteine in the blood.

Hyperinsulinaemia A condition in which there are excess levels of circulating insulin in the blood, also known as prediabetes.

Hyperkalaemia Is an elevated blood level of the electrolyte potassium.

Hyperkeratosis Abnormal thickening of the outer layer of the skin. *Adj.* hyperkeratotic.

Hyperkinesis Enhanced itch to pricking.

Hyperleptinaemia Increased serum leptin level.

Hyperlipoproteinaemia A metabolic disorder characterized by abnormally elevated concentrations of lipid/lipoprotein in the plasma, also known as hyperlipidaemia and hyperlipaemia.

Hypermenorrhoea Abnormally heavy or prolonged menstruation.

Hypermethylation An increase in the inherited methylation of cytosine and adenosine residues in DNA.

Hyperphagia Or polyphagia. Abnormally large ingestion of food beyond that needed for basic energy requirements.

Hyperpiesia Persistent and pathological high blood pressure for which no specific cause can be found.

Hyperplasia Increased cell production in a normal tissue or organ.

Hyperprebeta-LipoproteinaemiaIncreased concentrations of pre-beta-lipoproteins in the blood.

Hyperpropulsion Using water pressure as a force to move objects; used to dislodge calculi in the urethra.

Hyperpyrexia Is an abnormally high fever.

Hypertension Commonly referred to as 'high blood pressure' or HTN, is a medical condition in which the arterial blood pressure is chronically elevated.

Hypertensive Characterized or caused by increased tension or pressure as abnormally high blood pressure.

Hypertonia Abnormal increase in muscle tension and a reduced ability of the muscle to stretch.

Hypertriglyceridaemia or Hypertriglycemia A disorder that causes high triglycerides in the blood.

Hypertrophy Enlargement or overgrowth of an organ.

Hyperuricemia Is a condition characterized by abnormally high level of uric acid in the blood.

Hypoadiponectinaemia The state of having too low level of adiponectin, a major metabolic endocrine, responsible for regulating things like glucose uptake and lipolysis (the breakdown of fat deposits); low adiponectin is a risk factor for both type II diabetes and metabolic syndrome.

Hypoalbuminaemia A medical condition where levels of albumin in blood serum are abnormally low.

Hypocalcemic Tetany A disease caused by an abnormally low level of calcium in the blood and characterized by hyperexcitability of the neuromuscular system and results in carpopedal spasms.

Hypochlorhydria Refer to states where the production of gastric acid in the stomach is absent or low.

Hypocholesterolemic Cholesterol reducer, a substance that lowers blood cholesterol levels.

Hypocitraturia Low amount of citrate in the urine, an important risk factor for kidney stone formation.

Hypocorticism See Addison's Disease.

Hypocortisolism See Addison's Disease.

Hypoesthesia (or Hypaesthesia) Refers to a reduced sense of touch or sensation or a partial loss of sensitivity to sensory stimuli.

Hypoglycemic An agent that lowers the concentration of glucose (sugar) in the blood.

Hypoperfusion Decreased blood flow through an organ, characterized by an imbalance of oxygen demand and oxygen delivery to tissues.

Hypophagic Under-eating.

Hypospadias An abnormal birth defect in males in which the urethra opens on the under surface of the penis.

Hypotensive Characterized by or causing diminished tension or pressure, as abnormally low blood pressure.

Hypothermia A condition in which an organism's temperature drops below that required for normal metabolism and body functions.

Hypothermic Relating to hypothermia, with subnormal body temperature.

Hypoxaemia Is the reduction of oxygen specifically in the blood.

Hypoxia A shortage of oxygen in the body. *Adj.* hypoxic.

Hypoxia-Inducible Factors (HIFs) Transcription factors that respond to changes in available oxygen in the cellular environment, specifically to deficiency in oxygen.

ICAM-1 (Intercellular Adhesion Molecule 1) Also known as CD54 (cluster of differentiation 54), is a protein that in humans is encoded by the ICAM1 gene.

IC_{50} The median maximal inhibitory concentration; a measure of the effectiveness of a compound in inhibiting biological or biochemical function.

I.C.V. (Intra-cerebroventricular) Injection of chemical into the right lateral ventricle of the brain.

Ichthyotoxic A substance which is poisonous to fish.

Icterus Jaundice, yellowish pigmentation of the skin.

Icteric Hepatitis An infectious syndrome of hepatitis characterized by jaundice, nausea, fever, right-upper quadrant pain, enlarged liver and transaminitis (increase in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)).

Icterus Neonatorum Jaundice in newborn infants.

Idiopathic Of no apparent physical cause.

Idiopathic Sudden Sensorineural Hearing Loss (ISSHL) Is sudden hearing loss where clinical assessment fails to reveal a cause.

Ig Gastric intubation, insertion of Levin tube through the nasal passage to the stomach.

IgE Immunoglobulin E. A class of antibody that plays a role in allergy.

IGFsInsulin-like growth factors, polypeptides with high sequence similarity to insulin.

IgG Immunoglobulin G. The most abundant immunoglobulin (antibody) and is one of the major activators of the complement pathway.

IgM Immunoglobulin M. Primary antibody against A and B antigens on red blood cells.

IKAP Is a scaffold protein of the IvarKappa Beta kinase complex and a regulator for kinases involved in pro-inflammatory cytokine signalling.

IKappa B Or IkB-beta, a protein of the NF-Kappa-B inhibitor family.

Ileus A temporary disruption of intestinal peristalsis due to nonmechanical causes.

Immune Modulator A substance that affects or modulates the functioning of the immune system.

Immunodeficiency A state in which the immune system's ability to fight infectious disease is compromised or entirely absent.

Immunogenicity The property enabling a substance to provoke an immune response. *Adj.* immunogenic.

Immunoglobulin Class Switching Ig Class Switching A biological mechanism that changes a B cell's production of antibody from one class to another.

Immunomodulatory Capable of modifying or regulating one or more immune functions.

Immunoreactive Reacting to particular antigens or haptens.

Immunostimulant Agent that stimulates an immune response.

Immunosuppression Involves a process that reduces the activation or efficacy of the immune system.

Immunotoxin A man-made protein that consists of a targeting portion linked to a toxin.

Impaired Glucose Tolerance (IGT) A prediabetic state of dysglycemia associated with insulin resistance and increased risk of cardiovascular pathology and also a risk factor for mortality.

Impetigo A contagious, bacterial skin infection characterized by blisters that may itch, caused by a *Streptococcus* bacterium or *Staphylococcus aureus* and mostly seen in children.

Impotence A sexual dysfunction characterized by the inability to develop or maintain an erection of the penis.

Incontinence (Faecal) The inability to control bowel's movement.

Incontinence (Urine) The inability to control urine excretion.

Incretin A group of gastrointestinal hormones that cause an increase in the amount of insulin released from the beta cells of the islets of Langerhans after a meal; members include GIP and GLP-1.

Index of Structural Atypia (ISA) Index of structural abnormality.

Induration Hardened, as a soft tissue that becomes extremely firm, sclerosis.

Infarct An area of living tissue that undergoes necrosis as a result of obstruction of local blood supply.

Infarction Is the process of tissue death (necrosis) caused by blockage of the tissue's blood supply.

Inflammation A protective response of the body to infection, irritation or other injury, aimed at destroying or isolating the injuries and characterized by redness, pain, warmth and swelling.

Influenza A viral infection that affects mainly the nose, throat, bronchi and, occasionally, lungs.

Infusion A liquid extract obtained by steeping something (e.g. herbs) that are more volatile or dissolve readily in water, to release their active ingredients without boiling.

Inguinal Hernia An hernia into the inguinal canal of the groin.

Inhalant A medicinal substance that is administered as a vapour into the upper respiratory passages.

iNOS, Inducible Nitric Oxide Synthases Through its product, nitric oxide (NO), may contribute to the induction of germ cell apoptosis. It plays a crucial role in early sepsis-related microcirculatory dysfunction.

Inotropic Affecting the force of muscle contraction.

Insecticide An agent that destroys insects. *Adj.* insecticidal.

Insomnia A sleeping disorder characterized by the inability to fall asleep and/or the inability to remain asleep for a reasonable amount of time.

Insulin A peptide hormone composed of 51 amino acids produced in the islets of Langerhans in the pancreas causes cells in the liver, muscle and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle. Insulin deficiency is often the cause of diabetes, and exogenous insulin is used to control diabetes.

Insulin Homeostasis Blood sugar regulation.

Insulin-like Growth Factors (IGFs) Polypeptides with high sequence similarity to insulin. They are part of a complex system that cells employ to communicate with their physiologic environment.

Insulin-Mimetic To act like insulin.

Insulin Resistance A condition where the natural hormone insulin becomes less effective at reducing blood sugars.

Insulinogenic Associated with or stimulating the production of insulin.

Insulinotropic Stimulating or affecting the production and activity of insulin.

Integrase An enzyme produced by a retrovirus (such as HIV) that enables its genetic material to be integrated into the DNA of the infected cell.

Interferons (IFNs) Are natural cell-signalling glycoproteins known as cytokines produced by the cells of the immune system of most vertebrates in response to challenges such as viruses, parasites and tumour cells.

Interleukins A group of naturally occurring proteins and is a subset of a larger group of cellular messenger molecules called cytokines, which are modulators of cellular behaviour.

Interleukin-1 (IL-1) A cytokine that could induce fever, control lymphocytes, increase the number of bone marrow cells and cause degeneration of bone joints. Also called endogenous pyrogen, lymphocyte-activating factor, haemopoetin-1 and mononuclear cell factor, amongst others, that IL-1 is composed of two distinct proteins, now called IL-1α and IL-1β.

Interleukin 1 Beta (IL-1β) A cytokine protein produced by activated macrophages. Cytokine is an important mediator of the inflammatory response and is involved in a variety of cellular activities, including cell proliferation, differentiation and apoptosis.

Interleukin 2 (IL-2) A type of cytokine immune system signalling molecule that is instrumental in the body's natural response to microbial infection.

Interleukin-2 Receptor (IL-2R) A heterotrimeric protein expressed on the surface of certain immune cells, such as lymphocytes, that binds and responds to a cytokine called IL-2.

Interleukin-6 (IL-6) An interleukin that acts as both a pro-inflammatory and antiinflammatory cytokine.

Interleukin 8 (I-8) A cytokine produced by macrophages and other cell types such as epithelial cells and is one of the major mediators of the inflammatory response.

Intermediate-Density Lipoproteins (IDL) Is one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL and HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream. IDL is further degraded to form LDL particles and, like LDL, can also promote the growth of atheroma and increase cardiovascular diseases.

Intermittent Claudication An aching, crampy, tired and sometimes burning pain in the legs that comes and goes, caused by peripheral vascular disease. It usually occurs when walking and disappears after rest.

Interoceptive Relating to stimuli arising from within the body.

Interstitium The space between cells in a tissue.

Interstitial Pertaining to the interstitium.

Intertrigo An inflammation (rash) caused by microbial infection in skin folds.

Intima Innermost layer of an artery or vein.

Intoxicant Substance that produce drunkenness or intoxication.

Intracavernosal Within the corpus cavernosum, columns of erectile tissues forming the body of the penis.

Intraperitoneal (i.p.) The term used when a chemical is contained within or administered through the peritoneum (the thin, transparent membrane that lines the walls of the abdomen).

Intrathecal (i.t.) Through the theca of the spinal cord into the subarachnoid space.

Intromission The act of putting one thing into another.

Intubation Refers to the placement of a tube into an external or internal orifice of the body.

Iodine (I) Is an essential chemical element that is important for hormone development in the human body. Lack of iodine can lead to an enlarged thyroid gland (goitre) or other iodine deficiency disorders including mental retardation and stunted growth in babies and children. Iodine is found in dairy products, seafood, kelp, seaweeds, eggs, some vegetables and iodized salt.

IP See Intraperitoneal.

IP3R3 Inositol 1,4,5-triphosphate receptor type 3, is an intracellular calcium release channel that mediates calcium release from the endoplasmic reticulum.

Iron (Fe) Is essential to most life forms and to normal human physiology. In humans, iron is an essential component of proteins involved in oxygen transport and for haemoglobin. It is also essential for the regulation of cell growth and differentiation. A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance and decreased immunity. Conversely, excess amounts of iron can result in toxicity and even death. Dietary sources include certain cereals, dark green leafy vegetables, dried fruit, legumes, seafood, poultry, and meat.

Ischemia An insufficient supply of blood to an organ, usually due to a blocked artery.

Ischuria Retention or suppression of urine.

Isoflavones A subgroup of flavonoids in which the basic structure is a 3-phenyl chromane skeleton. They act as phytoestrogens in mammals. See Flavonoids.

Isomers Substances that are composed of the same elements in the same proportions and hence have the same molecular formula but differ in properties because of differences in the arrangement of atoms.

Isoprostanes Unique prostaglandin-like compounds generated in vivo from the free radical-catalyzed peroxidation of essential fatty acids.

Jamu Traditional Indonesian herbal medicine.

Janus Kinase (JAK)–Signal Transducer and Activator of Transcription (STAT) Signalling Are essential molecules in cytokine signal transduction pathways involved in cancer development and progression.

Jaundice Refers to the yellow colour of the skin and whites of the eyes caused by excess bilirubin in the blood.

JNK Jun N-terminal kinase, also known as stress-activated protein kinase (SAPK), belongs to the family of MAP kinases.

Jurkat Cells A line of T lymphocyte cells that are used to study acute T cell leukaemia.

KB Cell A cell line derived from a human carcinoma of the nasopharynx, used as an assay for antineoplastic (antitumour) agents.

Kaliuresis The presence of excess potassium in the urine.

Kallikreins Peptidases (enzymes that cleave peptide bonds in proteins), a subgroup of the serine protease family; they liberate kinins from kininogens. Kallikreins are targets of active investigation by drug researchers as possible biomarkers for cancer.

Kaposi Sarcoma A cancerous tumour of the connective tissues caused by the human herpes virus-8 and is often associated with AIDS.

Kaposi Sarcoma Herpes Virus (KSHV) Also known as human herpes virus-8, is a gamma 2 herpes virus or rhadinovirus. It plays an important role in the pathogenesis of Kaposi sarcoma (KS), multicentric Castleman's disease (MCD) of the plasma cell type and primary effusion lymphoma and occurs in HIV patients.

Karyolysis Dissolution and disintegration of the nucleus when a cell dies.

Karyorrhexis Destructive fragmentation of the nucleus of a dying cell whereby its chromatin disintegrates into formless granules.

Keloids Benign dermal tumours characterized by fibroblastic proliferation and excessive accumulation of collagen.

Keratin A sulphur-containing protein which is a major component in skin, hair, nails, hooves, horns and teeth.

Keratinocyte Is the major constituent of the epidermis, constituting 95 % of the cells found there.

Keratinophilic Having an affinity for keratin.

Keratitis Inflammation of the cornea.

Keratolysis Softening and separation of the horny layer of the epidermis.

Keratolytic Pertaining to keratolysis.

Keratomalacia An eye disorder that leads to a dry cornea.

Kidney Stones Calculi are hardened mineral deposits that form in the kidney.

Kinin Is any of various structurally related polypeptides, such as bradykinin, that act locally to induce vasodilation and contraction of smooth muscle.

Kininogen Either of two plasma α2-globulins that are kinin precursors.

Ki-67 Human protein associated with cell proliferation.

Knockout Gene knockout is a genetic technique in which an organism is engineered to carry genes that have been made inoperative.

Kunitz Protease Inhibitors A type of protein contained in legume seeds which functions as a protease inhibitor.

Kupffer Cells Are resident macrophages of the liver and play an important role in its normal physiology and homeostasis as well as participating in the acute and chronic responses of the liver to toxic compounds.

L-DOPA L-3,4-dihydroxyphenylalanine, is an amino acid that is formed in the liver and converted into dopamine in the brain.

Labour Process of childbirth involving muscular contractions.

Lacrimation Secretion and discharge of tears.

Lactagogue An agent that increases or stimulates milk flow or production. Also called a galactagogue.

Lactate Dehydrogenase (LDH) Enzyme that catalyzes the conversion of lactate to pyruvate.

Lactation Secretion and production of milk.

Lactic Acidosis Is a condition caused by the buildup of lactic acid in the body. It leads to acidification of the blood (acidosis) and is considered a distinct form of metabolic acidosis.

LAK Cell A lymphokine-activated killer cell, i.e. a white blood cell that has been stimulated to kill tumour cells.

Laminin A glycoprotein component of connective tissue basement membrane that promotes cell adhesion.

Laparotomy A surgical procedure involving an incision through the abdominal wall to gain

access into the abdominal cavity. *Adj.* laparotomized.

Larvacidal An agent which kills insect or parasite larva.

Laryngitis Is an inflammation of the larynx.

Laxation Bowel movement.

Laxatives Substances that are used to promote bowel movement.

LC 50 Median lethal concentration; see LD 50.

LD 50 Median lethal dose. The dose required to kill half the members of a tested population. Also called LC 50 (median lethal concentration).

LDL See Low-Density Lipoprotein.

LDL Cholesterol See Low-Density Lipoprotein.

LDL Receptor (LDLr) A low-density lipoprotein receptor gene.

Lectins Are sugar-binding proteins that are highly specific for their sugar moieties that agglutinate cells and/or precipitate glycoconjugates. They play a role in biological recognition phenomena involving cells and proteins.

Leishmaniasis A disease caused by protozoan parasites that belong to the genus *Leishmania* and is transmitted by the bite of certain species of sand fly.

Lenitive Palliative; easing pain or discomfort.

Lenticular Opacity Also known as or related to cataract.

Leprosy A chronic bacterial disease of the skin and nerves in the hands and feet and, in some cases, the lining of the nose. It is caused by the *Mycobacterium leprae.* Also called Hansen's disease.

Leptin Is a 16 kDa protein hormone with important effects in regulating body weight, metabolism and reproductive function.

Lequesne Algofunctional Index Is a widespread international instrument (ten questions survey) and recommended by the World Health Organization (WHO) for outcome measurement in hip and knee diseases such as osteoarthritis.

Leukocyte White blood corpuscles, colourless, without haemoglobin that help to combat infection.

Leucoderma A skin abnormality characterized by white spots, bands and patches on the skin; they can also be caused by fungus and tinea. Also see Vitiligo.

Leucorrhoea Commonly known as whites, refers to a whitish discharge from the female genitals

Leukemia, Leukaemia A cancer of the blood or bone marrow and is characterized by an abnormal proliferation (production by multiplication) of blood cells, usually white blood cells (leukocytes).

Leukemogenic Relating to leukaemia, causing leukaemia.

Leukocytopenia Abnormal decrease in the number of leukocytes (white blood cells) in the blood.

Leukomyelopathy Any diseases involving the white matter of the spinal cord.

Leukopenia A decrease in the number of circulating white blood cells.

Leukoplakia Condition characterized by white spots or patches on mucous membranes, especially of the mouth and vulva.

Leukotriene A group of hormones that cause the inflammatory symptoms of hay fever and asthma.

Levarterenol See Norepinephrine.

LexA Repressor Or repressor LexA is repressor enzyme that represses SOS response genes coding for DNA polymerases required for repairing DNA damage.

Leydig Cells Also called interstitial cells of Leydig, are found adjacent to the seminiferous tubules in the testicle. They produce testosterone in response to luteinizing hormone.

Libido Sexual urge.

Lichen Planus a chronic mucocutaneous disease that affects the skin, tongue and oral mucosa.

Ligroin A volatile, inflammable fraction of petroleum, obtained by distillation and used as a solvent.

Limbic System Complex set of brain structures, including the hypothalamus, amygdala, hippocampus, anterior thalamic nuclei, septum, limbic cortex and fornix that control various functions such as emotion, behaviour, motivation, memory and olfaction.

Liniment Liquid preparation rubbed on skin used to relieve muscular aches and pains.

Linterized Starch Starch that has undergone prolonged acid treatment.

Lipodiatic Having lipid and lipoprotein lowering property.

Lipodystrophy A medical condition characterized by abnormal or degenerative conditions of the body's adipose tissue.

Lipogenesis Is the process by which acetyl-CoA is converted to fats.

Lipolysis Is the breakdown of fat stored in fat cells in the body.

Liposomes Artificially prepared vesicles made of lipid bilayer.

Lipotoxicity Refers to tissues diseases that may occur when fatty acids spill over in excess of the oxidative needs of those tissues and enhances metabolic flux into harmful pathways of nonoxidative metabolism.

Lipotropic Refers to compounds that help catalyze the breakdown of fat during metabolism in the body, e.g. chlorine and lecithin.

Lipoxygenase A family of iron-containing enzymes that catalyze the dioxygenation of polyunsaturated fatty acids in lipids containing a cis,cis-1,4-pentadiene structure.

Lithiasis Formation of urinary calculi (stones) in the renal system (kidneys, ureters, urinary bladder, urethra) and can be of any one of several compositions.

Lithogenic Promoting the formation of calculi (stones).

Lithontripic Removes stones from kidney and gall bladder.

Liver X Receptors Nuclear hormones that function as central transcriptional regulators for lipid homeostasis.

Lotion A liquid suspension or dispersion of chemicals for external application to the body.

LoVo Cells Colon cancer cells.

Low-Density Lipoprotein (LDL) Is a type of lipoprotein that transports cholesterol and triglycerides from the liver to peripheral tissues. High levels of LDL cholesterol can signal medical problems like cardiovascular disease, and it is sometimes called 'bad cholesterol'.

LRP1 Low-density lipoprotein receptor-related protein-1, plays a role in intracellular signalling functions as well as in lipid metabolism.

LTB4 A type of leukotriene, is a major metabolite in neutrophil polymorphonuclear leukocytes. It stimulates polymorphonuclear cell function (degranulation, formation of oxygen-centred free radicals, arachidonic acid release and metabolism). It induces skin inflammation.

Luciferase Is a generic name for enzymes commonly used in nature for bioluminescence.

Lumbago Is the term used to describe general lower back pain.

Lung Abscess Necrosis of the pulmonary tissue and formation of cavities containing necrotic debris or fluid caused by microbial infections.

Lusitropic An agent that affects diastolic relaxation.

Lutein A carotenoid, occurs naturally as yellow or orange pigment in some fruits and leafy vegetables. It is one of the two carotenoids contained within the retina of the eye. Within the central macula, zeaxanthin predominates, whereas in the peripheral retina, lutein predominates. Lutein is necessary for good vision and may also help prevent or slow down atherosclerosis, the thickening of arteries, which is a major risk for cardiovascular disease.

Luteinising Hormone (LH) A hormone produced by the anterior pituitary gland. In females, it triggers ovulation. In males, it stimulates the production of testosterone to aid sperm maturation.

Luteolysis Is the structural and functional degradation of the corpus luteum (CL) that occurs at the end of the luteal phase of both the oestrous and menstrual cycles in the absence of pregnancy. *Adj*. luteolytic

Luteotropic Stimulating the formation of the corpus luteum.

Lymphadenitis The inflammation or enlargement of a lymph node caused by microbial infection.

Cervical Lymphadenitis Inflammation of the lymph nodes in the neck, usually caused by an infection.

Lymphatitis Inflammation of lymph vessels and nodes.

Lymphadenopathy A term meaning 'disease of the lymph nodes'—lymph node enlargement.

Lymphadenomegaly Is the enlargement of the lymph node/nodes.

Lymphoblastic Pertaining to the production of lymphocytes.

Lymphocyte A small white blood cell (leukocyte) that plays a large role in defending the body against disease. Lymphocytes are responsible for immune responses. There are two main types of lymphocytes: B cells and T cells. Lymphocytes secrete products (lymphokines) that modulate the functional activities of many other types of cells and are often present at sites of chronic inflammation.

Lymphocyte B Cells The B cells make antibodies that attack bacteria and toxins.

Lymphocyte T Cells T cells attack body cells themselves when they have been taken over by viruses or have become cancerous.

Lymphoma A type of cancer involving cells of the immune system called lymphocytes.

Lymphopenia Abnormally low number of lymphocytes in the blood.

Lysosomes Are small, spherical organelles containing digestive enzymes (acid hydrolases) and other proteases (cathepsins).

Maceration Softening or separating of parts by soaking in a liquid.

Macrophage A type of large leukocyte that travels in the blood but can leave the bloodstream and enter tissue; like other leukocytes it protects the body by digesting debris and foreign cells.

Macular Degeneration A disease that gradually destroys the macula, the central portion of the retina, reducing central vision.

Macules Small circumscribed changes in the colour of skin that are neither raised (elevated) nor depressed.

Maculopapular Describes a rash characterized by raised, spotted lesions.

Magnesium (Mg) Is the fourth most abundant mineral in the body and is essential to good health. It is important for normal muscle and nerve function, steady heart rhythm, immune system and strong bones. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure and is known to be involved in energy metabolism and protein synthesis and plays a role in preventing and managing disorders such as hypertension, cardiovascular disease and diabetes. Dietary sources include legumes (e.g. soya bean and by-products), nuts, whole unrefined grains, fruit (e.g. banana, apricots), okra and green leafy vegetables.

MAK Cell Macrophage-activated killer cell. Activated macrophage that is much more phagocytic than monocytes.

Malaise A feeling of weakness, lethargy or discomfort as of impending illness.

Malaria Is an infection of the blood by *Plasmodium* parasite that is carried from person to person by mosquitoes. There are four species of malaria parasites that infect man: *Plasmodium falciparum*, so-called malignant tertian fever, is the most serious disease; *Plasmodium vivax*, causing a relapsing form of the disease; *Plasmodium malariae*; and *Plasmodium ovale*.

Malassezia A fungal genus (previously known as *Pityrosporum*) classified as yeasts, naturally found on the skin surfaces of many animals including humans. It can cause hypopigmentation on the chest or back if it becomes an opportunistic infection.

Mammalian Target of Rapamycin (mTOR) Pathway that regulates mitochondrial oxygen consumption and oxidative capacity.

Mammogram An X-ray of the breast to detect tumours.

Mandibular Relating to the mandible, the human jaw bone.

Manganese Is an essential element for heath. It is an important constituent of some enzymes and an activator of other enzymes in physiologic processes. Manganese superoxide dismutase (MnSOD) is the principal antioxidant enzyme in the mitochondria. Manganese-activated enzymes play important roles in the metabolism of carbohydrates, amino acids and cholesterol. Manganese is the preferred cofactor of enzymes called glycosyltransferases which are required for the synthesis of proteoglycans that

are needed for the formation of healthy cartilage and bone. Dietary source include whole grains, fruit, legumes (soybean and by-products), green leafy vegetables, beetroot and tea.

MAO Activity Monoamine oxidase activity.

MAPK (Mitogen-Activated Protein Kinase) These kinases are strongly activated in cells subjected to osmotic stress, UV radiation, dysregulated K^+ currents, RNA-damaging agents and a multitude of other stresses, as well as inflammatory cytokines, endotoxin and withdrawal of a trophic factor . The stress-responsive MAPKs mediate a plethora of cellular responses to such stressful stimuli, including apoptosis and production of inflammatory and immunoregulatory cytokines in diverse cell systems.

Marasmus Is one of the three forms of serious protein-energy malnutrition.

Mastectomy Surgery to remove a breast.

Masticatory A substance chewed to increase salivation. Also called sialogue.

Mastitis A bacterial infection of the breast which usually occurs in breastfeeding mothers.

Matrix Metalloproteinases (MMP) A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e. extracellular matrix proteins). Matrix metalloproteinases are involved in wound healing, angiogenesis and tumour cell metastasis. See also Metalloproteinase.

MBC Minimum bacterial concentration. The lowest concentration of antibiotic required to kill an organism.

MCP-1 Monocyte chemotactic protein-1.Plays a role in the recruitment of monocytes to sites of infection and injury. It is a member of small inducible gene (SIG) family.

MDA Malondialdehyde is one of the most frequently used indicators of lipid peroxidation.

Measles An acute, highly communicable rash illness due to a virus transmitted by direct contact with infectious droplets or, less commonly, by airborne spread.

Mechanonociceptors Sensory neurons that are mechanically sensitive found in all of the paraspinal connective tissues including ligament, joint capsule, annulus fibrosus of the intervertebral disc, muscle, tendon and skin. They respond to a noxious (damaging) mechanical load.

Medial Preoptic Area Is located at the rostral end of the hypothalamus; it is important for the regulation of male sexual behaviour.

Megaloblastic Anaemia An anaemia that results from inhibition of DNA synthesis in red blood cell production, often due to a deficiency of vitamin B12 or folate and is characterized by many large immature and dysfunctional red blood cells (megaloblasts) in the bone marrow.

Melaena (Melena) Refers to the black, 'tarry' faeces that are associated with gastrointestinal haemorrhage.

Melanogenesis Production of melanin by living cells.

Melanoma Malignant tumour of melanocytes which are found predominantly in skin but also in the bowel and the eye and appear as pigmented lesions.

Melatonin A hormone produced in the brain by the pineal gland; it is important in the regulation of the circadian rhythms of several biological functions.

Menarche The first menstrual cycle, or first menstrual bleeding, in female human beings.

Menorrhagia Heavy or prolonged menstruation; too-frequent menstrual periods.

Menopausal Refer to permanent cessation of menstruation.

Menses See Menstruation.

MenstruationThe approximately monthly discharge of blood from the womb in women of childbearing age who are not pregnant. Also called menses. *Adj.* menstrual.

Mesangial Cells Are specialized cells around blood vessels in the kidneys, at the mesangium.

Mesothelioma Is an aggressive cancer affecting the membrane lining of the lungs and abdomen.

Metabolic Syndrome (MetS) Represents a combination of cardiometabolic risk factors, including visceral obesity, glucose intolerance or type 2 diabetes, elevated triglycerides, reduced HDL cholesterol and hypertension.

Metabonome Complete set of metabolically regulated elements in cells.

Metabolomics Is the scientific study of chemical processes involving metabolites.

Metalloproteinase Enzymes that break down proteins and requiring zinc or calcium atoms for proper function.

Metallothionein (MT) A family of cysteine-rich, low molecular weight (500–14,000 Da) proteins.

Meta-analysis A statistical procedure that combines the results of several studies that address a set of related research hypotheses.

Metaphysis Is the portion of a long bone between the epiphyses and the diaphysis of the femur.

Metaphyseal Pertaining to the metaphysis.

Metaplasia Transformation of one type of one mature differentiated cell type into another mature differentiated cell type.

Metastasis Is the movement or spreading of cancer cells from one organ or tissue to another.

Metestrus the quiescent period of sexual inactivity between oestrous cycles.

Metropathy Any disease of the uterus especially of the myometrium.

Metroptosis The slipping or falling out of place of an organ (as the uterus).

Metrorrhagia Uterine bleeding at irregular intervals, particularly between the expected menstrual periods.

Mevinolin A potent inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase).

MHC Acronym for major histocompatibility complex, a large cluster of genes found on the short arm of chromosome 6 in most vertebrates that encodes MHC molecules. MHC molecules play an important role in the immune system and autoimmunity.

MHC 11 Molecules Class II MHC molecules belong to a group of molecules known as the immunoglobulin supergene family, which includes immunoglobulins, T cell receptors, CD4, CD8 and others.

MIC Minimum inhibitory concentration. Lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism.

Micelle A submicroscopic aggregation of molecules.

Micellization Formation process of micelles.

Microangiopathy Or microvascular disease, is an angiopathy affecting small blood vessels in the body.

Microfilaria A pre-larval parasitic worm of the family Onchocercidae, found in the vector and in the blood or tissue fluid of human host.

Micronuclei Small particles consisting of acentric fragments of chromosomes or entire chromosomes, which lag behind at anaphase of cell division.

Microsomal PGE2 Synthase Is the enzyme that catalyzes the final step in prostaglandin E2 (PGE2) biosynthesis.

Microvasculature The finer vessels of the body, as the arterioles, capillaries and venules.

Micturition Urination, act of urinating.

Migraine A neurological syndrome characterized by altered bodily perceptions, severe, painful headaches and nausea.

Mimosine Is an alkaloid, β-3-hydroxy-4 pyridone amino acid; it is a toxic nonprotein free amino acid and is an antinutrient.

Mineral Apposition Rate MAR, rate of addition of new layers of mineral on the trabecular surfaces of bones.

Miscarriage Spontaneous abortion.

Mitochondrial Complex I The largest enzyme in the mitochondrial respiratory oxidative phosphorylation system.

Mitochondrial Permeability Transition (MPT) Is an increase in the permeability of the mitochondrial membranes to molecules of less than 1,500 Da in molecular weight. MPT is one of the major causes of cell death in a variety of conditions.

Mitogen An agent that triggers mitosis and elicits all the signals necessary to induce cell proliferation.

Mitogenic Able to induce mitosis or transformation.

Mitogenicity Process of induction of mitosis.

Mitomycin A chemotherapy drug that is given as a treatment for several different types of

cancer, including breast, stomach, oesophagus and bladder cancers.

Mitosis Cell division in which the nucleus divides into nuclei containing the same number of chromosomes.

MMP Matrix metalloproteinases, a group of peptidases involved in degradation of the extracellular matrix (ECM).

Mnestic Pertaining to memory.

Molecular Docking Is a key tool in structural molecular biology and computer-assisted drug design.

Molluscidal Destroying molluscs like snails.

MOLT4 Cells MOLT4 cells are lymphoblast-like in morphology and are used for studies of apoptosis, tumour cytotoxicity, tumorigenicity, as well as for antitumour testing.

Molybdenum (Mo) Is an essential element that forms part of several enzymes such as xanthine oxidase involved in the oxidation of xanthine to uric acid and use of iron. Molybdenum concentrations also affect protein synthesis, metabolism and growth. Dietary sources include meat, green beans, eggs, sunflower seeds, wheat flour, lentils and cereal grain.

Monoamine Oxidase A (MAOA) Is an isozyme of monoamine oxidase. It preferentially deaminates norepinephrine (noradrenaline), epinephrine (adrenaline), serotonin and dopamine.

Monoaminergic Of or pertaining to neurons that secrete monoamine neurotransmitters (e.g. dopamine, serotonin).

Monoclonal Antibodies Are produced by fusing single antibody-forming cells to tumour cells grown in culture.

Monocyte Large white blood cell that ingest microbes, other cells and foreign matter.

Monogalactosyl Diglyceride Are the major lipid components of chloroplasts.

Monorrhagia Is heavy bleeding and that is usually defined as periods lasting longer than 7 days or excessive bleeding.

Morbidity A diseased state or symptom or can refer either to the incidence rate or to the prevalence rate of a disease.

Morelloflavone A biflavonoid extracted from *Garcinia dulcis*, has shown antioxidative, antiviral and antiinflammatory properties.

Morphine The major alkaloid of opium and a potent narcotic analgesic.

mTOR, the Mammalian (or Mechanistic) Target of Rapamycin Regulates a wide range of cellular and developmental processes by coordinating signalling responses to mitogens, nutrients and various stresses.

MTTP Microsomal triglyceride transfer protein that is required for the assembly and secretion of triglyceride-rich lipoproteins from both enterocytes and hepatocytes.

MUC 5AC Mucin 5AC, a secreted gel-forming protein mucin with a high molecular weight of about 641 kDa.

Mucositis Painful inflammation and ulceration of the mucous membranes lining the digestive tract.

Mucous Relating to mucus.

Mucolytic Capable of reducing the viscosity of mucus or an agent that so acts.

Mucus Viscid secretion of the mucous membrane.

Multidrug Resistance (MDR) Ability of a living cell to show resistance to a wide variety of structurally and functionally unrelated compounds.

Muscarinic Receptors Are G protein-coupled acetylcholine receptors found in the plasma membranes of certain neurons and other cells.

Mutagen An agent that induces genetic mutation by causing changes in the DNA.

Mutagenic Capable of inducing mutation (used mainly for extracellular factors such as X-rays or chemical pollution).

Myalgia Muscle pain.

Myc Codes for a protein that binds to the DNA of other genes and is therefore a transcription facor, found on chromosome 8 in human.

Mycosis An infection or disease caused by a fungus.

Myelocyte Is a young cell of the granulocytic series, occurring normally in bone marrow, but not in circulating blood.

Myeloid Leukaemia (Chronic) A type of cancer that affects the blood and bone marrow, characterized by excessive number of white blood cells.

Myeloma Cancer that arise in the plasma cells a type of white blood cells.

Myeloperoxidase (MPO) Is a peroxidase enzyme most abundantly present in neutrophil

granulocytes (a subtype of white blood cells). It is an inflammatory enzyme produced by activated leukocytes that predicts risk of coronary heart disease.

Myeloproliferative Disorder Disease of the bone marrow in which excess cells are produced.

Myelosuppressive Causing bone marrow suppression.

Myelotoxicity State of being toxic to myeloid tissues, the bone marrow.

Myocardial Relating to heart muscles tissues.

Myocardial infarction (MI) Is the rapid development of myocardial necrosis caused by a critical imbalance between oxygen supply and demand of the myocardium.

Myocardial Ischemia An intermediate condition in coronary artery disease during which the heart tissue is slowly or suddenly starved of oxygen and other nutrients.

Myocardial Lipidosis Is the accumulation of fat droplets in myocardial fibres.

Myoclonus Brief, involuntary twitching of a muscle or a group of muscles.

Myogenesis The formation of muscular tissue, especially during embryonic development.

Myopathy A muscular disease wherein the muscle fibres do not function for any one of many reasons, resulting in muscular weakness.

Myopia Near or short sightedness.

Myosarcoma A malignant muscle tumour.

Myotonia Dystrophica An inherited disorder of the muscles and other body systems characterized by progressive muscle weakness, prolonged muscle contractions (myotonia), clouding of the lens of the eye (cataracts), cardiac abnormalities, balding and infertility.

Myotube A developing skeletal muscle fibre or cell with a tubular appearance and a centrally located nucleus.

Myringosclerosis Also known as tympanosclerosis or intratympanic tympanosclerosis, is a condition caused by calcification of collagen tissues in the tympanic membrane of the middle ear.

Myotonia A symptom of certain neuromuscular disorders characterized by the slow relaxation of the muscles after voluntary contraction or electrical stimulation.

Myotube A developing skeletal muscle fibre with a tubular appearance.

N-NitrosomorpholineA human carcinogen.

N-NitrosoprolineAn indicator for N-nitrosation of amines.

Nicotinamide Adenine Dinucleotide Phosphate (NADP) A coenzyme comprising nicotinamide mononucleotide coupled by pyrophosphate linkage to adenosine 2′,5′-bisphosphate; it acts as an electron carrier in numerous reactions, being alternately oxidized (NADP+) and reduced (NADPH).

NADPH The reduced form of nicotinamide adenine dinucleotide phosphate that serves as an electron carrier.

NAFLD Non-alcoholic fatty liver disease.

Narcotic An agent that produces narcosis; in moderate doses it dulls the senses, relieves pain and induces sleep, and in excessive dose it cause stupor, coma, convulsions and death.

Nasopharynx Upper part of the alimentary continuous with the nasal passages.

Natriorexia Excessive intake of sodium evoked by sodium depletion. *Adj.* natriorexic, natriorexigenic.

Natriuresis The discharge of excessive large amount of sodium through urine. *Adj.* natriuretic.

Natural Killer Cells (NK Cells) A type of cytotoxic lymphocyte that constitutes a major component of the innate immune system.

Natural Killer T (NKT) Cells A heterogeneous group of T cells that share properties of both T cells and natural killer (NK) cells.

Nausea Sensation of unease and discomfort in the stomach with an urge to vomit.

Necropsy See Autopsy.

Necrosis Morphological changes that follow cell death, usually involving nuclear and cytoplasmic changes.

Neointima A new or thickened layer of arterial intima formed especially on a prosthesis or in atherosclerosis by migration and proliferation of cells from the media.

Neonatal *Adj.* of or relating to newborn infants or an infant.

Neoplasia Abnormal growth of cells, which may lead to a neoplasm or tumour.

Neoplasm Tumour, any new and abnormal growth, specifically one in which cell multiplication is uncontrolled and progressive. Neoplasms may be benign or malignant.

Neoplastic Transformation Conversion of a tissue with a normal growth pattern into a malignant tumour.

Neovascularization Is the development of tiny, abnormal, leaky blood vessels inside the eye.

Neovasculature Formation of new blood vessels.

Nephrectomized Kidneys surgically removed.

Nephrectomy Surgical removal of the kidney.

Nephric Relating to or connected with a kidney.

Nephrin Is a protein necessary for the proper functioning of the renal filtration barrier.

Nephritic Syndrome Is a collection of signs (known as a syndrome) associated with disorders affecting the kidneys, more specifically glomerular disorders.

Nephritis Is inflammation of the kidney.

Nephrolithiasis Process of forming a kidney stone in the kidney or lower urinary tract.

Nephropathy A disorder of the kidney.

Nephrotic Syndrome Nonspecific disorder in which the kidneys are damaged, causing them to leak large amounts of protein from the blood into the urine.

Nephrotoxicity Poisonous effect of some substances, both toxic chemicals and medication, on the kidney.

Nerve Growth Factor (NGF) A small protein that induces the differentiation and survival of particular target neurons (nerve cells).

Nervine A nerve tonic that acts therapeutically upon the nerves, particularly in the sense of a sedative that serves to calm ruffled nerves.

Neural Tube Defects (NTDs) Are common birth defects of the brain and spinal cord.

NEU 4 Sialidase This protein belongs to a family of glycohydrolytic enzymes, which remove terminal sialic acid residues from various sialo derivatives, such as glycoproteins, glycolipids, oligosaccharides and gangliosides.

Neuralgia Is a sudden, severe painful disorder of the nerves.

Neuraminidase Glycoside hydrolase enzymes that cleaves the glycosidic linkages of neuraminic acids.

Neuraminidase Inhibitors A class of antiviral drugs targeted at the influenza viruses whose mode of action consists of blocking the function of the viral neuraminidase protein, thus preventing the virus from reproducing.

Neurasthenia A condition with symptoms of fatigue, anxiety, headache, impotence, neuralgia and impotence.

Neurasthenic A substance used to treat nerve pain and/or weakness (i.e. neuralgia and sciatica).

Neurite Refers to any projection from the cell body of a neuron.

Neuritis An inflammation of the nerve characterized by pain, sensory disturbances and impairment of reflexes. *Adj.* neuritic.

Neuritogenesis The first step of neuronal differentiation and takes place as nascent neurites bud from the immediate postmitotic neuronal soma.

Neuroblastoma A common extracranial cancer that forms in nerve tissues, common in infancy.

Neuroendocrine *Adj.* of, relating to or involving the interaction between the nervous system and the hormones of the endocrine glands.

Neurogenesis Process by which neurons are generated from neural stem and progenitor cells.

Neurogenic Originating from the nerves of the nervous system.

Neuroleptic Refers to the effects on cognition and behaviour of antipsychotic drugs that reduce confusion, delusions, hallucinations and psychomotor agitation in patients with psychoses.

Neuroma Is a growth or tumour of nerve tissue.

Neuropathy A collection of disorders that occurs when the peripheral nervous systems are damaged, causing pain and numbness in the hands and feet.

Neuropharmacological Relating the effects of drugs on the neurosystem.

Neuroradiology Is a subspecialty of radiology focusing on the diagnosis and characterization of abnormalities of the central and peripheral nervous system. *Adj.* neuroradiologic.

Neurotrophic Relating to neutrophy, i.e. the nutrition and maintenance of nervous tissue.

Neutropenia A disorder of the blood, characterized by abnormally low levels of neutrophils.

Neutrophil Type of white blood cell, specifically a form of granulocyte.

Neurotrophin Protein that induce the survival, development and function of neurons.

NF-kappa B (NF-κB) Nuclear factor kappa B, is an ubiquitous rapid response transcription factor in cells involved in immune and inflammatory reactions.

Niacin Vitamin B3. See Vitamin B3.

Niacinamide An amide of niacin, also known as nicotinamide. See Vitamin B3.

NIH3T3 Cells A mouse embryonic fibroblast cell line used in the cultivation of keratinocytes.

Nidation Implantation.

Niosomes Are novel, vesicular, drug delivery systems composed of nonionic surfactants instead of phospholipids; they are capable of entrapping hydrophilic and hydrophobic drugs.

Nitrogen (N) Is an essential building block of amino and nucleic acids and proteins and is essential to all living organisms. Protein-rich vegetables like legumes are rich food sources of nitrogen.

NK Cells Natural killer cells. A type of cytotoxic lymphocyte that constitutes a major component of the innate immune system.

NK1.1+T (NKT) cells A type of natural killer T (NKT) cells. See Natural Killer T Cells.

NMDA Receptor N-methyl-D-ASPARTATE receptor. The predominant molecular device for controlling synaptic plasticity and memory function. A brain receptor activated by the amino acid glutamate, which when excessively stimulated may cause cognitive defects in Alzheimer's disease.

Nociceptive Causing pain, responding to a painful stimulus.

Nociceptors Specialized peripheral sensory neurons that respond to potentially damaging stimuli by sending nerve signals to the spinal cord and brain.

Non-osteogenicFibromata of bone, a benign tumour of bone which shows no evidence of ossification.

Non-alcoholic Fatty Liver Disease One cause of a fatty liver, occurring when fat is deposited (steatosis) in the liver not due to excessive alcohol use.

Nootropics Are substances which are claimed to boost human cognitive abilities (the functions and capacities of the brain). Also popularly referred to as 'smart drugs', 'smart nutrients', 'cognitive enhancers' and 'brain enhancers'.

Noradrenalin See Norepinephrine.

Norepinephrine A substance, both a hormone and neurotransmitter, secreted by the adrenal medulla and the nerve endings of the sympathetic nervous system to cause vasoconstriction and increases in heart rate, blood pressure and the sugar level of the blood. Also called levarterenol, noradrenalin.

Normoglycaemic Having the normal amount of glucose in the blood.

Normotensive Having normal blood pressure.

Nosebo A harmless substance that when taken by a patient is associated with unpleasant or harmful effects due to negative expectations or the psychological state of the person.

Nosocomial Infections Infections which are a result of treatment in a hospital or a healthcare service unit, but secondary to the patient's original condition.

NPC1L1 Niemann–Pick C1-like 1 gene that plays a major role in cholesterol homeostasis. It is critical for the uptake of cholesterol across the plasma membrane of the intestinal enterocyte.

Nrf2 NF-E2-related factor 2, a transcription factor that activates ARE-containing genes.

Nrf2/ARE Pathway Plays an important role in inducing phase II detoxifying enzymes and antioxidant proteins and has been considered a potential target for cancer chemoprevention because it eliminates harmful reactive oxygen species or reactive intermediates generated from carcinogens.

Nuclear Factor Erythroid 2-Related Factor 2 (Nrf2) A transcription factor that plays a major role in response to oxidative stress by binding to antioxidant-responsive elements that regulate many hepatic phase I and II enzymes as well as hepatic efflux transporters.

Nucleosomes Fundamental repeating subunits of all eukaryotic chromatin, consisting of a DNA chain coiled around a core of histones.

Nulliparous Term used to describe a woman who has never given birth.

Nyctalopia Night blindness, impaired vision in dim light and in the dark, due to impaired function of certain specialized vision cells.

Nystagmus Fast, involuntary movements of the eyes.

Nycturia Excessive urination at night, especially common in older men.

Occludin A novel integral membrane protein localizing at tight junctions. *Cf.* tight junction.

Occlusion Closure or blockage (as of a blood vessel).

Occlusive Peripheral Arterial Disease (PAOD) Also known as peripheral vascular disease (PVD) or peripheral arterial disease (PAD) refers to the obstruction of large arteries not within the coronary, aortic arch vasculature or brain. PVD can result from atherosclerosis, inflammatory processes leading to stenosis, an embolism or thrombus formation.

Oculomotor Nerve The third of 12 paired cranial nerves.

Odds Ratio A statistical measure of effect size, describing the strength of association or nonindependence between two binary data values.

Odontalgia Toothache. *Adj.* odontalgic.

Odontopathy Any disease of the teeth.

Oedema Formerly known as dropsy or hydropsy, is characterized swelling caused by abnormal accumulation of fluid beneath the skin or in one or more cavities of the body. It usually occurs in the feet, ankles and legs, but it can involve the entire body.

Oedematogenic Producing or causing oedema.

Oestrogen Female hormone produced by the ovaries that play an important role in the oestrous cycle in women.

Oestrogen Receptor (ER) Is a protein found in high concentrations in the cytoplasm of breast, uterus, hypothalamus and anterior hypophysis cells; ER levels are measured to determine a breast CA's potential for response to hormonal manipulation.

Oestrogen Receptor Negative (ER-) Tumour is not driven by oestrogen and needs another test to determine the most effective treatment.

Oestrogen Receptor Positive (ER+) Means that oestrogen is causing the tumour to grow and that the breast cancer should respond well to hormone suppression treatments.

Oestrogenic Relating to oestrogen or producing oestrous.

Oestrous Sexual excitement or heat of female or period of this characterized by changes in the sex organs.

Oligoarthritis An inflammation of two, three or four joints.

Oligonucleosome A series of nucleosomes.

Oligospermia or Oligozoospermia Refers to semen with a low concentration of sperm, commonly associated with male infertility.

Oligoanuria Insufficient urine volume to allow administration of necessary fluids, etc.

Oliguria Decreased production of urine.

Omega-3 Fatty Acids are essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the $n-3$ position. Dietary sources of omega-3 fatty acids include fish oil and certain plant/nut oils. The three most nutritionally important omega-3 fatty acids are alpha-linolenic acid, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Research indicates that omega-3 fatty acids are important in health promotion and disease and can help prevent a wide range of medical problems, including cardiovascular disease, depression, asthma and rheumatoid arthritis.

Omega-6 Fatty Acids Are essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the $n-6$ position. Omega-6 fatty acids are considered essential fatty acids (EFAs) found in vegetable oils, nuts and seeds. They are essential to human health but cannot be made in the body. Omega-6 fatty acids—found in vegetable oils, nuts and seeds—are a beneficial part of a heart-healthy eating. Omega-6 and omega-3 PUFA play a crucial role in heart and brain function and in normal growth and development. Linoleic acid (LA) is the main omega-6 fatty acid in foods, accounting for 85–90 % of the dietary omega-6 PUFA. Other omega-6 acids include gamma-linolenic acid or GLA, sometimes called gamoleic acid, eicosadienoic acid, arachidonic acid and docosadienoic acid.

Omega-9 Fatty Acids Are not essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the $n-9$ position. Some $n-9$s are common components of animal fat and vegetable oil. Two n − 9 fatty acids important in industry are oleic acid (18:1, $n-9$), which is a main component of olive oil and erucic acid (22:1, $n-9$), which is found in rapeseed, wallflower seed and mustard seed.

Oncogenes Genes carried by tumour viruses that are directly and solely responsible for the neoplastic (tumorous) transformation of host cells.

Oncosis Accidental cell death. Also referred to swelling necrosis.

Ophthalmia Severe inflammation of eye or the conjunctiva or deeper structures of the eye. Also called ophthalmitis.

Ophthalmia (Sympathetic) Inflammation of both eyes following trauma to one eye.

Ophthalmopathy An autoimmune disease where the thyroid gland is overactive leading to ocular manifestations.

Opiate Drug derived from the opium plant.

Opioid Receptors A group of G-protein-coupled receptors located in the brain and various organs that bind opiates or opioid substances.

Optic Placode An ectodermal placode from which the lens of the embryonic eye develops. Also called lens placode.

ORAC (Oxygen Radical Absorbance Capacity) A method of measuring antioxidant capacities in biological samples.

Oral Submucous Fibrosis A chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucosa tissues.

Oral Thrush An infection of yeast fungus, *Candida albicans*, in the mucous membranes of the mouth.

Orchidectomy Surgery to remove one or both testicles.

Orchidectomized With testis removed.

Orchitis An acute painful inflammatory reaction of the testis secondary to infection by different bacteria and viruses.

Orexigenic Increasing or stimulating the appetite.

Orofacial Dyskinesia Abnormal involuntary movements involving muscles of the face, mouth, tongue, eyes and, occasionally, the neck—may be unilateral or bilateral and constant or intermittent.

Oropharyngeal Relating to the oropharynx.

Oropharynx Part of the pharynx between the soft palate and the epiglottis.

Ostalgia, Ostealgia Pain in the bones. Also called osteodynia.

Osteoarthritis Is the deterioration of the joints that becomes more common with age.

Osteoarthrosis Chronic noninflammatory bone disease.

Osteoblast A mononucleate cell that is responsible for bone formation.

Osteoblastic Relating to osteoblasts.

Osteocalcin A noncollagenous protein found in bone and dentin. Also referred to as bone gamma-carboxyglutamic acid-containing protein.

Osteoclasts A kind of bone cell that removes bone tissue by removing its mineralized matrix.

Osteoclastogenesis The production of osteoclasts.

Osteodynia Pain in the bone.

Osteogenic Derived from or composed of any tissue concerned in bone growth or repair.

Osteomalacia Refers to the softening of the bones due to defective bone mineralization.

Osteomyelofibrosis A myeloproliferative disorder in which fibrosis and sclerosis finally lead to bone marrow obliteration.

Osteopenia Reduction in bone mass, usually caused by a lowered rate of formation of new bone that is insufficient to keep up with the rate of bone destruction.

Osteoporosis A disease of bone that leads to an increased risk of fracture.

Osteoprotegerin Also called osteoclastogenesis inhibitory factor (OCIF), a cytokine, which can inhibit the production of osteoclasts.

Osteosacrcoma A malignant bone tumour. Also called osteogenic sarcoma.

Otalgia Earache, pain in the ear.

Otic Placode A thickening of the ectoderm on the outer surface of a developing embryo from which the ear develops.

Otitis Inflammation of the inner or outer parts of the ear.

Otitis Media Inflammation of the middle ear.

Otorrhoea Running drainage (discharge) exiting the ear.

Otopathy Disease of the ear.

Ovariectomized With one or two ovaries removed.

Ovariectomy Surgical removal of one or both ovaries.

Oxidation The process of adding oxygen to a compound, dehydrogenation or increasing the electronegative charge.

Oxidoreductase Activity Catalysis of an oxidation-reduction (redox) reaction, a reversible chemical reaction. One substrate acts as a hydrogen or electron donor and becomes oxidized, while the other acts as hydrogen or electron acceptor and becomes reduced.

Oxygen Radical Absorbance Capacity (ORAC) A method of measuring antioxidant capacities in biological samples.

Oxytocic *Adj.* hastening or facilitating childbirth, especially by stimulating contractions of the uterus.

Oxytocin Is a mammalian hormone that also acts as a neurotransmitter in the brain. It is best known for its roles in female reproduction: it is released in large amounts after distension of the cervix and vagina during labour and after stimulation of the nipples, facilitating birth and breastfeeding, respectively.

Oxyuriasis Infestation by pinworms.

Ozoena Discharge of the nostrils caused by chronic inflammation of the nostrils.

P13-K Is a lipid kinase enzyme involved in the regulation of a number of cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer.

P13-K/AKT Signalling Pathway Shown to be important for an extremely diverse array of cellular activities—most notably cellular proliferation and survival.

P21 Also known as cyclin-dependent kinase inhibitor 1 or CDK-interacting protein 1, is a potent cyclin-dependent kinase inhibitor.

p21waf1/cip1 Encodes a cyclin-dependent kinase inhibitor that is transcriptionally activated by the p53 tumour suppressor gene, transforming growth factor beta 1 (TGF-beta 1), AP2 and other pathways, all regulating apoptosis and the cell cycle.

P300/CBP Are transcriptional coactivators that play critical roles in integrating multiple signal-dependent transcription events and may have specific roles in tumour suppression pathways.

P53 Also known as protein 53 or tumour protein 53, is a tumour suppressor protein that in humans is encoded by the TP53 gene.

P65 Transcription Factor Is a protein that in humans is encoded by the RELA gene. Its alternative name is nuclear factor NF-kappa-B p65 subunit.

P-Glycoprotein (P-gp, ABCB1, MDR1) A cell membrane-associated drug-exporting protein that transports a variety of drug substrates from cancer cells.

P-Selectin Also known as CD62P, GMP-140, LLECAM-3 and PADGEM and is a member of the selectin family. It is expressed by activated platelets and endothelial cells.

pACREB Phosphorylated cAMP (adenosine 3′5′ cyclic monophosphate)-response element binding protein.

Palliative Relieving pain without alleviating the underlying problem.

Palpebral Ptosis The abnormal drooping of the upper lid, caused by partial or total reduction in levator muscle function.

Palpitation Rapid pulsation or throbbing of the heart.

Paludism State of having symptoms of malaria characterized by high fever and chills.

Pancreatectomized Having undergone a pancreatectomy.

Pancreatectomy Surgical removal of all or part of the pancreas.

Pancreatitis Inflammation of the pancreas.

Pancytopenia A haematological condition in which there is a reduction in the number of red and white blood cells, as well as platelets.

Pantothenic Acid Vitamin B5. See Vitamin B5.

Papain A protein-degrading enzyme used medicinally and to tenderize meat.

Papilloma A benign epithelial tumour growing outwardly like in fingerlike fronds.

Papule A small, solid, usually inflammatory elevation of the skin that does not contain pus.

Paradontosis Is the inflammation of gums and other deeper structures, including the bone.

Paralytic Person affected with paralysis, pertaining to paralysis.

Paraoxonase An enzyme that protects against oxidation of low-density lipoprotein and affects the risk of coronary artery disease.

Parasitemia Presence of parasites in blood. *Adj.* parasitemic.

Parasympathetic Nervous System Subsystem of the nervous systems that slows the heart rate and increases intestinal and gland activity and relaxes the sphincter muscles.

Parasympathomimetic Having an action resembling that caused by stimulation of the parasympathetic nervous system.

Paraesthesia A sensation of tingling, burning, pricking or numbness of a person's skin with no apparent long-term physical effect. Also known as 'pains and needles'.

Parenteral Administration Administration by intravenous, subcutaneous or intramuscular routes.

Paresis A condition characterized by partial loss of movement or impaired movement.

Paraesthesia Is an abnormal sensation of the skin, such as burning, numbness, itching, hyperaesthesia (increased sensitivity) or tingling, with no apparent physical cause.

Parotitis Inflammation of salivary glands.

Paroxysm A sudden outburst of emotion or action, a sudden attack and recurrence or intensification of a disease.

Paroxystic Relating to an abnormal event of the body with an abrupt onset and an equally sudden return to normal.

PARP See Poly (ADP-ribose) polymerase.

Pars Compacta Is a portion of the substantia nigra (a brain structure located in the midbrain).

Parturition Act of childbirth.

PCAF P300/CBP-associated factor. A histone acetyl transferase (HAT) that plays a role in regulation of transciton and cell cycly progression and differentiation.

PCE/PCN Ratio Polychromatic erythrocyte/normochromatic erythrocyte ratio used as a measure of cytotoxic effects.

PCNA Proliferating cell nuclear antigen, an auxiliary protein of DNA polymerase delta involved in modulating eukaryotic DNA replication.

PDEF Acronym for prostate-derived ETS factor, an ETS (epithelial-specific E26 transforming sequence) family member that has been identified as a potential tumour suppressor.

PDGFs Platelet-derived growth factors constitute a group of growth factors that play a significant role in blood vessel formation and the growth of blood vessels.

PDGR Receptor (Platelet-Derived Growth Factor Receptor) Are cell surface tyrosine kinase receptors for members of the platelet-derived growth factor (PDGF) family.

Pectoral Pertaining to or used for the chest and respiratory tract.

pERK Phosphorylated extracellular signal-regulated kinase, protein kinases involved in many cell functions.

Peliosis See Purpura.

Pellagra Is a systemic nutritional wasting disease caused by a deficiency of vitamin B3 (niacin).

Pemphigus Neonatorum Staphylococcal scalded skin syndrome, a bacterial disease of infants, characterized by elevated vesicles or blebs on a normal or reddened skin.

Peptic Ulcer A sore in the lining of the stomach or duodenum, the first part of the small intestine.

Peptide YY A short (36 amino acid) pancreatic protein released by cells in the ileum and colon in response to feeding.

Percutaneous Pertains to a medical procedure where access to inner organs or tissues is done via needle puncture of the skin.

Perfusion To force fluid through the lymphatic system or blood vessels to an organ or tissue.

Periapical Periodontitis Is the inflammation of the tissue adjacent to the tip of the tooth's root.

Perifuse To flush a fresh supply of bathing fluid around all of the outside surfaces of a small piece of tissue immersed in it.

Perilipins Highly phosphorylated adipocyte proteins that are localized at the surface of the lipid droplet.

Perimenopause Is the phase before menopause actually takes place, when ovarian hormone production is declining and fluctuating. *Adj.* perimenopausal.

Periodontal Ligament (PDL) Is a group of specialized connective tissue fibres that essentially attach a tooth to the bony socket.

Periodontitis Is a severe form of gingivitis in which the inflammation of the gums extends to the supporting structures of the tooth. Also called pyorrhoea.

Peripheral Arterial Disease (PAD) Is a disease in which plaque builds up in the arteries that carry blood to your head, organs and limbs.

Peripheral Neuropathy Refers to damage to nerves of the peripheral nervous system.

Peripheral Neuropathic Pain (PNP) Refers to situations where nerve roots or peripheral nerve trunks have been damaged by mechanical and/or chemical stimuli that exceeded the physical capabilities of the nervous system. Symptoms may include pain, paraesthesia, dysaesthesia, spasm, weakness, hypoesthesia or anaesthesia.

Peripheral Vascular Disease (PVD) See Peripheral Artery Occlusive Disease.

Peristalsis A series of organized, wave-like muscle contractions that occur throughout the digestive tract.

PERK A transmembrane protein kinase of the PEK family resident in the endoplasmic reticulum (ER) membrane and is linked to insulin processing.

Perlingual Through or by way of the tongue.

Perniosis An abnormal reaction to cold that occurs most frequently in women, children and the elderly. Also called chilblains.

Per Os (P.O.) Oral administration.

Peroxisome Proliferator-Activated Receptors (PPARs) A family of nuclear receptors that are involved in lipid metabolism, differentiation, proliferation, cell death and inflammation.

Peroxisome Proliferator-Activated Receptor Alpha (**PPAR-Alpha**) A nuclear receptor protein, transcription factor and a major regulator of lipid metabolism in the liver.

Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ) A type II nuclear receptor protein that regulates fatty acid storage and glucose metabolism.

Pertussis Whooping cough, severe cough.

Peyer's Patches Patches of lymphoid tissue or lymphoid nodules on the walls of the ileal-small intestine.

PGE-2 Prostaglandin E2. A hormonelike substance that is released by blood vessel walls in response to infection or inflammation that acts on the brain to induce fever.

Phagocytes Are the white blood cells that protect the body by ingesting (phagocytosing) harmful foreign particles, bacteria and dead or dying cells. *Adj.* phagocytic.

Phagocytosis Is process the human body uses to destroy dead or foreign cells.

Pharmacognosis The branch of pharmacology that studies the composition, use and history of drugs.

Pharmacodynamics Branch of pharmacology dealing with the effects of drugs and the mechanism of their action.

Pharmacokinetics Branch of pharmacology concerned with the movement of drugs within the body including processes of absorption, distribution, metabolism and excretion in the body.

Pharmacopoeia Authoritative treatise containing directions for the identification of drug samples and the preparation of compound medicines and published by the authority of a government or a medical or pharmaceutical society and in a broader sense is a general reference work for pharmaceutical drug specifications.

Pharyngitis, Pharyngolaryngitis Inflammation of the pharynx and the larynx.

Pharyngolaryngeal Pertaining to the pharynx and larynx.

Phase II Drug-Metabolizing Enzymes Play an important role in biotransformation of endogenous compounds and xenobiotics to more easily excretable forms as well as in the metabolic inactivation of pharmacologically active compounds. Phase II drug-metabolizing enzymes are mainly transferases.

Phenolics Class of chemical compounds consisting of a hydroxyl group (–OH) bonded directly to an aromatic hydrocarbon group.

Pheochromocytoma Is a rare neuroendocrine tumour that usually originates from the adrenal glands' chromaffin cells, causing overproduction of catecholamines, powerful hormones that induce high blood pressure and other symptoms.

Phlebitis Is an inflammation of a vein, usually in the legs.

Phlegm Abnormally viscid mucus secreted by the mucosa of the respiratory passages during certain infectious processes.

Phlegmon A spreading, diffuse inflammation of the soft or connective tissue due to infection by Streptococci bacteria.

Phloroglucinol A white, crystalline compound used as an antispasmodic, analytical reagent and decalcifier of bone specimens for microscopic examination.

Phosphatidylglycerol Is a glycerophospholipid found in pulmonary active surface lipoprotein and consists of a L-glycerol 3-phosphate backbone ester-bonded to either saturated or unsaturated fatty acids on carbons 1 and 2.

Phosphatidylinositol 3-kinases (PI 3-Kinases or PI3Ks) A group of enzymes involved in cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer.

Phosphatidylserine A phosphoglyceride phospholipid that is one of the key building blocks of cellular membranes, particularly in the nervous system. It is derived from soy lecithin.

Phosphaturia A urinary tract condition of excessive urine phosphorus, causing urine to appear cloudy or murky coloured. Also called hypophosphatemia.

Phosphodiesterases A diverse family of enzymes that hydrolyze cyclic nucleotides and thus play a key role in regulating intracellular levels of the second messengers cAMP and cGMP and hence cell function.

Phosphoenolpyruvate C Kinase (PEPCK) An enzyme in the lyase family used in the metabolic pathway of gluconeogenesis.

Phospholipase An enzyme that hydrolyzes phospholipids into fatty acids and other lipophilic substances.

Phospholipase A2 (PLA2) A small lipolytic enzyme that releases fatty acids from the second carbon group of glycerol. Plays an essential role in the synthesis of prostaglandins and leukotrienes.

Phospholipase C Enzymes that cleaves phospholipase.

Phospholipase C Gamma (PLC Gamma) Enzymes that cleave phospholipase in cellular proliferation and differentiation, and its enzymatic activity is upregulated by a variety of growth factors and hormones.

Phosphorus (P) Is an essential mineral that makes up 1 % of a person's total body weight and is found in the bones and teeth. It plays an important role in the body's utilization of carbohydrates and fats, in the synthesis of protein for the growth, maintenance and repair of cells and tissues. It is also crucial for the production of ATP, a molecule the body uses to store energy. Main sources are meat and milk; fruits and vegetables provide small amounts.

Photoaging Is the term that describes damage to the skin caused by intense and chronic exposure to sunlight resulting in premature aging of the skin.

Photocarcinogenesis Represents the sum of a complex of simultaneous and sequential biochemical events that ultimately lead to the occurrence of skin cancer caused by exposure to the sun.

Photodermatoses Skin disorders caused by exposure to sunlight.

Photophobia Abnormal visual intolerance to light.

Photopsia An affection of the eye, in which the patient perceives luminous rays, flashes, coruscations, etc.

Photosensitivity Sensitivity towards light.

Phthisis An archaic name for tuberculosis.

Phytohaemagglutinin A lectin found in plant that is involved in the stimulation of lymphocyte proliferation.

Phytonutrients Certain organic components of plants that are thought to promote human health. Fruits, vegetables, grains, legumes, nuts and teas are rich sources of phytonutrients. Phytonutrients are not 'essential' for life. Also called phytochemicals.

Phytosterols A group of steroid alcohols, cholesterol-like phytochemicals naturally occurring in plants like vegetable oils, nuts and legumes.

Piebaldism Rare autosomal dominant disorder of melanocyte development characterized by distinct patches of skin and hair that contain no pigment.

Piles See Haemorrhoids.

PI3K Phosphoinositide 3-kinase.

PI13K/AKT Signalling Pathways Are involved in the modulation of cell survival, cell cycle progression and cellular growth in cancer.

Pityriasis Lichenoides Is a rare skin disorder of unknown aetiology characterized by multiple papules and plaques.

PKC Protein kinase C, a membrane-bound enzyme that phosphorylates different intracellular proteins and raised intracellular Ca levels.

PKC Delta Inhibitors Protein kinase C delta inhibitors that induce apoptosis of haematopoietic cell lines.

Placebo A sham or simulated medical intervention.

Placode A platelike epithelial thickening in the embryo where some organ or structure later develops.

Plantar Verruca Wart occurring on the sole of the foot.

Plasma The yellow-coloured liquid component of blood, in which blood cells are suspended.

Plasma Kallikrein A serine protease, synthesized in the liver and circulates in the plasma.

Plasmalemma Plasma membrane.

Plasmin A proteinase enzyme that is responsible for digesting fibrin in blood clots.

Plasminogen The proenzyme of plasmin, whose primary role is the degradation of fibrin in the vasculature.

Plasminogen Activator Inhibitor-1 (PAI-1) Also known as endothelial plasminogen activator inhibitor or serpin E1, is a serine protease inhibitor (serpin) that functions as the principal inhibitor of tissue plasminogen activator (tPA) and urokinase (uPA), the activators of plasminogen and hence fibrinolysis (the physiological breakdown of blood clots).

Plaster Poultice.

Platelet-Activating Factor (PAF) Is an acetylated derivative of glycerophosphorylcholine, released by basophils and mast cells in immediate hypersensitive reactions and macrophages and neutrophils in other inflammatory reactions. One of its main effects is to induce platelet aggregation.

PLC Gamma Phospholipase C gamma plays a central role in signal transduction.

Pleurisy Is an inflammation of the pleura, the lining of the pleural cavity surrounding the lungs, which can cause painful respiration and other symptoms. Also known as pleuritis.

Pneumonia An inflammatory illness of the lung caused by bacteria or viruses.

Pneumotoxicity Damage to lung tissues.

Poliomyelitis Is a highly infectious viral disease that may attack the central nervous system and is characterized by symptoms that range from a mild non-paralytic infection to total paralysis in a matter of hours. Also called polio or infantile paralysis.

Poly (ADP-Ribose) Polymerase (PARP) A protein involved in a number of cellular processes especially DNA repair and programmed cell death.

Polyarthritis Is any type of arthritis which involves five or more joints.

Polychromatic Erythrocyte (PCE) An immature red blood cell containing RNAthat can be differentiated by appropriate staining techniques from a normochromatic erythrocyte (NCE), which lacks RNA.

Polycystic Kidney Disease Is a kidney disorder passed down through families in which multiple cysts form on the kidneys, causing them to become enlarged.

Polycystic Ovary Syndrome Imbalance of woman's sex hormone. This imbalance may cause changes in menstrual cycle, skin changes, small cysts in the ovary and problem in getting pregnant.

Polycythaemia A type of blood disorder characterized by the production of too many red blood cells.

Polymorphonuclear Having a lobed nucleus. Used especially of neutrophilic white blood cells.

Polyneuritis Widespread inflammation of the nerves.

Polyneuritis Gallinarum A nervous disorder in birds and poultry.

Polyneuropathy Simultaneous malfunction of many peripheral nerves throughout the body.

Polyp A growth that protrudes from a mucous membrane.

Polyphagia Medical term for excessive hunger or eating.

Polyposis Describes a condition where there are a lot of polyps.

Polyuria A condition characterized by the passage of large volumes of urine with an increase in urinary frequency.

Pomade A thick oily dressing.

Porphyrin Any of a class of water-soluble, nitrogenous biological pigments.

Postherpetic Neuralgia (PHN) Is neuralgia (pain in the nerves) caused by the varicella herpes zoster virus. The pain may last for more than a month or more after a shingles infection occurred.

Postpartum Depression Depression after pregnancy. Also called postnatal depression.

Postprandial After mealtime.

Potassium (K) Is an element that is essential for the body's growth and maintenance. It keeps a normal water balance between the cells and body fluids, for cellular enzyme activities and plays an essential role in the response of nerves to stimulation and in the contraction of muscles. Potassium is found in many plant foods and fish (tuna, halibut): chard, mushrooms, spinach, fennel, kale, mustard greens, Brussels sprouts, broccoli, cauliflower, cabbage winter squash, eggplant, cantaloupe, tomatoes, parsley, cucumber, bell pepper, turmeric, ginger root, apricots, strawberries, avocado and banana.

Poultice Is a soft moist mass, often heated and medicated, that is spread on cloth over the skin to treat an aching, inflamed or painful part of the body. Also called cataplasm.

PPARs Peroxisome proliferator-activated receptors. A group of nuclear receptor proteins that function as transcription factors regulating the expression of genes.

PR Interval Is the time (in seconds) from the beginning of the P wave (onset of atrial depolarization) to the beginning of the QRS complex.

Prebiotics A category of functional food, defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improve host health. *Cf.* probiotics.

Pre-ecamplasiaToxic condition of pregnancy characterized by high blood pressure, abnormal weight gain, proteinuria and oedema.

Prenidatory Phase Pre-implantation phase.

Prepubertal Before puberty, pertaining to the period of accelerated growth preceding gonadal maturity.

Pregnane X Receptor (PXR; NR1I2) Is a ligand-activated transcription factor that plays a role not only in drug metabolism and transport but also in various other biological processes.

Pregnenolone A steroid hormone produced by the adrenal glands, involved in the steroidogenesis of other steroid hormones like progesterone, mineralocorticoids, glucocorticoids, androgens and oestrogens.

Prenidatory Referring to the time period between fertilization and implantation.

Prenylated Flavones Flavones with an isoprenyl group in the 8-position has been reported to have good antiinflammatory properties.

Proangiogenic Promote angiogenesis (formation and development of new blood vessels).

Probiotication Enhancement with beneficial probiotic bacteria such as *Lactobacillus* species that can prevent the growth of intestinal pathogenic microflora.

Probiotics Are dietary supplements and live microorganisms containing potentially beneficial bacteria or yeasts that are taken into the alimentary system for healthy intestinal functions. *Cf.* prebiotics.

Proctitis An inflammation of the rectum that causes discomfort, bleeding and, occasionally, a discharge of mucus or pus.

Procyanidin Also known as proanthocyanidin, oligomeric proanthocyanidin, leukocyanidin, leucoanthocyanin, is a class of flavanols found in many plants. It has antioxidant activity and plays a role in the stabilization of collagen and maintenance of elastin.

Progestational Of or relating to the phase of the menstrual cycle immediately following

ovulation, characterized by secretion of progesterone.

Proglottid One of the segments of a tapeworm.

Prognosis Medical term to describe the likely outcome of an illness.

Prokinetic Or gastroprokinetic. Substance that enhances gastrointestinal motility by increasing the frequency of contractions in the small intestine or making them stronger.

Prolactin A hormone produced by the pituitary gland. It stimulates the breasts to produce milk in pregnant women. It is also present in males but its role is not well understood.

Prolapse A common condition where the bladder, uterus and or bowel protrudes into the vagina.

Prolapsus To fall or slip out of place.

Prolapsus Ani Eversion of the lower portion of the rectum and protruding through the anus, common in infancy and old age.

Proliferating Cell Nuclear Antigen (PCNA) A new marker to study human colonic cell proliferation.

Proliferative Vitreoretinopathy (PVR) A most common cause of failure in retinal reattachment surgery, characterized by the formation of cellular membrane on both surfaces of the retina and in the vitreous.

Promastigote The flagellate stage in the development of trypanosomatid protozoa, characterized by a free anterior flagellum.

Promyelocytic Leukaemia A subtype of acute myelogenous leukaemia (AML), a cancer of the blood and bone marrow.

Pro-oxidants Chemicals that induce oxidative stress, either through creating reactive oxygen species or inhibiting antioxidant systems.

Prophylaxis Prevention or protection against disease.

Proptosis See Exophthalmos.

Prostacyclin A prostaglandin that is a metabolite of arachidonic acid, inhibits platelet aggregation and dilates blood vessels.

Prostaglandins A family of C 20 lipid compounds found in various tissues, associated with muscular contraction and the inflammation response such as swelling, pain, stiffness, redness and warmth.

Prostaglandin E2 (PEG –2) One of the prostaglandins, a group of hormonelike substances that participate in a wide range of body functions such as the contraction and relaxation of smooth muscle, the dilation and constriction of blood vessels, control of blood pressure and modulation of inflammation.

Prostaglandin E Synthase An enzyme that in humans is encoded by the glutathione-dependent PTGES gene.

Prostanoids Term used to describe a subclass of eicosanoids (products of COX pathway) consisting of: the prostaglandins (mediators of inflammatory and anaphylactic reactions), the thromboxanes (mediators of vasoconstriction) and the prostacyclins (active in the resolution phase of inflammation).

Prostate A gland that surrounds the urethra at the bladder in the male.

Prostate Cancer A disease in which cancer develops in the prostate, a gland in the male reproductive system. Symptoms include pain, difficulty in urinating, erectile dysfunction and other symptoms.

Prostate-Specific Antigen (PSA) A protein produced by the cells of the prostate gland.

Protein Kinase C (PKC) A family of enzymes involved in controlling the function of other proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins. PKC enzymes play important roles in several signal transduction cascades.

Protein Tyrosine Phosphatase (PTP) A group of enzymes that remove phosphate groups from phosphorylated tyrosine residues on proteins.

Proteinase A protease (enzyme) involved in the hydrolytic breakdown of proteins, usually by splitting them into polypeptide chains.

Proteinuria Means the presence of an excess of serum proteins in the urine.

Proteolysis Cleavage of the peptide bonds in protein forming smaller polypeptides. *Adj.* proteolytic.

Proteomics The large-scale study of proteins, particularly their structures and functions.

Prothrombin Blood-clotting protein that is converted to the active form, factor IIa or thrombin, by cleavage.

Prothyroid Good for thyroid function.

Protheolithic Proteolytic; see Proteolysis.

Proto-oncogene A normal gene which, when altered by mutation, becomes an oncogene that can contribute to cancer.

Prurigo A general term used to describe itchy eruptions of the skin.

Pruritis Defined as an unpleasant sensation on the skin that provokes the desire to rub or scratch the area to obtain relief; itch, itching. *Adj.* pruritic.

PSA Prostate-specific antigen. A protein which is secreted into ejaculate fluid by the healthy prostate. One of its functions is to aid sperm movement.

Psoriasis A common chronic, noncontagious autoimmune dermatosis that affects the skin and joints.

Psychoactive Having effects on the mind or behaviour.

Psychonautics Exploration of the psyche by means of approaches such as meditation, prayer, lucid dreaming and brain wave entrainment.

Psychotomimetic Hallucinogenic.

Psychotropic Capable of affecting the mind, emotions and behaviour.

PTEN Phosphatase and tensin homolog. A tumour suppressor gene.

Ptosis Also known as drooping eyelid; caused by weakness of the eyelid muscle and damage to the nerves that control the muscles or looseness of the skin of the upper eyelid.

Phthisis Silicosis with tuberculosis.

Ptosis Drooping of the upper eye lid.

PTP Protein tyrosine phosphatase.

PTPIB Protein tyrosine phosphatase 1B.

Puerperal Pertaining to childbirth.

Puerperium Post-partum period.

Pulmonary Embolism A blockage (blood clot) of the main artery of the lung.

Purgative A substance used to cleanse or purge, especially causing the immediate evacuation of the bowel.

Purpura Is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. Also called peliosis.

Purulent Containing pus discharge.

Purulent Sputum Sputum containing, or consisting of, pus.

Pustule Small, inflamed, pus-filled lesions.

Pyelonephritis An ascending urinary tract infection that has reached the pyelum (pelvis) of the kidney.

Pyoderma Bacterial skin infection.

Pyodermatitis Refers to inflammation of the skin.

Pyorrhoea See Periodontitis.

Pyretic Referring to fever.

Pyrexia Fever of unknown origin.

Pyridoxal A chemical form of vitamin B6. See Vitamin B6.

Pyridoxamine A chemical form of vitamin B6. See Vitamin B6.

Pyridoxine A chemical form of vitamin B6. See Vitamin B6.

Pyrolysis Decomposition or transformation of a compound caused by heat. *Adj.* pyrolytic.

PYY Peptide A 36 amino acid peptide secreted by L cells of the distal small intestine and colon that inhibits gastric and pancreatic secretion.

QT Interval Is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. A prolonged QT interval is a biomarker for ventricular tachyarrhythmias and a risk factor for sudden death.

Quorum Sensing (QS) The control of gene expression in response to cell density, is used by both Gram-negative and Gram-positive bacteria to regulate a variety of physiological functions.

Radiodermatitis A skin disease associated with prolonged exposure to ionizing radiation.

Radiolysis The dissociation of molecules by radiation.

Radioprotective Serving to protect or aiding in protecting against the injurious effect of radiations.

RAGE Is the receptor for advanced glycation end products, a multiligand receptor that propagates cellular dysfunction in several inflammatory disorders, in tumours and in diabetes.

RAS See Renin-Angiotensin System or Recurrent Aphthous Stomatitis.

Rash A temporary eruption on the skin; see Uticaria.

Reactive Oxygen Species Species such as superoxide, hydrogen peroxide and hydroxyl

radical. At low levels, these species may function in cell signalling processes. At higher levels, these species may damage cellular macromolecules (such as DNA and RNA) and participate in apoptosis (programmed cell death).

Rec A Is a 38 kDa *Escherichia coli* protein essential for the repair and maintenance of DNA.

Receptor for Advanced Glycation End Products (RAGE) Is a member of the immunoglobulin superfamily of cell surface molecules; mediates neurite outgrowth and cell migration upon stimulation with its ligand, amphoterin.

Reticulocyte Nonnucleated stage in the development of the red blood cell.

Reticulocyte Lysate Cell lysate produced from reticulocytes, used as an in-vitro translation system.

Reticuloendothelial System Part of the immune system, consists of the phagocytic cells located in reticular connective tissue, primarily monocytes and macrophages.

Recurrent Aphthous Stomatitis or RAS Is a common, painful condition in which recurring ovoid or round ulcers affect the oral mucosa.

Redox Homeostasis Is considered as the cumulative action of all free radical reactions and antioxidant defenses in different tissues.

Refrigerant A medicine or an application for allaying heat, fever or its symptoms.

Renal Calculi Kidney stones.

Renal Interstitial Fibrosis Damage sustained by the kidneys' renal tubules and interstitial capillaries due to accumulation of extracellular waste in the wall of the small arteries and arterioles.

Renal Resistive Index (RRI) Measures the resistance of renal arterial flow to the kidney.

Renin Also known as an angiotensinogenase, is an enzyme that participates in the body's renin-angiotensin system (RAS).

Renin-Angiotensin System (RAS) Also called the renin-angiotensin-aldosterone system (RAAS), is a hormone system that regulates blood pressure and water (fluid) balance.

Reperfusion The restoration of blood flow to an organ or tissue that has had its blood supply cut-off, as after a heart attack.

Reporter Gene A transfected gene that produces a signal, such as green fluorescence, when it is expressed.

Resistin A cysteine-rich protein secreted by adipose tissue of mice and rats.

Resolutive A substance that induces subsidence of inflammation.

Resolvent Reduces inflammation or swelling.

Resorb To absorb or assimilate a product of the body such as an exudates or cellular growth.

Restenosis Is the reoccurrence of stenosis, a narrowing of a blood vessel, leading to restricted blood flow.

Resveratrol Is a phytoalexin produced naturally by several plants when under attack by pathogens such as bacteria or fungi. It is a potent antioxidant found in red grapes and other plants.

Retinal Ischemia Is a common cause of visual impairment and blindness.

Retinol A form of vitamin A; see Vitamin A.

Retinopathy A general term that refers to some form of non-inflammatory damage to the retina of the eye.

Revulsive Counterirritant, used for swellings.

Rhabdomyolysis Breakdown of muscle fibres leading to the release of muscle fibre content (myoglobin) into the bloodstream.

Rheumatic Pertaining to rheumatism or to abnormalities of the musculoskeletal system.

Rheumatism, Rheumatic Disorder, Rheumatic Diseases Refers to various painful medical conditions which affect bones, joints, muscles and tendons. Rheumatic diseases are characterized by the signs of inflammation—redness, heat, swelling and pain.

Rheumatoid Arthritis (RA) Is a chronic, systemic autoimmune disorder that most commonly causes inflammation and tissue damage in joints (arthritis) and tendon sheaths, together with anaemia.

Rhinitis Irritation and inflammation of some internal areas of the nose and the primary symptom of rhinitis is a runny nose.

Rhinopathy Disease or malformation of the nose.

Rhinoplasty Is surgery to repair or reshape the nose.

Rhinorrhoea Commonly known as a runny nose, characterized by an unusually significant amount of nasal discharge.

Rhinosinusitis Inflammation of the nasal cavity and sinuses.

Rho GTPases Rho-guanosine triphosphate hydrolase enzymes are molecular switches that regulate many essential cellular processes, including actin dynamics, gene transcription, cell-cycle progression and cell adhesion.

Ribosome Inactivating Proteins Proteins that are capable of inactivating ribosomes.

Rickets Is a softening of the bones in children potentially leading to fractures and deformity.

Ringworm Dermatophytosis, a skin infection caused by fungus.

Roborant Restoring strength or vigour, a tonic.

Rotavirus The most common cause of infectious diarrhoea (gastroenteritis) in young children and infants, one of several viruses that causes infections called stomach flu.

Rubefacient A substance for external application that produces redness of the skin, e.g. by causing dilation of the capillaries and an increase in blood.

Ryanodine receptor Intracellular Ca++ channels in animal tissues like muscles and neurons.

SC Abbreviation for subcutaneous, beneath the layer of skin.

S-T Segment The portion of an electrocardiogram between the end of the QRS complex and the beginning of the T wave. Elevation or depression of the S-T segment is the characteristics of myocardial ischemia or injury and coronary artery disease.

Salve Medical ointment used to soothe the head or body surface.

Sapraemia See Septicaemia.

Sarcoma Cancer of the connective or supportive tissue (bone, cartilage, fat, muscle, blood vessels) and soft tissues.

Sarcopenia Degenerative loss of skeletal muscle mass and strength associated with aging.

Sarcoplasmic Reticulum A special type of smooth endoplasmic reticulum found in smooth and striated muscle.

SARS Severe acute respiratory syndrome. The name of a potentially fatal new respiratory disease in humans which is caused by the SARS coronavirus (SARS-CoV).

Satiety State of feeling satiated, fully satisfied (appetite or desire).

Scabies A transmissible ectoparasite skin infection characterized by superficial burrows, intense pruritus (itching) and secondary infection.

Scarlatina Scarlet fever, an acute, contagious disease caused by infection with group A streptococcal bacteria.

Schwann Cells Or neurolemmocytes, are the principal supporting cells of the peripheral nervous system; they form the myelin sheath of a nerve fibre.

Schistosomiasis Is a parasitic disease caused by several species of fluke of the genus *Schistosoma*. Also known as bilharzia, bilharziosis or snail fever.

Schizophrenia A psychotic disorder (or a group of disorders) marked by severely impaired thinking, emotions and behaviours.

Sciatica a condition characterized by pain deep in the buttock often radiating down the back of the leg along the sciatic nerve.

Scleroderma a disease of the body's connective tissue. The most common symptom is a thickening and hardening of the skin, particularly of the hands and face.

Scrofula A tuberculous infection of the skin on the neck caused by the bacterium *Mycobacterium tuberculosis*.

Scrophulosis See Scrofula.

Scurf Abnormal skin condition in which small flakes or sales become detached.

Scurvy A state of dietary deficiency of vitamin C (ascorbic acid) which is required for the synthesis of collagen in humans.

Secretagogue A substance that causes another substance to be secreted.

Sedative Having a soothing, calming or tranquilizing effect; reducing or relieving stress, irritability or excitement.

Seizure The physical findings or changes in behaviour that occur after an episode of abnormal electrical activity in the brain.

Selectins Are a family of cell adhesion molecules, e.g. selectin-E, selectin-L, selectin-P.

Selenium (Se) A trace mineral that is essential to good health but required only in tiny amounts; it is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. It is found in avocado, brazil nut, lentils, sunflower seeds, tomato, whole grain cereals, seaweed, seafood and meat.

Sensorineural Bradyacuasia Hearing impairment of the inner ear resulting from damage to the sensory hair cells or to the nerves that supply the inner ear.

Sepsis A condition in which the body is fighting a severe infection that has spread via the bloodstream.

Sequela An abnormal pathological condition resulting from a disease, injury or trauma.

Serine Proteinase Peptide hydrolases which have an active centre histidine and serine involved in the catalytic process.

Serotonergic Liberating, activated by or involving serotonin in the transmission of nerve impulses.

Serotonin A monoamine neurotransmitter synthesized in serotonergic neurons in the central nervous system.

Sepsis Is a potentially fatal medical condition characterized by a whole-body inflammatory response (called a systemic inflammatory response syndrome or SIRS) that is triggered by an infection.

Septicaemia A systemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood.

Sequelae A pathological condition resulting from a prior disease, injury or attack.

Sexual Potentiator Increases sexual activity and potency and enhances sexual performance due to increased blood flow and efficient metabolism.

Sexually Transmitted Diseases (STD) Infections that are transmitted through sexual activity.

SGOT, Serum Glutamic Oxaloacetic Transaminase An enzyme that is normally present in liver and heart cells. SGOT is released into blood when the liver or heart is damaged. Also called aspartate transaminase (AST).

SGPT, Serum Glutamic Pyruvic Transaminase An enzyme normally present in serum and body tissues, especially in the liver; it is released into the serum as a result of tissue injury. Also called Alanine transaminase (ALT).

Shiga–Like Toxin A toxin produced by the bacterium *Escherichia coli* which disrupts the function of ribosomes. Also known as verotoxin.

Shiga Toxigenic *Escherichia coli* (STEC) Comprises a diverse group of organisms capable of causing severe gastrointestinal disease in humans.

Shiga Toxin A toxin produced by the bacterium *Shigella dysenteriae*, which disrupts the function of ribosomes.

Shingles Skin rash caused by the Zoster virus (same virus that causes chicken pox) and is medically termed herpes zoster.

Sialogogue Salivation promoter, a substance used to increase or promote the excretion of saliva.

Sialoproteins Glycoproteins that contain sialic acid as one of their carbohydrates.

Sialyation Reaction with sialic acid or its derivatives; used especially with oligosaccharides.

Sialyltransferases Enzymes that transfer sialic acid to nascent oligosaccharide.

Sickle-Cell Disease Is an inherited blood disorder that affects red blood cells. People with sickle-cell disease have red blood cells that contain mostly haemoglobin S, an abnormal type of haemoglobin. Sometimes these red blood cells become sickle shaped (crescent shaped) and have difficulty passing through small blood vessels.

Side Stitch Is an intense stabbing pain under the lower edge of the ribcage that occurs while exercising.

Signal Transduction Cascade Refers to a series of sequential events that transfer a signal through a series of intermediate molecules until final regulatory molecules, such as transcription factors, are modified in response to the signal.

Silicon (Si) Is required in minute amounts by the body and is important for the development of healthy hair and the prevention of nervous disorders. Lettuce is the best natural source of Silicon.

Sinapism Signifies an external application, in the form of a soft plaster, or poultice.

Sinusitis Inflammation of the nasal sinuses.

SIRC Cells Statens Serum Institut Rabbit Cornea (SIRC) cell line.

SIRT 1 Stands for sirtuin (silent mating type information regulation 2 homolog) 1. It is an enzyme that deacetylates proteins that contribute to cellular regulation.

Sirtuin Also called Sir2 proteins a class of proteins that possess either histone deacetylase or mono-ribosyltransferase activity.

6-Keto-PGF1 Alpha A physiologically active and stable hydrolysis product of Epoprostenol, found in nearly all mammalian tissues.

Skp1 (S-Phase Kinase-Associated Protein 1) Is a core component of SCF ubiquitin ligases and mediates protein degradation.

Smads A family of intracellular proteins that mediate signalling by members of the TGF-beta (transforming growth factor beta) superfamily.

Smad2/3 A key signalling molecule for TGF-beta.

Smad7 A TGFβ type 1 receptor antagonist.

Smallpox Is an acute, contagious and devastating disease in humans caused by *Variola* virus and have resulted in high mortality over the centuries.

Snuff Powder inhaled through the nose.

SOD Superoxide dismutase, is an enzyme that repairs cells and reduces the damage done to them by superoxide, the most common free radical in the body.

Sodium (Na) Is an essential nutrient required for health. Sodium cations are important in neuron (brain and nerve) function and in influencing osmotic balance between cells and the interstitial fluid and in maintenance of total body fluid homeostasis. Extra intake may cause a harmful effect on health. Sodium is naturally supplied by salt intake with food.

Soleus Muscle Smaller calf muscle lower down the leg and under the gastrocnemius muscle.

Somites Mesodermal structures formed during embryonic development that give rise to segmented body parts such as the muscles of the body wall.

Soporific A sleep-inducing drug.

SOS Response A global response to DNA damage in which the cell cycle is arrested and DNA repair and mutagenesis are induced.

Soyasapogenins Triterpenoid products obtained from the acid hydrolysis of soyasaponins, designated soyasapogenols A, B, C, D and E.

Soyasaponins Bioactive saponin compounds found in many legumes.

Spasmogenic Inducing spasm.

Spasmolytic Checking spasms; see Antispasmodic.

Spermatorrhoea Medically an involuntary ejaculation/drooling of semen usually nocturnal emissions.

Spermidine An important polyamine in DNA synthesis and gene expression.

Spina Bifida A congenital birth defect caused by the incomplete closing of the embryonic neural tube.

Sphingolipid A member of a class of lipids derived from the aliphatic amino alcohol, sphingosine.

Spleen Organ that filters blood and prevents infection.

Spleen Tyrosine Kinase (SYK) Is an enigmatic protein tyrosine kinase functional in a number of diverse cellular processes such as the regulation of immune and inflammatory responses.

Splenitis Inflammation of the spleen.

Splenocyte Is a monocyte, one of the five major types of white blood cell, and is characteristically found in the splenic tissue.

Splenomegaly Is an enlargement of the spleen.

Sprain To twist a ligament or muscle of a joint without dislocating the bone.

Sprue Is a chronic disorder of the small intestine caused by sensitivity to gluten, a protein found in wheat and rye and to a lesser extent oats and barley . It causes poor absorption by the intestine of fat, protein, carbohydrates, iron, water and vitamins A, D, E and K.

Sputum Matter coughed up and usually ejected from the mouth, including saliva, foreign material, and substances such as mucus or phlegm, from the respiratory tract.

SREBP-1 See Sterol Regulatory Element-Binding Protein-1.

Stanch To stop or check the flow of a bodily fluid like blood from a wound.

Statin A type of lipid-lowering drug.

STAT3 Signal transducer and activator of transcription 3, a transcription factor, plays a key role in many cellular processes such as cell growth and apoptosis.

Status Epilepticus Refers to a life-threatening condition in which the brain is in a state of persistent seizure.

STD Sexually transmitted disease.

Steatorrhoea Is the presence of excess fat in faeces which appear frothy, foul smelling and floats because of the high fat content.

Steatohepatitis Liver disease, characterized by inflammation of the liver with fat accumulation in the liver.

Steatosis Refers to the deposition of fat in the interstitial spaces of an organ like the liver, fatty liver disease.

Sterility Inability to produce offspring. Also called asepsis.

Steroidogenic Relating to steroidogenesis.

Steroidogenesis The production of steroids, as by the adrenal glands.

Sterol Regulatory Element-Binding Protein-1 (SREBP1) Is a key regulator of the transcription of numerous genes that function in the metabolism of cholesterol and fatty acids.

Stimulant A substance that promotes the activity of a body system or function.

Stomachic Digestive stimulant, an agent that stimulates or strengthens the activity of the stomach; used as a tonic to improve the appetite and digestive processes.

Stomatitis Oral inflammation and ulcers, may be mild and localized or severe, widespread and painful.

Stomatology Medical study of the mouth and its diseases.

Stool Faeces.

Strangury Is the painful passage of small quantities of urine which are expelled slowly by straining with severe urgency; it is usually accompanied with the unsatisfying feeling of a remaining volume inside and a desire to pass something that will not pass.

Straub Tail Condition in which an animal carries its tail in an erect (vertical or nearly vertical) position.

STREPs Sterol regulatory element binding proteins, a family of transcription factors that regulate lipid homeostasis by controlling the expression of a range of enzymes required for endogenous cholesterol, fatty acid, triacylglycerol and phospholipid synthesis.

Stria Terminalis A structure in the brain consisting of a band of fibres running along the lateral margin of the ventricular surface of the thalamus.

Striae Gravidarum A cutaneous condition characterized by stretch marks on the abdomen during and following pregnancy.

Stricture An abnormal constriction of the internal passageway within a tubular structure such as a vessel or duct

Strongyloidiasis An intestinal parasitic infection in humans caused by two species of the parasitic nematode *Strongyloides.* The nematode or round worms are also called thread worms.

Styptic A short stick of medication, usually anhydrous aluminium sulphate (a type of alum) or titanium dioxide, which is used for stanching blood by causing blood vessels to contract at the site of the wound. Also called haemostatic pencil. See Antihaemorrhagic.

Subarachnoid Haemorrhage Is bleeding in the area between the brain and the thin tissues that cover the brain.

Substance P A neuropeptide that functions as a neurotransmitter and neuromodulator and is associated with the sensation of pain.

Substantia Nigra Is a dark-coloured brain structure located in the midbrain that play an important role in reward, addiction and movement.

Sudatory Medicine that causes or increases sweating. Also see Sudorific.

Sudorific A substance that causes sweating.

Sulphur Sulphur is an essential component of all living cells. Sulphur is important for the synthesis of sulphur-containing amino acids, all polypeptides, proteins and enzymes such as glutathione, an important sulphur-containing tripeptide which plays a role in cells as a source of chemical reduction potential. Sulphur is also important for hair formation. Good plant sources are garlic, onion, leeks

and other Alliaceous vegetables, Brassicaceous vegetables like cauliflower, cabbages, Brussels sprout, kale, legumes (beans, green and red gram, soybeans), horse radish, water cress and wheat germ.

Superior Mesenteric Artery (SMA) Arises from the anterior surface of the abdominal aorta, just inferior to the origin of the celiac trunk, and supplies the intestine from the lower part of the duodenum to the left colic flexure and the pancreas.

Superoxidae Mutase (SOD) Antioxidant enzyme.

Suppuration The formation of pus, the act of becoming converted into and discharging pus.

Supraorbital Located above the orbit of the eye.

Sural Nerve Sensory nerve comprising collateral branches off of the common tibial and common fibular nerve.

SYK, Spleen Tyrosine Kinase Is a human protein and gene. SYK plays a similar role in transmitting signals from a variety of cell surface receptors including CD74, Fc Receptor and integrins.

Sympathetic Nervous System The part of the autonomic nervous system originating in the thoracic and lumbar regions of the spinal cord that in general inhibits or opposes the physiological effects of the parasympathetic nervous system, as in tending to reduce digestive secretions or speed up the heart.

Synaptic Plasticity The ability of neurons to change the number and strength of their synapses.

Synaptogenesis The formation of synapses.

Synaptoneurosomes Purified synapses containing the pre- and postsynaptic termini.

SynaptosoAmes Isolated terminal of a neuron.

Syncope Fainting, sudden loss of consciousness followed by the return of wakefulness.

Syndactyly Webbed toes, a condition where two or more digits are fused together.

Syneresis Expulsion of liquid from a gel, as contraction of a blood clot and expulsion of liquid.

Syngeneic Genetically identical or closely related, so as to allow tissue transplant; immunologically compatible.

Synovial Lubricating fluid secreted by synovial membranes, as those of the joints.

Synoviocyte Located in the synovial membrane, there are two types: type A cells are more numerous, have phagocytic characteristics and produce degradative enzymes, and type B cells produce synovial fluid, which lubricates the joint and nurtures nourishes the articular cartilage.

Syphilis Is perhaps the best known of all the STDs. Syphilis is transmitted by direct contact with infection sores, called chancres, syphitic skin rashes or mucous patches on the tongue and mouth during kissing, necking, petting or sexual intercourse. It can also be transmitted from a pregnant woman to a foetus after the fourth month of pregnancy.

System Lupus Erythematosus A long-term autoimmune disorder that may affect the skin, joints, kidneys, brain and other organs. Symptoms may include chest pain, fatigue, fever, hair loss, malaise, mouth sores, sensitivity to sunlight and skin rash (butterfly rash).

Systolic The blood pressure when the heart is contracting. It is specifically the maximum arterial pressure during contraction of the left ventricle of the heart.

T cells Or T lymphocytes, a type of white blood cell that plays a key role in the immune system.

Tachyarrhythmia Any disturbance of the heart rhythm in which the heart rate is abnormally increased.

Tachycardia A false heart rate applied to adults to rates over 100 beats per minute.

Tachykinins Neuropeptide transmitters that are widely distributed and active in the central nervous system and periphery, rapidly acting secretagogues and cause smooth muscle contraction and vasodilation (hypotension).

Tachyphylaxia A decreased response to a medicine given over a period of time so that larger doses are required to produce the same response.

Tachypnea Abnormally fast breathing.

Taenia A parasitic tapeworm or flatworm of the genus, *Taenia.*

Taeniacide An agent that kills tapeworms.

Tardive Dyskinesia A disorder characterized by repetitive, involuntary, purposeless movements in the body such as grimacing, tongue protrusion, lip smacking, puckering and pursing

of the lips and rapid eye blinking. Rapid, involuntary movements of the limbs, torso and fingers may also occur.

Tau Is a class of microtubule-associated protein (MAP) in neuronal and glial cells.

Tau-1 (Ser198/199/202), pS396 (Ser396), and pS214 (Ser214) Epitopes Serine phosphorylation sites of tau-1.

Tau Phosphorylation Plays an important role in neurodegenerative diseases and regulated by protein kinases and phosphatases.

TBARS See Thiobarbituric Acid Reactive Substances.

T Cell A type of white blood cell that attacks virus-infected cells, foreign cells and cancer cells.

TCA Cycle See Tricarboxylic Acid Cycle.

TCID50 Median tissue culture infective dose; that amount of a pathogenic agent that will produce pathological change in 50 % of cell cultures.

Telencephalon The cerebral hemispheres, the largest divisions of the human brain.

Teletherapy A noninvasive procedure using external beam radiotherapy treatments.

Telomerase Enzyme that acts on parts of chromosomes known as telomeres.

Temporomandibular Joint Fisorder (TMJD or TMD Syndrome) A disorder characterized by acute or chronic inflammation of the temporomandibular joint that connects the mandible to the skull.

Tendonitis Is inflammation of a tendon.

Tenesmus A strong desire to defaecate.

Teratogen Is an agent that can cause malformations of an embryo or foetus. *Adj.* teratogenic.

Testicular Torsion Twisting of the spermatic cord, which cuts off the blood supply to the testicle and surrounding structures within the scrotum.

Tetanus An acute, potentially fatal disease caused by tetanus bacilli multiplying at the site of an injury and producing an exotoxin that reaches the central nervous system producing prolonged contraction of skeletal muscle fibres. Also called lockjaw.

Tete Acute dermatitis caused by both bacterial and fungal infection.

Tetter Any of a number of skin diseases.

TGF-Beta Transforming growth factor beta is a protein that controls proliferation, cellular differentiation and other functions in most cells.

Th cells or T Helper Cells A subgroup of lymphocytes that helps other white blood cells in immunologic processes.

Th 1 Cells Helper cells that play an important role in the immune system.

Th 17 Cells A subset of T helper cells producing interleukin 17.

Thalassemia Major Is a genetic blood disorder that causes the body to manufacture an abnormal form of haemoglobin.

Thelarche The beginning of secondary (postnatal) breast development, usually occurring at the beginning of puberty in girls.

Thermogenic Tending to produce heat, applied to drugs or food (fat burning food).

Thermogenesis Is the process of heat production in organisms.

Thermonociceptors Or thermal nociceptors, sensory receptors that are stimulated by noxious heat or cold at various temperature.

Thiobarbituric Acid Reactive Substances (TBARS) A well-established method for screening and monitoring lipid peroxidation.

Thixotropy The property exhibited by certain gels of becoming fluid when stirred or shaken and returning to the semisolid state upon standing.

3-β-HSD Or 3-β-hydroxysteroid dehydrogenase/δ-5-4 isomerase is an enzyme that catalyzes the synthesis of progesterone from pregnenolone.

Thrombocythaemia A blood condition characterized by a high number of platelets in the blood.

Thrombocytopenia A condition when the bone marrow does not produce enough platelets (thrombocytes) like in leukaemia.

Thromboembolism Formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the bloodstream to plug another vessel. Cf. deep vein thrombosis.

Thrombogenesis Formation of a thrombus or blood clot.

Thrombophlebitis Occurs when there is inflammation and clot in a surface vein.

Thromboplastin An enzyme liberated from blood platelets that converts prothrombin into

thrombin as blood starts to clot. Also called thrombokinase.

Thrombosis The formation or presence of a thrombus (clot).

Thromboxanes Any of several compounds, originally derived from prostaglandin precursors in platelets that stimulate aggregation of platelets and constriction of blood vessels.

Thromboxane B2 The inactive product of thromboxane.

Thrombus A fibrinous clot formed in a blood vessel or in a chamber of the heart.

Thrush A common mycotic infection caused by yeast, *Candida albicans*, in the digestive tract or vagina. In children it is characterized by white spots on the tongue.

Thymocytes Are T cell precursors which develop in the thymus.

Thyrotoxicosis Or hyperthyroidism, an overactive thyroid gland, producing excessive circulating free thyroxine and free triiodothyronine, or both.

Tight Junction Associated areas of two cells whose membranes join together forming a virtually impermeable barrier to fluid.

TIMP-3 A human gene belongs to the tissue inhibitor of matrix metalloproteinases (MMP) gene family. See MMP.

Tincture Solution of a drug in alcohol.

Tinea Ringworm, fungal infection on the skin.

Tinea favosa See Favus.

Tinea cruris Ringworm of the groin.

Tinea imbricata (also called Tokelau) An eruption characterized by concentric rings of overlapping scales forming papulosquamous patches scattered over the body; it occurs in tropical climates especially prevalent in southwest Polynesia and is caused by the fungus *Trichophyton concentricum*.

Tinea pedis Fungal infection of the foot. Also called Athletes' foot.

Tinnitus A noise in the ears, as ringing, buzzing, roaring, clicking, etc.

Tisane An herbal infusion used as tea or for medicinal purposes.

Tissue Plasminogen Activator (t-PA) A serine protease involved in the breakdown of blood clots.

TNF Alpha Cachexin or cachectin and formally known as tumour necrosis factor-alpha, a cytokine involved in systemic inflammation. Primary role of TNF is in the regulation of immune cells. TNF is also able to induce apoptotic cell death, to induce inflammation, and to inhibit tumorigenesis and viral replication.

Tocolytics Medications used to suppress premature labour.

Tocopherol Fat-soluble organic compounds belonging to vitamin E group. See Vitamin E.

Tocotrienol Fat-soluble organic compounds belonging to vitamin E group. See Vitamin E.

Tolerogenic Producing immunological tolerance.

Toll-Like Receptors (TLRs) A class of proteins that play a key role in the innate immune system.

Tonic Substance that acts to restore, balance, tone, strengthen or invigorate a body system without overt stimulation or depression.

Tonic Clonic Seizure A type of generalized seizure that affects the entire brain.

Tonsillitis An inflammatory condition of the tonsils due to bacteria, allergies or respiratory problems.

TOP2 A Topoisomerase II alpha enzyme.

Topoisomerases A class of enzymes involved in the regulation of DNA supercoiling.

Topoisomerase Inhibitors A new class of anticancer agents with a mechanism of action aimed at interrupting DNA replication in cancer cells.

Total Parenteral Nutrition (TPN) Is a method of feeding that bypasses the gastrointestinal tract.

Toxemia Is the presence of abnormal substances in the blood, but the term is also used for a serious condition in pregnancy that involves hypertension and proteinuria. Also called pre-eclampsia.

Tracheitis Is a bacterial infection of the trachea; also known as bacterial tracheitis or acute bacterial tracheitis.

Trachoma A contagious disease of the conjunctiva and cornea of the eye, producing painful sensitivity to strong light and excessive tearing.

TRAIL Acronym for tumour necrosis factor-related apoptosis-inducing ligand, is a cytokine that preferentially induces apoptosis in tumour cells.

Tranquilizer A substance drug used in calming person suffering from nervous tension or anxiety.

Transaminase Also called aminotransferase is an enzyme that catalyzes a type of reaction between an amino acid and an α-keto acid.

Transaminitis Increase in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) to >5 times the upper limit of normal.

Transcatheter Arterial Chemoembolization (TACE) Is an interventional radiology procedure involving percutaneous access of to the hepatic artery and passing a catheter through the abdominal artery aorta followed by radiology. It is used extensively in the palliative treatment of unresectable hepatocellular carcinoma (HCC)

Transcriptional Activators Are proteins that bind to DNA and stimulate transcription of nearby genes.

Transcriptional Coactivator PGC-1 A potent transcriptional coactivator that regulates oxidative metabolism in a variety of tissues.

Transcriptome Profiling To identify genes involved in peroxisome assembly and function.

Transforming Growth Factor Beta (TGF-β) A protein that controls proliferation, cellular differentiation and other functions in most cells.

Transient Receptor Potential Vanilloid 1 (TRPV1) Receptor also known as capsaicin receptor and vanilloid receptor, is a Ca 2+ permeable nonselective cation channel localized on a subset of primary sensory neurons and can be activated by physical and chemical stimuli.

TRAP 6 Thrombin receptor-activating peptide with 6 amino acids.

Tremorine A chemical that produces a tremor resembling Parkinsonian tremor.

Tremulous Marked by trembling, quivering or shaking.

Triacylglycerols Or triacylglyceride, is a glyceride in which the glycerol is esterified with three fatty acids.

Tricarboxylic Acid Cycle (TCA Cycle) A series of enzymatic reactions in aerobic organisms involving oxidative metabolism of acetyl units and producing high-energy phosphate compounds, which serve as the main source of cellular energy. Also called citric acid cycle, Krebs cycle.

Trichophytosis Infection by fungi of the genus *Trichophyton*.

Trigeminal Neuralgia (TN) Is a neuropathic disorder of one or both of the facial trigeminal nerves, also known as prosopalgia.

Triglycerides A type of fat (lipids) found in the blood stream.

Trismus Continuous contraction of the muscles of the jaw, specifically as a symptom of tetanus, or lockjaw; inability to open mouth fully.

TrKB receptor Also known as TrKB tyrosine kinase, a protein in humans that acts as a catalytic receptor for several neurotrophins.

Trolox Equivalent Measures the antioxidant capacity of a given substance, as compared to the standard, Trolox also referred to as TEAC (Trolox equivalent antioxidant capacity).

Trypanocidal Destructive to trypanosomes.

Trypanosomes Protozoan of the genus *Trypanosoma.*

Trypanosomiasis Human disease or an infection caused by a trypanosome.

Trypsin An enzyme of pancreatic juice that hydrolyzes proteins into smaller polypeptide units.

Trypsin Inhibitor Small protein synthesized in the exocrine pancreas which prevents conversion of trypsinogen to trypsin, so protecting itself against trypsin digestion.

TRPV1 See Transient Receptor Potential Vanilloid 1.

Tuberculosis (TB) Is a bacterial infection of the lungs caused by a bacterium called *Mycobacterium tuberculosis,* characterized by the formation of lesions (tubercles) and necrosis in the lung tissues and other organs.

Tumorigenesis Formation or production of tumours.

Tumour An abnormal swelling of the body other than those caused by direct injury.

Tussis A cough.

Tympanic Membrane Eardrum.

Tympanitis Infection or inflammation of the inner ear.

Tympanophonia Increased resonance of one's own voice, breath sounds, arterial murmurs, etc., noted especially in disease of the middle ear.

Tympanosclerosis See Myringosclerosis.

Tyrosinase A copper containing enzyme found in animals and plants that catalyzes the oxidation of phenols (such as tyrosine) and the production of melanin and other pigments from tyrosine by oxidation.

Ubiquitin Ligase Also called an E3 ubiquitin ligase, is a protein that targets other proteins to be broken down (degraded) within cells.

UCP1 An uncoupling protein found in the mitochondria of brown adipose tissue used to generate heat by non-shivering thermogenesis.

UCP-2 Enzyme Uncoupling protein 2 enzyme. A mitochondrial protein expressed in adipocytes.

Ulcer An open sore on an external or internal body surface usually accompanied by disintegration of tissue and pus.

Ulcerative Colitis Is one of 2 types of inflammatory bowel disease—a condition that causes the bowel to become inflamed and red.

Ulemorrhagia Bleeding of the gums.

Ulitis Inflammation of the gums.

Unguent Ointment.

Unilateral Ureteral Obstruction Unilateral blockage of urine flow through the ureter of 1 kidney, resulting in a backup of urine, distension of the renal pelvis and calyces and hydronephrosis.

Uraemia An excess in the blood of urea, creatinine and other nitrogenous end products of protein and amino acids metabolism, more correctly referred to as azotaemia.

Urethra Tube conveying urine from the bladder to the external urethral orifice.

Urethritis Is an inflammation of the urethra caused by infection.

Uricemia An excess of uric acid or urates in the blood.

Uricosuric Promoting the excretion of uric acid in the urine.

Urinary Pertaining to the passage of urine.

Urinogenital Relating to the genital and urinary organs or functions.

Urodynia Pain on urination.

Urokinase Also called urokinase-type plasminogen (u-PA), is a serine protease enzyme in human urine that catalyzes the conversion of plasminogen to plasmin. It is used clinically as a thrombolytic agent.

Urokinase-Type Plasminogen (u-PA) Plays a key role in tumour invasion and metastasis. Also see Urokinase.

Urolithiasis Formation of stone in the urinary tract (kidney bladder or urethra).

Urticant A substance that causes wheals to form.

Urticaria Or hives, is a skin condition, commonly caused by an allergic reaction, that is characterized by raised red skin welts.

Uterine Relating to the uterus.

Uterine Prolapse Occurs when weakened or damaged muscles and ligaments allow the uterus to slip into the vagina.

Uterine Relaxant An agent that relaxes the muscles in the uterus.

Uterine Stimulant An agent that stimulates the uterus (and often employed during active childbirth).

Uterotonic Giving muscular tone to the uterus.

Uterotrophic Causing an effect on the uterus.

Uterus Womb.

Vaginal Dystrophy A condition in which the outer part of the vagina becomes dry and the skin thickens or thins.

Vaginitis Infectious or non-infectious inflammation of the vaginal mucosa.

Vaginopathy Any disease of the vagina.

Vagotomy The surgical cutting of the vagus nerve to reduce acid secretion in the stomach.

Vagus nerve A cranial nerve, that is, a nerve connected to the brain. The vagus nerve has branches to most of the major organs in the body, including the larynx, throat, windpipe, lungs, heart and most of the digestive system

Variola Or smallpox, a contagious disease unique to humans, caused by either of two virus variants, *Variola major* and *Variola minor*. The disease is characterized by fever, weakness and skin eruption with pustules that form scabs that leave scars.

Varicose Veins Are veins that have become enlarged and twisted.

Vasa Vasorum Is a network of small blood vessels that supply large blood vessels. *Pl.* vasa vasori.

Vascular Endothelial Growth Factor (VEGF) A polypeptide chemical produced by cells that stimulates the growth of new blood vessels.

Vasculogenesis The process of blood vessel formation occurring by a de novo production of endothelial cells.

Vasoconstrictor Drug that causes constriction of blood vessels.

Vasodilator Drug that causes dilation or relaxation of blood vessels.

Vasodilatory Causing the widening of the lumen of blood vessels.

Vasomotor Symptoms Menopausal symptoms characterized by hot flushes and night sweats.

Vasospasm Refers to a condition in which blood vessels spasm, leading to vasoconstriction and subsequently to tissue ischemia and death (necrosis).

VCAM-1 (Vascular Cell Adhesion Molecule-1) Also known as CD106, contains six or seven immunoglobulin domains and is expressed on both large and small vessels only after the endothelial cells are stimulated by cytokines.

VEGF Vascular endothelial growth factor.

Venereal Disease (VD) Term given to the diseases syphilis and gonorrhoea.

Venule A small vein, especially one joining capillaries to larger veins.

Vermifuge A substance used to expel worms from the intestines.

Verotoxin A Shiga-like toxin produced by *Escherichia coli,* which disrupts the function of ribosomes, causing acute renal failure.

Verruca A contagious and painful wart on the sole of the foot.

Verruca plana Is a reddish-brown or flesh-coloured, slightly raised, flat-surfaced, well-demarcated papule on the hand and face. Also called flat wart.

Verruca vulgaris Small painless warts on the skin caused by the human papillomavirus.

Vertigo An illusory, sensory perception that the surroundings or one's own body are revolving; dizziness.

Very-Low-Density Lipoprotein (VLDL) A type of lipoprotein made by the liver. VLDL is one of the five major groups of lipoproteins (chylomicrons, VLDL, intermediate-density lipoprotein, low-density lipoprotein, high-density lipoprotein (HDL)) that enable fats and cholesterol to move within the water-based solution of the bloodstream. VLDL is converted in the bloodstream to low-density lipoprotein (LDL).

Vesical Calculus Calculi (stones) in the urinary bladder

Vesicant A substance that causes tissue blistering.

Vestibular Relating to the sense of balance.

Vestibular Disorders Includes symptoms of dizziness, vertigo and imbalance; it can be result from or worsened by genetic or environmental conditions.

Vestibular System Includes parts of the inner ear and brain that process sensory information involved with controlling balance and eye movement.

Vibrissa Stiff hairs that are located especially about the nostrils.

Viremia A medical condition where viruses enter the bloodstream and hence have access to the rest of the body.

Visceral Fat Intra-abdominal fat, is located inside the peritoneal cavity, packed in between internal organs and torso.

Vitamin Any complex, organic compound, found in various food or sometimes synthesized in the body, required in tiny amounts and are essential for the regulation of metabolism, normal growth and function of the body.

Vitamin A Retinol, fat-soluble vitamins that play an important role in vision, bone growth, reproduction, cell division and cell differentiation and help regulate the immune system in preventing or fighting off infections. Vitamin A that is found in colourful fruits and vegetables is called provitamin A carotenoid. They can be made into retinol in the body. Deficiency of vitamin A results in night blindness and keratomalacia.

Vitamin B1 Also called thiamine, water-soluble vitamins, dissolve easily in water, and in general, are readily excreted from the body they are not readily stored, consistent daily intake is important. It functions as coenzyme in the

metabolism of carbohydrates and branched chain amino acids and other cellular processes. Deficiency results in beri-beri disease.

Vitamin B2 Also called riboflavin, an essential water-soluble vitamin that functions as coenzyme in redox reactions. Deficiency causes ariboflavinosis.

Vitamin B3 Comprises niacin and niacinamide, water-soluble vitamin that function as coenzyme or co-substrate for many redox reactions and is required for energy metabolism. Deficiency causes pellagra.

Vitamin B5 Also called pantothenic acid, a water-soluble vitamin that function as coenzyme in fatty acid metabolism. Deficiency causes paraesthesia.

Vitamin B6 Water-soluble vitamin, exists in three major chemical forms: pyridoxine, pyridoxal and pyridoxamine. Vitamin B6 is needed in enzymes involved in protein metabolism, red blood cell metabolism, efficient functioning of nervous and immune systems and haemoglobin formation. Deficiency causes anaemia and peripheral neuropathy.

Vitamin B7 Also called biotin or vitamin H, an essential water-soluble vitamin, is involved in the synthesis of fatty acids amino acids and glucose, in energy metabolism. Biotin promotes normal health of sweat glands, bone marrow, male gonads, blood cells, nerve tissue, skin and hair. Deficiency causes dermatitis and enteritis.

Vitamin B9 Also called folic acid, an essential water-soluble vitamin. Folate is especially important during periods of rapid cell division and growth such as infancy and pregnancy. Deficiency during pregnancy is associated with birth defects such as neural tube defects. Folate is also important for production of red blood cells and prevent anaemia. Folate is needed to make DNA and RNA, the building blocks of cells. It also helps prevent changes to DNA that may lead to cancer.

Vitamin B12 A water-soluble vitamin, also called cobalamin as it contains the metal cobalt. It helps maintain healthy nerve cells and red blood cells and in DNA production. Vitamin B12 is bound to the protein in food. Deficiency causes megaloblastic anaemia.

Vitamin C Also known as ascorbic acid is an essential water-soluble vitamin. It functions as cofactor for reactions requiring reduced copper or iron metalloenzyme and as a protective antioxidant. Deficiency of vitamin C causes scurvy.

Vitamin D A group of fat-soluble, prohormone vitamin, the two major forms of which are vitamin D2 (or ergocalciferol) and vitamin D3 (or cholecalciferol). Vitamin D obtained from sun exposure, food and supplements is biologically inert and must undergo two hydroxylations in the body for activation. Vitamin D is essential for promoting calcium absorption in the gut and maintaining adequate serum calcium and phosphate concentrations to enable normal growth and mineralization of bone and prevent hypocalcemic tetany. Deficiency causes rickets and osteomalacia. Vitamin D has other roles in human health, including modulation of neuromuscular and immune function, reduction of inflammation and modulation of many genes encoding proteins that regulate cell proliferation, differentiation and apoptosis.

Vitamin E Is the collective name for a group of fat-soluble compounds and exists in eight chemical forms (alpha-, beta-, gamma- and delta-tocopherol and alpha-, beta-, gamma- and delta-tocotrienol). It has pronounced antioxidant activities stopping the formation of reactive oxygen species when fat undergoes oxidation and help prevent or delay the chronic diseases associated with free radicals. Besides its antioxidant activities, vitamin E is involved in immune function, cell signalling, regulation of gene expression and other metabolic processes. Deficiency is very rare but can cause mild haemolytic anaemia in newborn infants.

Vitamin K A group of fat**-**soluble vitamin and consist of vitamin K1 which is also known as phylloquinone or phytomenadione (also called phytonadione) and vitamin K2 (menaquinone, menatetrenone). Vitamin K plays an important role in blood clotting. Deficiency is very rare but can cause bleeding diathesis.

Vitamin P A substance or mixture of substances obtained from various plant sources, identified

as citrin or a mixture of bioflavonoids, thought to but not proven to be useful in reducing the extent of haemorrhage.

Vitiligo A chronic skin disease that causes loss of pigment, resulting in irregular pale patches of skin. It occurs when the melanocytes, cells responsible for skin pigmentation, die or are unable to function. Also called leucoderma.

Vitreoretinopathy See Proliferative Vitreoretinopathy.

VLA-4 Very late antigen-4, expressed by most leukocytes, but it is observed on neutrophils under special conditions.

VLDL See Very Low-Density Lipoproteins.

Vomitive Substance that causes vomiting.

Vulnerary Wound healer, a substance used to heal wounds and promote tissue formation.

Vulva-Vaginal Erythema Abnormal redness and inflammation of the skin in the vagina.

Wart An infectious skin tumour caused by a viral infection.

Welt See Wheal.

Wheal A firm, elevated swelling of the skin. Also called a weal or welt.

White fat White adipose tissue (WAT) in mammals, store of energy. Cf. brown fat.

Whitlow Painful infection of the hand involving 1 or more fingers that typically affects the terminal phalanx.

Whooping Cough Acute infectious disease usually in children caused by a *Bacillus* bacterium and accompanied by catarrh of the respiratory passages and repeated bouts of coughing.

Wnt signalling Pathway Is a network of proteins involved in embryogenesis and cancer and also in normal physiological processes.

X-Linked Agammaglobulinemia Also known as X-linked hypogammaglobulinaemia, XLA, Bruton type agammaglobulinemia, Bruton syndrome or sex-linked agammaglobulinemia; a rare x-linked genetic disorder that affects the body's ability to fight infection.

Xanthine Oxidase A flavoprotein enzyme containing a molybdenum cofactor (Moco) and (Fe2S2) clusters, involved in purine metabolism. In humans, inhibition of xanthine oxidase reduces the production of uric acid and prevents hyperuricemia and gout.

Xanthones Unique class of biologically active phenol compounds with the molecular formula C13H8O2 possessing antioxidant properties, discovered in the mangosteen fruit.

Xenobiotics A chemical (as a drug, pesticide or carcinogen) that is foreign to a living organism.

Xenograft A surgical graft of tissue from one species to an unlike species.

Xerophthalmia A medical condition in which the eye fails to produce tears.

Yaws An infectious tropical infection of the skin, bones and joints caused by the spirochete bacterium *Treponema pertenue,* characterized by papules and papilloma with subsequent deformation of the skins, bone and joints. Also called framboesia.

yGCN5 A histone acetyl transferase (HAT) that plays a role in regulation of transcription, cell cycle progression and differentiation.

Yellow Fever Is a viral disease that is transmitted to humans through the bite of infected mosquitoes. Illness ranges in severity from an influenza-like syndrome to severe hepatitis and haemorrhagic fever. Yellow fever virus (YFV) is maintained in nature by mosquito-borne transmission between nonhuman primates.

Zeaxanthin A common carotenoid, found naturally as coloured pigments in many fruit vegetables and leafy vegetables. It is important for good vision and is one of the two carotenoids contained within the retina of the eye. Within the central macula, zeaxanthin predominates, whereas in the peripheral retina, lutein predominates.

Zinc (Zn) Is an essential mineral for health. It is involved in numerous aspects of cellular metabolism: catalytic activity of enzymes, immune function, protein synthesis, wound healing, DNA synthesis and cell division. It also supports normal growth and development during pregnancy, childhood and adolescence and is required for proper sense of taste and smell. Dietary sources include beans, nuts, pumpkin seeds, sunflower seeds, whole wheat bread and animal sources.

ZO1 Protein A high molecular weight tight junction-associated protein.

Scientific Glossary

Abaxial Facing away from the axis, as of the surface of an organ.

Abortive Imperfectly formed.

Abscission Shedding of leaves, flowers or fruits following the formation of the abscission zone.

Acaulescent Lacking a stem or stem very much reduced.

Accrescent Increasing in size after flowering or with age.

Achene A dry, small, one-seeded, indehiscent one-seeded fruit formed from a superior ovary of one carpel as in sunflower.

Acid Soil Soil that maintains a pH of less than 7.0.

Acidulous Acid or sour in taste.

Actinomorphic Having radial symmetry, capable of being divided into symmetrical halves by any plane, refers to a flower, calyx or corolla.

Aculeate Having sharp prickles.

Acuminate Tapering gradually to a sharp point.

Acute (Botany) Tapering at an angle of less than 90° before terminating in a point as of leaf apex and base.

Adaxial Side closest to the stem axis.

Aldephous Having stamens united together by their filaments.

Adherent Touching without organic fusion as of floral parts of different whorls.

Adnate United with another unlike part as of stamens attached to petals.

Adpressed Lying close to another organ but not fused to it.

Adventitious Arising in abnormal positions, e.g. roots arising from the stem, branches or leaves; buds arising elsewhere than in the axils of leaves.

Adventive Not native to and not fully established in a new habitat or environment; locally or temporarily naturalized, e.g. an adventive weed.

Aestivation Refers to positional arrangement of the floral parts in the bud before it opens.

Akinete A thick-walled dormant cell derived from the enlargement of a vegetative cell. It serves as a survival structure.

Alfisols Soil with a clay-enriched subsoil and relatively high native fertility, having undergone only moderate leaching, containing aluminium, iron and with at least 35 % base saturation, meaning that calcium, magnesium and potassium are relatively abundant.

Alkaline Soil Soil that maintains a pH above 7.0, usually containing large amounts of calcium, sodium and magnesium and is less soluble than acidic soils.

Alkaloids Naturally occurring bitter, complex organic-chemical compounds containing basic nitrogen and oxygen atoms and having various pharmacological effects on humans and other animals.

Alternate Leaves or buds that are spaced along opposite sides of stem at different levels.

Allomorphic With a shape or form different from the typical.

Alluvial Soil A fine-grained fertile soil deposited by water flowing over flood plains or in river beds.

Alluvium Soil or sediments deposited by a river or other running water.

Amplexicaul Clasping the stem as base of certain leaves.

Anatomizing Interconnecting network as applied to leaf veins.

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Andisols Are soils formed in volcanic ash and containing high proportions of glass and amorphous colloidal materials.

Androdioecious With male flowers and bisexual flowers on separate plants.

Androecium Male parts of a flower, comprising the stamens of one flower.

Androgynophore A stalk bearing both the androecium and gynoecium above the perianth of the flower.

Androgynous With male and female flowers in distinct parts of the same inflorescence.

Andromonoecious Having male flowers and bisexual flowers on the same plant.

Angiosperm A division of seed plants with the ovules borne in an ovary.

Annual A plant which completes its life cycle within a year.

Annular Shaped like or forming a ring.

Annulus Circle or ringlike structure or marking; the portion of the corolla which forms a fleshy, raised ring.

Anthelate An open, paniculate cyme.

Anther The part of the stamen containing pollen sac which produces the pollen.

Antheriferous Containing anthers.

Anthesis The period between the opening of the bud and the onset of flower withering.

Anthocarp A false fruit consisting of the true fruit and the base of the perianth.

Anthocyanidins Are common plant pigments. They are the sugar-free counterparts of anthocyanins.

Anthocyanins A subgroup of antioxidant flavonoids and are glucosides of anthocyanidins. They occur as water-soluble vacuolar pigments that may appear red, purple or blue according to pH in plants.

Antipetala Situated opposite petals.

Antisepala Situated opposite sepals.

Antrorse Directed forward upwards.

Apetalous Lacking petals as of flowers with no corolla.

Apical meristem Active growing point. A zone of cell division at the tip of the stem or the root.

Apically Towards the apex or tip of a structure.

Apiculate Ending abruptly in a short, sharp, small point.

Apiculum A short, pointed, flexible tip.

Apocarpous Carpels separate in single individual pistils.

Apopetalous With separate petals, not united to other petals.

Aposepalous With separate sepals, not united to other sepals.

Appressed Pressed closely to another structure but not fused or united.

Aquatic A plant living in or on water for all or a considerable part of its life span.

Arachnoid (Botany) Formed of or covered with long, delicate hairs or fibres.

Arborescent Resembling a tree; applied to nonwoody plants attaining tree height and to shrubs tending to become treelike in size.

Arbuscular Mycorrhiza (AM) A type of mycorrhiza in which the fungus (of the phylum Glomeromycota) penetrates the cortical cells of the roots of a vascular plant and form unique structures such as arbuscules and vesicles. These fungi help plants to capture nutrients such as phosphorus and micronutrients from the soil.

Archegonium A flask-shaped female reproductive organ in mosses, ferns and other related plants.

Areolate With areolea.

Areole (Botany) A small, specialized, cushion-like area on a cactus from which hairs, glochids, spines, branches or flowers may arise; an irregular angular specs marked out on a surface, e.g. fruit surface. *Pl.* areolea.

Aril Specialized outgrowth from the funiculus (attachment point of the seed) (or hilum) that encloses or is attached to the seed. *Adj.* arillate.

Arillode A false aril; an aril originating from the micropyle instead of from the funicle or chalaza of the ovule, e.g. mace of nutmeg.

Aristate Bristlelike part or appendage, e.g. awns of grains and grasses.

Aristulate Having a small, stiff, bristlelike part or appendage; a diminutive of aristate

Articulate Jointed; usually breaking easily at the nodes or point of articulation into segments.

Ascending Arched upwards in the lower part and becoming erect in the upper part.

Ascospore Spore produced in the ascus in Ascomycete fungi.

Ascus Is the sexual spore-bearing cell produced in Ascomycete fungi. *Pl.* asci.

Asperulous Refers to a rough surface with short, hard projections.

Attenuate Tapered or tapering gradually to a point.

Auricle An earlike appendage that occurs at the base of some leaves or corolla.

Auriculate Having auricles.

Awn A hair-like or bristlelike appendage on a larger structure.

Axil Upper angle between a lateral organ, such as a leaf petiole and the stem that bears it.

Axile Situated along the central axis of an ovary having two or more locules, as in axile placentation.

Axillary Arising or growing in an axil.

Baccate Beery like, pulpy or fleshy.

Barbate Bearded, having tufts of hairs.

Barbellae Short, stiff, hair-like bristles. *Adj.* barbellate.

Bark Is the outermost layers of stems and roots of woody plants.

Basal Relating to, situated at, arising from or forming the base.

Basaltic Soil Soil derived from basalt, a common extrusive volcanic rock.

Basidiospore A reproductive spore produced by Basidiomycete fungi.

Basidium A microscopic, spore-producing structure found on the hymenophore of fruiting bodies of Basidiomycete fungi.

Basifixed Attached by the base, as certain anthers are to their filaments.

Basionym The synonym of a scientific name that supplies the epithet for the correct name.

Beak A prominent apical projection, especially of a carpel or fruit. *Adj.* beaked.

Bearded Having a tuft of hairs.

Berry A fleshy or pulpy indehiscent fruit from a single ovary with the seed(s) embedded in the fleshy tissue of the pericarp.

Biconvex Convex on both sides.

Biennial Completing the full cycle from germination to fruiting in more than one, but not more than 2 years.

Bifid Forked, divided into two parts.

Bifoliolate Having two leaflets.

Bilabiate Having two lips as of a corolla or calyx with segments fused into an upper and lower lip.

Bipinnate Twice pinnate; the primary leaflets being again divided into secondary leaflets.

Bipinnatisect Refers to a pinnately compound leaf, in which each leaflet is again divided into pinnae.

Biserrate Doubly serrate; with smaller regular, asymmetric teeth on the margins of larger teeth.

Bisexual Having both sexes, as in a flower bearing both stamens and pistil, hermaphrodite or perfect.

Biternate Twice ternate; with three pinnae each divided into three pinnules.

Blade Lamina; part of the leaf above the sheath or petiole.

Blotched See Variegated.

Bole Main trunk of tree from the base to the first branch.

Brachyblast A short, axillary, densely crowded branchlet or shoot of limited growth, in which the internodes elongate little or not at all.

Bracket Fungus Shelf fungus.

Bract A leaflike structure, different in form from the foliage leaves, associated with an inflorescence or flower. *Adj.* bracteate.

Bracteate Possessing bracts.

Bracteolate Having bracteoles.

Bracteole A small, secondary, bract-like structure borne singly or in a pair on the pedicel or calyx of a flower. *Adj.* bracteolate.

Bran Hard outer layer of grain and comprises the aleurone and pericarp. It contains important antioxidant, vitamins and fibre.

Bristle A stiff hair.

Bulb A modified underground axis that is short and crowned by a mass of usually fleshy, imbricate scales. *Adj.* bulbous.

Bulbil A small bulb or bulb-shaped body, especially one borne in the leaf axil or an inflorescence, and usually produced for asexual reproduction.

Bullate Puckered, blistered.

Burr Type of seed or fruit with short, stiff bristles or hooks or may refer to a deformed type of wood in which the grain has been misformed.

Bush Low, dense shrub without a pronounced trunk.

Buttress Supporting, projecting outgrowth from base of a tree trunk as in some Rhizophoraceae and Moraceae.

Caducous Shedding or falling early before maturity refers to sepals and petals.

Caespitose Growing densely in tufts or clumps; having short, closely packed stems.

Calcareous Composed of or containing lime or limestone.

Calcrete A hardpan consisting gravel and sand cemented by calcium.

Callus A condition of thickened raised mass of hardened tissue on leaves or other plant parts often formed after an injury but sometimes a normal feature. A callus also can refer to an undifferentiated plant cell mass grown on a culture medium. *N.* callosity; *Pl.* calli, callosities; *Adj.* callose.

Calyptra The protective cap or hood covering the spore case of a moss or related plant.

Calyptrate Operculate, having a calyptra.

Calyx Outer floral whorl usually consisting of free sepals or fused sepals (calyx tube) and calyx lobes. It encloses the flower while it is still a bud. *Adj.* calycine.

Calyx Lobe One of the free upper parts of the calyx which may be present when the lower part is united into a tube.

Calyx Tube The tubular fused part of the calyx, often cup shaped or bell shaped, when it is free from the corolla.

Campanulate Shaped like a bell refers to calyx or corolla.

Canaliculate Having groove or grooves.

Candelabriform Having the shape of a tall branched candlestick.

Canescent Covered with short, fine whitish or greyish hairs or down.

Canopy Uppermost leafy stratum of a tree.

Cap See Pileus.

Capitate Growing together in a head. Also means enlarged and globular at the tip.

Capitulum A flower head or inflorescence having a dense cluster of sessile, or almost sessile, flowers or florets.

Capsule A dry, dehiscent fruit formed from two or more united carpels and dehiscing at maturity by sections called valves to release the seeds. *Adj.* capsular.

Carinate Keeled.

Carpel A simple pistil consisting of ovary, ovules, style and stigma. *Adj.* carpellary.

Carpogonium Female reproductive organ in red algae. *Pl.* carpogonia.

Carpophore Part of the receptacle which is lengthened between the carpels as a central axis; any fruiting body or fruiting structure of a fungus.

Cartilaginous Sinewy, having a firm, tough, flexible texture (in respect of leaf margins).

Caruncle (Botany) Fleshy structure attached to the seed of certain plants.

Caryopsis A simple dry, indehiscent fruit formed from a single ovary with the seed coat united with the ovary wall as in grasses and cereals.

Cataphyll A reduced or scarcely developed leaf at the start of a plant's life (i.e. cotyledons) or in the early stages of leaf development.

Catkin A slim, cylindrical, pendulous flower spike usually with unisexual flowers.

Caudate Having a narrow, tail-like appendage.

Caudex Thickened, usually underground base of the stem.

Caulescent Having a well-developed aerial stem.

Cauliflory Botanical term referring to plants which flower and fruit from their main stems or woody trunks. *Adj.* cauliflorus.

Cauline Borne on the aerial part of a stem.

Chaffy Having thin, membranous scales in the inflorescence as in the flower heads of the sunflower family.

Chalaza The basal region of the ovule where the stalk is attached.

Chamaephyte A low-growing perennial plant whose dormant overwintering buds are borne at or just above the surface of the ground.

Chartaceous Papery, of paper-like texture.

Chasmogamous Describing flowers in which pollination takes place while the flower is open.

Chatoyant Having a velvety sheen or lustre.

Chloroplast A chlorophyll-containing organelle (plastid) that gives the green colour to leaves and stems. Plastids harness light energy that is used to fix carbon dioxide in the process called photosynthesis.

Chromoplast Plastid containing coloured pigments apart from chlorophyll.

Chromosomes Thread-shaped structures that occur in pairs in the nucleus of a cell, containing the genetic information of living organisms.

Cilia Hairs along the margin of a leaf or corolla lobe.

Ciliate With a fringe of hairs on the margin as of the corolla lobes or leaf.

Ciliolate Minutely ciliate.

Cilium A straight, usually erect hair on a margin or ridge. *Pl.* cilia.

Cincinnus A monochasial cyme in which the lateral branches arise alternately on opposite sides of the false axis.

Circinate Spirally coiled, with the tip innermost.

Circumscissile Opening by a transverse line around the circumference as of a fruit.

Cladode The modified photosynthetic stem of a plant whose foliage leaves are much reduced or absent. *Cf.* cladophyll, phyllode.

Cladophyll A photosynthetic branch or portion of a stem that resembles and functions as a leaf, like in asparagus. *Cf.* cladode, phyllode.

Clamp Connection In the Basidiomycetes fungi, a lateral connection or outgrowth formed between two adjoining cells of a hypha and arching over the septum between them.

Clavate Club shaped thickened at one end refer to fruit or other organs.

Claw The conspicuously narrowed basal part of a flat structure.

Clay A naturally occurring material composed primarily of fine-grained minerals like kaolinite, montmorillonite-smectite or illite which exhibit plasticity through a variable range of water content and which can be hardened when dried and/or fired.

Clayey Resembling or containing a large proportion of clay.

Cleft Incised halfway down.

Cleistogamous Refers to a flower in which fertilization occurs within the bud, i.e. without the flower opening. *Cf.* chasmogamous.

Climber Growing more or less upwards by leaning or twining around another structure.

Clone All the plants reproduced, vegetatively, from a single parent, thus having the same genetic make-up as the parent.

Coccus One of the sections of a distinctly lobed fruit which becomes separate at maturity; sometimes called a mericarp. *Pl.* cocci.

Coenocarpium A fleshy, multiple pseudocarp formed from an inflorescence rather than a single flower.

Coherent Touching without organic fusion, referring to parts normally together, e.g. floral parts of the same whorl. *Cf.* adherent, adnate, connate.

Collar Boundary between the above- and below ground parts of the plant axis.

Colliculate Having small elevations.

Column A structure formed by the united style, stigma and stamen(s) as in Asclepiadaceae and Orchidaceae.

Comose Tufted with hairs at the ends as of seeds.

Composite Having two types of florets as of the flowers in the sunflower family, Asteraceae.

Compost Organic matter (like leaves, mulch and manure) that breaks down in soil releasing its nutrients.

Compound Describes a leaf that is further divided into leaflets or pinnae or flower with more than a single floret.

Compressed Flattened in one plane.

Conceptacles Specialized cavities of marine algae that contain the reproductive organs.

Concolorous Uniformly coloured, as in upper and lower surfaces. *Cf.* discolorous

Conduplicate Folded together lengthwise.

Cone A reproductive structure composed of an axis (branch) bearing sterile bract-like organs and seed or pollen-bearing structures. Applied to Gymnospermae, Lycopodiaceae, Casuarinaceae and also in some members of Proteaceae.

Conic Cone shaped, attached at the broader end.

Conic-Capitate A cone-shaped head of flowers.

Connate Fused to another structure of the same kind. *Cf*. adherent, adnate, coherent.

Connective The tissue separating two lobes of an anther.

Connivent Converging.

Conspecific Within or belonging to the same species.

Contorted Twisted.

Convolute Refers to an arrangement of petals in a bud where each has one side overlapping the adjacent petal.

Cordate Heart shaped as of leaves.

Core Central part.

Coriaceous Leathery texture as of leaves.

Corm A short, swollen, fleshy, underground plant stem that serves as a food storage organ used by some plants to survive winter or other adverse conditions

Cormel A miniature, new corm produced on a mature corm.

Corn Silk The long, filamentous styles that grow as a silky tuft or tassel at the tip of an ear of corn.

Corolla The inner floral whorl of a flower, usually consisting of free petals or a petals fused forming a corolla tube and corolla lobes. *Adj.* corolline.

Corona A crown-like section of the staminal column, usually with the inner and outer lobes as in the **Stapelieae**.

Coroniform Crown shaped, as in the pappus of Asteraceae.

CortexThe outer of the stem or root of a plant, bounded on the outside by the epidermis and on the inside by the endodermis containing undifferentiated cells.

Corymb A flat-topped, short, broad inflorescence, in which the flowers, through unequal pedicels, are in one horizontal plane and the youngest in the centre. *Adj.* corymbose.

Costa A thickened, linear ridge or the midrib of the pinna in ferns. *Adj.* costate.

Costapalmate Having definite costa (midrib) unlike the typical palmate leaf, but the leaflets are arranged radially like in a palmate leaf.

Cotyledon The primary seed leaf within the embryo of a seed.

Cover Crop Crop grown in between trees or in fields primarily to protect the soil from erosion, to improve soil fertility and to keep off weeds.

Crenate Round toothed or scalloped as of leaf margins.

Crenulate Minutely crenate, very strongly scalloped.

Crested Frilled and ruffled edge.

Crispate Weakly undulating edge.

Crisped With a curled or twisted edge.

Cristate Having or forming a crest or crista.

Crozier Shaped like a shepherd's crook.

Crustaceous Like a crust, having a hard crust or shell.

Cucullate Having the shape of a cowl or hood, hooded.

Culm The main aerial stem of the Gramineae (grasses, sedges, rushes and other monocots).

Culm Sheath The plant casing (similar to a leaf) that protects the young bamboo shoot during growth, attached at each node of culm.

Cultigen Plant species or race known only in cultivation.

Cultivar Cultivated variety; an assemblage of cultivated individuals distinguished by any characters significant for the purposes of agriculture, forestry or horticulture and which, when reproduced, retains its distinguishing features.

Cuneate Wedge shaped, obtriangular.

Cupular Cup shaped, having a cupule.

Cupule A small cup-shaped structure or organ, like the cup at the base of an acorn.

Cusp An elongated, usually rigid, acute point. *Cf.* mucro.

Cuspidate Terminating in or tipped with a sharp firm point or cusp. *Cf.* mucronate.

Cuspidulate Constricted into a minute cusp. *Cf.* cuspidate.

Cyathiform In the form of a cup, a little widened at the top.

Cyathium A specialized type of inflorescence of plants in the genus Euphorbia and Chamaesyce in which the unisexual flowers are clustered together within a bract-like envelope. *Pl.* cyathia.

Cylindric Tubular or rod shaped.

Cylindric-Acuminate Elongated and tapering to a point.

Cymbiform Boat shaped, elongated and having the upper surface decidedly concave.

Cyme An inflorescence in which the lateral axis grows more strongly than the main axis with the oldest flower in the centre or at the ends. *Adj.* cymose

Cymule A small cyme or one or a few flowers.

Cystidium A relatively large cell found on the hymenium of a Basidiomycete, for example, on the surface of a mushroom.

Cystocarp Fruitlike structure (sporocarp) developed after fertilization in the red algae.

Deciduous Falling off or shedding at maturity or a specific season or stage of growth.

Decorticate To remove the bark, rind or husk from an organ; to strip of its bark; to come off as a skin.

Decompound As of a compound leaf; consisting of divisions that are themselves compound.

Decumbent Prostrate, laying or growing on the ground but with ascending tips. *Cf.* ascending, procumbent.

Decurrent Having the leaf base tapering down to a narrow wing that extends to the stem.

Decussate Having paired organs with successive pairs at right angles to give four rows as of leaves.

Deflexed Bent downwards.

Degumming Removal of gum deposits (phosphatides, entrained oil and meal particles) from crude edible oils traditionally done with water. Water degumming process also remove hydrophilic substances such as sugars from the oil.

Dehisce To split open at maturity, as in a capsule.

Dehiscent Splitting open at maturity to release the contents. *Cf.* indehiscent.

Deltate Triangular shape.

Deltoid Shaped like an equilateral triangle.

Dendritic Branching from a main stem or axis like the branches of a tree.

Dentate With sharp, rather coarse teeth perpendicular to the margin.

Denticulate Finely toothed.

Diageotropic The tendency of growing parts, such as roots, to grow at right angle to the line of gravity.

Diadelphous Having stamens in two bundles as in Papilionaceae flowers.

Dichasium A cymose inflorescence in which the branches are opposite and approximately equal. *Pl.* dichasia; *Adj.* dichasial.

Dichotomous divided into two parts.

Dicotyledon Angiosperm with two cotyledons.

Didymous Arranged or occurring in pairs as of anthers, having two lobes.

Digitate Having digits or fingerlike projections.

Dikaryophyses Or dendrophydia, irregularly, strongly branched terminal hyphae in the Hymenomycetes (class of Basidiomycetes) fungi.

Dimorphic Having or occurring in two forms, as of stamens of two different lengths or a plant having two kinds of leaves.

Dioecious With male and female unisexual flowers on separate plants. *Cf.* monoecious.

Diploid A condition in which the chromosomes in the nucleus of a cell exist as pairs, one set being derived from the female parent and the other from the male.

Diplobiontic Life Cycle Life cycle that exhibits alternation of generations, which features of spore-producing multicellular sporophytes and gamete-producing multicellular gametophytes. Mitoses occur in both the diploid and haploid phases.

Diplontic Life Cycle Or gametic meiosis, wherein instead of immediately dividing meiotically to produce haploid cells, the zygote divides mitotically to produce a multicellular diploid individual or a group of more diploid cells.

Diplochory Seed dispersal involving two or more modes.

Dipterocarpus Trees of the family Dipterocarpaceae, with two-winged fruit found mainly in tropical lowland rainforest.

Disc (Botany) Refers to the usually disc-shaped receptacle of the flower head in Asteraceae; also the fleshy nectariferous organ usually between the stamens and ovary; also used for the enlarged style-end in Proteaceae.

Disc Floret The central, tubular 4 or 5 toothed or lobed floret on the disc of an inflorescence, as of flower head of Asteraceae.

Disciform Flat and rounded in shaped. *Cf.* discoid, radiate.

Discoid Resembling a disc; having a flat, circular form; disc-shaped. *Cf.* disciform, radiate.

Discolorous Having two colours, as of a leaf which has different colours on the two surfaces. *Cf.* concolorous.

Disomic Having one or more chromosomes present twice but without the entire genome doubled.

Dispersal Dissemination of seeds.

Distal Site of any structure farthest from the point of attachment. *Cf.* proximal.

Distichous Referring to two rows of upright leaves in the same plane.

Dithecous Having two thecae.

Divaricate Diverging at a wide angle.

Domatium A part of a plant (e.g. a leaf) that has been modified to provide protection for other organisms. *Pl.* domatia.

Dormancy A resting period in the life of a plant during which growth slows or appears to stop.

Dorsal Referring to the back surface.

Dorsifixed Attached to the back as of anthers.

Drupaceous Resembling a drupe.

Drupe A fleshy fruit with a single seed enclosed in a hard shell (endocarp) which is tissue embedded in succulent tissue (mesocarp) surrounded by a thin outer skin (epicarp). *Adj.* drupaceous.

Drupelet A small drupe.

Ebracteate Without bracts.

Echinate Bearing stiff, stout, bristly, prickly hairs.

Edaphic Refers to plant communities that are distinguished by soil conditions rather than by the climate.

Eglandular Without glands. *Cf.* glandular.

Elaioplasts A type of leucoplast that is specialized for the storage of lipids in plants.

Elaiosome Fleshy lipid-rich structures that are attached to the seeds of many plant species.

Ellipsoid A 3-dimensional shape; elliptic in outline.

Elliptic Having a 2-dimensional shape of an ellipse or flattened circle.

Elongate Extended, stretched out.

Emarginate Refers to leaf with a broad, shallow notch at the apex. *Cf.* retuse.

Embryo (Botany) A minute rudimentary plant contained within a seed or an archegonium, composed of the embryonic axis (shoot end and root end).

Endemic Prevalent in or peculiar to a particular geographical locality or region.

Endocarp The hard innermost layer of the pericarp of many fruits.

Endosperm Tissue that surrounds and nourishes the embryo in the angiosperm seed. It contains starchy carbohydrates, proteins and small amounts of vitamins and minerals.

Endospermous Refers to seeds having an endosperm.

Ensiform Shaped like the blade of a sword, long and narrow with sharp edges and a pointed tip.

Endotrophic As of mycorrhiza obtaining nutrients from inside.

Ensilage The process of preserving green food for livestock in an undried condition in airtight conditions. Also called silaging.

Entire Having a smooth, continuous margin without any incisions or teeth as of a leaf.

Entisols Soils that do not show any profile development other than an A horizon.

Ephemeral Transitory, short lived.

Epicalyx A whorl of bracts, subtending and resembling a calyx.

Epicarp Outermost layer of the pericarp of a fruit.

Epicormic Attached to the corm.

Epicotyl The upper portion of the embryonic axis, above the cotyledons and below the first true leaves.

Epigeal Above grounds with cotyledons raised above ground.

Epiparasite An organism parasitic on another that parasitizes a third.

Epipetalous Borne on the petals, as of stamens.

Epiphyte A plant growing on, but not parasitic on, another plant, deriving its moisture and nutrients from the air and rain, e.g. some Orchidaceae. *Adj.* epiphytic.

Epithet Name.

Erect Upright, vertical.

Essential Oils Volatile products obtained from a natural source; refers to volatile products obtained by steam or water distillation in a strict sense.

Etiolation To cause (a plant) to develop without chlorophyll by preventing exposure to sunlight.

Eutrophic Having waters rich in mineral and organic nutrients that promote a proliferation of plant life, especially algae, which reduces the dissolved oxygen content and often causes the extinction of other organisms.

Excentric Off the true centre.
Excrescence Abnormal outgrowth.
Excurrent Projecting beyond the tip, as the midrib of a leaf or bract.
Exserted Sticking out, protruding beyond some enclosing organ, as of stamens which project beyond the corolla or perianth.
Exstipulate Without stipules. *Cf.* stipulate.
Extra-floral Outside the flower.
Extrorse Turned outwards or away from the axis as of anthers. *Cf.* introrse, latrorse.
Falcate sickle shaped, crescent shaped.
Fascicle A cluster or bundle of stems, flowers, stamens. *Adj.* fasciculate.
Fasciclode Staminode bundles.
Fastigiate A tree in which the branches grow almost vertically.
Ferrosols Soils with an iron oxide content of greater than 5 %.
Ferruginous Rust coloured, reddish-brown.
Fertile Having functional sexual parts which are capable of fertilization and seed production. *Cf.* sterile.
Filament The stalk of a stamen supporting and subtending the anther.
Filiform Having the form of or resembling a thread or filament.
Fimbriate Fringed.
Fixed Oils Nonvolatile oils, triglycerides of fatty acids.
Flaccid Limp and weak.
Flag Leaf The uppermost leaf on the stem.
Flaky In the shape of flakes or scales.
Flexuous Zigzagging, sinuous, bending, as of a stem.
Floccose Covered with tufts of soft woolly hairs.
Floral Tube A flower tube usually formed by the basal fusion of the perianth and stamens.
Floret One of the small individual flowers of sunflower family or the reduced flower of the grasses, including the lemma and palea.
Flower The sexual reproductive organ of flowering plants, typically consisting of gynoecium, androecium and perianth or calyx and/or corolla and the axis bearing these parts.
Fluted As of a trunk with grooves and folds.
Fodder Plant material, fresh or dried fed to animals.
Foliaceous Leaf like.
Foliage Leaves of the plant.
Foliar Pertaining to a leaf.
Foliolate Pertaining to leaflets, used with a number prefix to denote the number of leaflets.
Foliose Leaf like.
Follicle (Botany) A dry fruit, derived from a single carpel and dehiscing along one suture.
Forb Any herb that is not grass or grass like.
Foveolate Surface pitted with shallow depressions.
Free Central Placentation The arrangement of ovules on a central column that is not connected to the ovary wall by partitions, as in the ovaries of the carnation and primrose.
Frond The leaf of a fern or cycad.
Fruit Ripened ovary with adnate parts.
Frutescent Shrubby.
Fugacious Shedding off early.
Fulvous Yellow, tawny.
Funiculus (Botany) Short stalk which attaches the ovule to the ovary wall.
Fuscescent Dusky.
Fusiform A 3-dimensional shape; spindle shaped, i.e. broad in the centre and tapering at both ends thick, but tapering at both ends.
Gall Flower Short-styled flowers that do not develop into a fruit but are adapted for the development of a specific wasp within the fruit, e.g. in the fig.
Gamete A reproductive cell that fuses with another gamete to form a zygote. Gametes are haploid, (they contain half the normal (diploid) number of chromosomes); thus, when two fuse, the diploid number is restored.
Gametophyte The gamete-producing phase in a plant characterized by alternation of generations.
Gamosepalous With sepals united or partially united.
Genome Complete set of genetic material of an organism.
Geniculate Bent like a knee; refers to awns and filaments.
Geocarpic Where the fruit are pushed into the soil by the gynophore and mature.

Geophyte A plant that stores food in an underground storage organ, e.g. a tuber, bulb or rhizome and has subterranean buds which form aerial growth.

Geotextile Are permeable fabrics which, when used in association with soil, have the ability to separate, filter, reinforce, protect or drain.

Germ Of cereal is the embryo of the seed or kernel. It contains vitamins B and E, folic acid, some protein, minerals and polyunsaturated fats.

Glabrescent Becoming glabrous.

Glabrous Smooth, hairless without pubescence.

Gland A secretory organ, e.g. a nectary, extrafloral nectary or a gland tipped, hair like or wart like organ. *Adj.* glandular; *Cf.* eglandular.

Glaucous Pale blue-green in colour, covered with a whitish bloom that rubs off readily.

Gley Soils A hydric soil which exhibits a greenish-blue-grey soil colour due to wetland conditions.

Globose Spherical in shape.

Globular A three-dimensional shape; spherical or orbicular; circular in outline.

Glochids Tiny, finely barbed hair-like spines found on the areoles of some cacti and other plants.

Glochidiate Having glochids.

Glochidote Plant having glochids.

Glume One of the two small, sterile bracts at the base of the grass spikelet, called the lower and upper glumes, due to their position on the rachilla. Also used in Apiaceae and Cyperaceae for the very small bracts on the spikelet in which each flower is subtended by one floral glume. *Adj.* glumaceous.

Grits Consist of coarsely ground corn or sometimes alkali-treated corn.

Groats Hulled, whole grains of various cereals, such as oats, wheat, barley or buckwheat, it includes the cereal germ, fibre-rich bran portion and endosperm of the grain.

Guttation The appearance of drops of xylem sap on the tips or edges of leaves of some vascular plants, such as grasses and bamboos.

Guttule Small droplet.

Gymnosperm A group of spermatophyte seed-bearing plants with ovules on scales, which are usually arranged in cone-like structures and not borne in an ovary. *Cf.* angiosperm.

Gynoecium The female organ of a flower; a collective term for the pistil, carpel or carpels.

Gynomonoecious Having female flowers and bisexual flowers on the same plant. *Cf.* andromonoecious.

Gynophore Stalk that bears the pistil/carpel.

Habit The general growth form of a plant, comprising its size, shape, texture and stem orientation; the locality in which the plant grows.

Halophyte A plant adapted to living in highly saline habitats. Also a plant that accumulates high concentrations of salt in its tissues. *Adj.* halophytic.

Hapaxanthic Refers to palms which flowers only once and then dies. Cf. pleonanthic.

Haploid Condition where nucleus or cell has a single set of unpaired chromosomes, the haploid number is designated as *n*.

Haplontic Life Cycle Or zygotic meiosis wherein meiosis of a zygote, immediately after karyogamy, produces haploid cells which produces more or larger haploid cells ending its diploid phase.

Hastate Having the shape of an arrowhead but with the basal lobes pointing outwards at right angles as of a leaf.

Hastula A piece of plant material at the junction of the petiole and the leaf blade; the hastula can be found on the top of the leaf, adaxial or the bottom, abaxial or both sides.

Heartwood Wood from the inner portion of a tree.

Heliophilous Sun loving, tolerates high level of sunlight.

Heliotropic Growing towards sunlight.

Herb A plant which is nonwoody or woody at the base only, the above ground stems usually being ephemeral. *Adj.* herbaceous.

Herbaceous Resembling an herb, having a habit of an herb.

Hermaphrodite Bisexual, bearing flowers with both androecium and gynoecium in the same flower. *Adj.* hermaphroditic.

Heterocyst A differentiated cyanobacterial cell that carries out nitrogen fixation.

Heterogamous Bearing separate male and female flowers, or bisexual and female

flowers, or florets in an inflorescence or flower head, e.g. some Asteraceae in which the ray florets may be neuter or unisexual and the disc florets may be bisexual. *Cf.* homogamous.

Heteromorphous Having two or more distinct forms. *Cf.* homomorphous.

Heterophyllous Having leaves of different form.

Heterosporous Producing spores of 2 sizes, the larger giving rise to megagametophytes (female), the smaller giving rise to microgametophytes (male). Refer to the ferns and fern allies. *Cf.* homosporous.

Heterostylous Having styles of two different lengths or forms.

Heterostyly The condition in which flowers on polymorphous plants have styles of different lengths, thereby facilitating cross-pollination.

Hilar Of or relating to a hilum.

Hilum The scar on a seed, indicating the point of attachment to the funiculus.

Hirsute Bearing long coarse hairs.

Hispid Bearing stiff, short, rough hairs or bristles.

Hispidulous Minutely hispid.

Histosol Soil comprising primarily of organic materials, having 40 cm or more of organic soil material in the upper 80 cm.

Hoary Covered with a greyish layer of very short, closely interwoven hairs.

Holdfast An organ or structure of attachment, especially the basal, root-like formation by which certain seaweeds or other algae are attached to a substrate.

Holocarpic Having the entire thallus developed into a fruiting body or sporangium.

Homochromous Having all the florets of the same colour in the same flower head. *Cf.* heterochromous.

Homogamous Bearing flowers or florets that do not differ sexually. *Cf.* heterogamous.

Homogenous Endosperm Endosperm with even surface that lacks invaginations or infoldings of the surrounding tissue.

Hormogonium A part of a filament of a cyanobacterium that detaches and grows by cell division into a new filament. *Pl.* hormogonia.

Homomorphous Uniform, with only one form. *Cf.* heteromorphous.

Homosporous Producing one kind of spores. Refer to the ferns and fern allies. *Cf.* heterosporous.

Hurd Fibre Long pith fibre of the stem.

Hyaline Colourless, almost transparent.

Hybrid The first generation progeny of the sexual union of plants belonging to different taxa.

Hybridisation The crossing of individuals from different species or taxa.

Hydathode A type of secretory tissue in leaves, usually of Angiosperms, that secretes water through pores in the epidermis or margin of the leaf.

Hydrophilous Water loving; requiring water in order to be fertilized, referring to many aquatic plants.

Hygrochastic Applied to plants in which the opening of the fruits is caused by the absorption of water.

Hygrophilous Living in water or moist places.

Hymenial cystidia The cells of the hymenium develop into basidia or asci, while in others some cells develop into sterile cells called cystidia.

Hymenium Spore-bearing layer of cells in certain fungi containing asci (Ascomycetes) or basidia (Basidiomycetes).

Hypanthium Cuplike receptacles of some dicotyledonous flowers formed by the fusion of the calyx, corolla and androecium that surround the ovary which bears the sepals, petals and stamens.

Hypha Is a long, branching filamentous cell of a fungus and also of unrelated Actinobacteria. *Pl.* hyphae.

Hypocotyl The portion of the stem below the cotyledons.

Hypodermis The cell layer beneath the epidermis of the pericarp.

Hypogeal Below ground as of germination of seed.

Hysteresis Refers to systems that may exhibit path dependence.

Imbricate Closely packed and overlapping. *Cf.* valvate.

Imparipinnate Pinnately compound with a single terminal leaflet and hence with an odd number of leaflets. *Cf.* paripinnate.

Inceptisols Old soils that have no accumulation of clays, iron, aluminium or organic matter.

Incised Cut jaggedly with very deep teeth.

Included Referring to stamens which do not project beyond the corolla or to valves which do not extend beyond the rim of a capsular fruit. *Cf.* exserted.

Incurved Curved inwards; curved towards the base or apex.

Indefinite Numerous and variable in number.

Indehiscent Not opening or splitting to release the contents at maturity as of fruit. *Cf.* dehiscent.

Indumentum Covering of fine hairs or bristles commonly found on external parts of plants.

Indurate To become hard, often the hardening developed only at maturity.

Indusium An enclosing membrane, covering the sorus of a fern. Also used for the modified style end or pollen-cup of some Goodeniaceae (including Brunoniaceae). *Adj.* indusiate.

Inferior Said of an ovary or fruit that has sepals, petals and stamens above the ovary. *Cf.* superior.

Inflated Enlarged and hollow except in the case of a fruit which may contain a seed. *Cf.* swollen.

Inflexed Bent or curved inwards or downwards, as petals or sepals.

Inflorescence A flower cluster or the arrangement of flowers in relation to the axis and to each other on a plant.

Infrafoliar Located below the leaves.

Infraspecific Referring to any taxon below the species rank.

Infructescence The fruiting stage of an inflorescence.

Inrolled Curved inwards.

Integuments Two distinct tissue layers that surround the nucellus of the ovule, forming the testa or seed coat when mature.

Intercalary Of growth, between the apex and the base; of cells, spores, etc., between two cells.

Interfoliar Inter leaf.

Internode Portion of the stem, culm, branch or rhizome between two nodes or points of attachment of the leaves.

Interpetiolar As of stipules positioned between petioles of opposite leaves.

Intrastaminal Within the stamens.

Intricate Entangled, complex.

Introduced Not indigenous; not native to the area in which it now occurs.

Introrse Turned inwards or towards the axis or pistil as of anthers. *Cf.* extrorse, latrorse.

Involucre A whorl of bracts or leaves that surround one to many flowers or an entire inflorescence.

Involute Having the margins rolled inwards, referring to a leaf or other flat organ.

Jugate Of a pinnate leaf; having leaflets in pairs.

Juvenile Young or immature, used here for leaves formed on a young plant which are different in morphology from those formed on an older plant.

Keel A longitudinal ridge, at the back of the leaf. Also the two lower fused petals of a 'pea' flower in the Papilionaceae, which form a boatlike structure around the stamens and styles. Also called carina. *Adj.* keeled. *Cf.* standard, wing.

Labellum The modified lowest of the three petals forming the corolla of an orchid, usually larger than the other two petals, and often spurred.

Lacerate Irregularly cleft.

Laciniate Fringed; having a fringe of slender, narrow, pointed lobes cut into narrow lobes.

Lamella A gill-shaped structure: fine sheets of material held adjacent to one another.

Lamina The blade of the leaf or frond.

Lanate Woolly, covered with long hairs which are loosely curled together like wool.

Lanceolate Lance shaped in outline, tapering from a broad base to the apex.

Landrace Plants adapted to the natural environment in which they grow, developing naturally with minimal assistance or guidance from humans and usually possess more diverse phenotypes and genotypes. They have not been improved by formal breeding programs.

Laterite Reddish-coloured soils rich in iron oxide, formed by weathering of rocks under oxidizing and leaching conditions, commonly found in tropical and subtropical regions. *Adj.* lateritic.

Latex A milky, clear or sometimes coloured sap of diverse composition exuded by some plants.

Latrorse Turned sideways, i.e. not towards or away from the axis as of anthers dehiscing longitudinally on the side. *Cf.* extrorse, introrse.

Lax Loose or limp, not densely arranged or crowded.

Leaflet One of the ultimate segments of a compound leaf.

Lectotype A specimen chosen after the original description to be the type.

Lemma The lower of two bracts (scales) of a grass floret, usually enclosing the palea, lodicules, stamens and ovary.

Lenticel Is a lens-shaped opening that allows gases to be exchanged between air and the inner tissues of a plant, commonly found on young bark, or the surface of the fruit.

Lenticellate Dotted with lenticels.

Lenticular Shaped like a biconvex lens. *Cf.* lentiform.

Lentiform Shaped like a biconvex lens. *Cf.* lenticular.

Leptomorphic Temperate, running bamboo rhizome; usually thinner then the culms they support and the internodes are long and hollow.

Liane A woody climbing or twining plant.

Ligneous Woody.

Lignotuber A woody, usually underground, tuberous rootstock often giving rise to numerous aerial stems.

Ligulate Small and tongue shaped or with a little tongue-shaped appendage or ligule, star shaped as of florets of Asteraceae.

Ligule A strap-shaped corolla in the flowers of Asteraceae; also a thin membranous outgrowth from the inner junction of the grass leaf sheath and blade. *Cf.* ligulate.

Limb The expanded portion of the calyx tube or the corolla tube or the large branch of a tree.

Linear A 2-dimensional shape, narrow with nearly parallel sides.

Linguiform Tongue shaped. *Cf.* ligulate.

Lipotubuloids Are cytoplasmic domains containing aggregates of lipid bodies surrounded by a network of microtubules, which join one lipid body with the others.

Lithosol A kind of shallow soils lacking well-defined horizons and composed of imperfectly weathered fragments of rock.

Littoral Of or on a shore, especially seashore.

Loam A type of soil made up of sand, silt and clay in relative concentration of 40 %, 40 %, 20 % respectively.

Lobed Divided but not to the base.

Loculicidal Opening into the cells, when a ripe capsule splits along the back.

Loculus Cavity or chamber of an ovary. *Pl.* loculi.

Lodicules Two small structures below the ovary which, at flowering, swell up and force open the enclosing bracts, exposing the stamens and carpel.

Lorate Strap shaped with obtuse tip.

Lyrate Pinnately lobed, with a large terminal lobe and smaller laterals ones which become progressively smaller towards the base.

Macronutrients Chemical elements which are needed in large quantities for growth and development by plants and include nitrogen, phosphorus, potassium and magnesium.

Maculate Spotted.

Mallee A growth habit in which several to many woody stems arise separately from a lignotuber; usually applied to certain low-growing species of *Eucalyptus.*

Mangrove A distinctive vegetation type of trees and shrubs with modified roots, often viviparous, occupying the saline coastal habitats that are subject to periodic tidal inundation.

Marcescent Withering or to decay without falling off.

Margin The edge of the leaf blade.

Medulla The pith in the stems or roots of certain plants, or the central portion of a thallus in certain lichens.

Megasporangium The sporangium containing megaspores in fern and fern allies. *Cf.* microsporangium.

Megaspore The large spore which may develop into the female gametophyte in heterosporous ferns and fern allies. *Cf.* microspore.

Megasporophyll A leaflike structure that bears megasporangia.

Megastrobilus Female cone, seed cone or ovulate cone, contains ovules within which, when fertilized by pollen, become seeds. The female cone structure varies more markedly between the different conifer families.

Meiosis The process of cell division that results in the formation of haploid cells from diploid cells to produce gametes.

Mericarp A 1-seeded portion of an initially syncarpous fruit (schizocarp) which splits apart at maturity. *Cf.* coccus.

Meristem The region of active cell division in plants, from which permanent tissue is derived. *Adj.* meristematic.

Merous Used with a number prefix to denote the basic number of the 3 outer floral whorls, e.g. a 5-merous flower may have 5 sepals, 10 petals and 15 stamens.

Mesic Moderately wet.

Mesocarp The middle layer of the fruit wall derived from the middle layer of the carpel wall. *Cf.* endocarp, exocarp, pericarp.

Mesophytes Terrestrial plants which are adapted to neither a particularly dry nor particularly wet environment.

Micropyle The small opening in a plant ovule through which the pollen tube passes in order to effect fertilization.

Microsporangium The sporangium containing microspores in pteridophytes. *Cf.* megasporangium.

Microspore A small spore which gives rise to the male gametophyte in heterosporous pteridophytes. Also for a pollen grain. *Cf.* megaspore.

Midvein The main vascular supply of a simple leaf blade or lamina. Also called midrib.

Mitosis Is a process of cell division which results in the production of two daughter cells from a single parent cell.

Mollisols Soils with deep, high organic matter, nutrient-enriched surface soil (A horizon), typically between 60 and 80 cm thick.

Monadelphous Applied to stamens united by their filaments into a single bundle.

Monocarpic Refers to plants that flower, set seeds and then die.

Monochasial A cyme having a single flower on each axis.

Monocotyledon Angiosperm having one cotyledon.

Monoecious Having both male and female unisexual flowers on the same individual plant. *Cf.* dioecious.

Monoembryonic Seed The seed contains only one embryo, a true sexual (zygotic) embryo, polyembryonic seed.

Monolete A spore that has a simple linear scar.

Monopodial With a main terminal growing point producing many lateral branches progressively. *Cf.* sympodial.

Monotypic Of a genus with one species or a family with one genus, in general, applied to any taxon with only one immediately subordinate taxon.

Montane Refers to highland areas located below the subalpine zone.

Mucilage A soft, moist, viscous, sticky secretion. *Adj.* mucilaginous.

Mucous Botany, slimy.

Mucro A sharp, pointed part or organ, especially a sharp terminal point, as of a leaf.

Mucronate Ending with a short, sharp tip or mucro, resembling a spine. Cf. cuspidate, muticous.

Mucronulate With a very small mucro; a diminutive of mucronate.

Mulch Protective cover of plant (organic) or non-plant material placed over the soil, primarily to modify and improve the effects of the local microclimate and to control weeds.

Multiple Fruit A fruit that is formed from a cluster of flowers.

Muricate Covered with numerous short hard outgrowths. *Cf.* papillose.

Muriculate With numerous minute hard outgrowths; a diminutive of muricate.

Muticous Blunt, lacking a sharp point. *Cf.* mucronate.

MYB Proteins Are a superfamily of transcription factors that play regulatory roles in developmental processes and defense responses in plants.

Mycorrhiza The mutualistic symbiosis (nonpathogenic association) between soil-borne fungi with the roots of higher plants.

Mycorrhiza (Vesicular Arbuscular) Endomycorrhiza living in the roots of higher plants producing inter-and intracellular fungal growth in root cortex and forming specific fungal structures, referred to as vesicles and arbuscles. *Abbrev.* VAM.

Myrmecochory Seed dispersal by ants.

Native A plant indigenous to the locality or region.

Naviculate Boat shaped.

Necrotic Applied to dead tissue.

Nectariferous Having one or more nectaries.

Nectary A nectar secretory gland; commonly in a flower, sometimes on leaves, fronds or stems.

Nervation Venation, a pattern of veins or nerves as of leaf.

Nixtamalization Refers to a process for the preparation of maize (corn), or other grain, in which the grains are soaked and cooked in an alkaline solution, usually limewater, and hulled.

Node The joint between segments of a culm, stem, branch or rhizome; the point of the stem that gives rise to the leaf and bud.

Nodule A small knoblike outgrowth, as those found on the roots of many leguminous, that contains *Rhizobium* bacteria which fix nitrogen in the soil.

Nom. ambig. Nomen ambiguum (Latin). Ambiguous name used in different senses which has become a long-persistent source of error.

Nom. cons. Nomen nonservandum (Latin). Name conserved in International Code of Botanical Nomenclature.

Nom. dub. Nomen dubium (Latin). An invalid proposed taxonomic name because it is not accompanied by a definition or description of the taxon to which it applies.

Nom. illeg. Nomen illegitimum (Latin). Illegitimate taxon deemed as superfluous at its time of publication either because the taxon to which it was applied already has a name, or because the name has already been applied to another plant.

Nom. invalid. Nomen invalidum (Latin). Invalid name according to International Code of Botanical Nomenclature.

Nom. nud. Nomen nudum (Latin). The name of a taxon which has never been validated by a description.

Nom. rej. Nomen rejiciendum (Latin). Name rejected in International Code of Botanical Nomenclature.

Notho (Subsp. or Var.) Prefix to the rank of a hybrid taxon below the rank of species.

Nucellus Central portion of an ovule in which the embryo sac develops.

Nucellar Embryony A form of seed reproduction in which the nucellar tissue which surrounds the embryo sac can produce additional embryos (polyembryony) which are genetically identical to the parent plant. This is found in many citrus species and in mango.

Nut A dry indehiscent 1-celled fruit with a hard pericarp.

Nutlet A small. 1-seeded, indehiscent lobe of a divided fruit.

Ob- Prefix meaning inversely or opposite to.

Obconic A 3-dimensional shape; inversely conic; cone shaped, conic with the vertex pointing downward.

Obcordate Inversely cordate, broad and notched at the tip; heart shaped but attached at the pointed end.

Obdeltate Inversely deltate; deltate with the broadest part at the apex.

Oblanceolate Inversely lanceolate, lance shaped but broadest above the middle and tapering towards the base as of leaf.

Oblate Having the shape of a spheroid with the equatorial diameter greater than the polar diameter; being flattened at the poles.

Oblong Longer than broad with sides nearly parallel to each other.

Obovate Inversely ovate, broadest above the middle.

Obpyramidal Resembling a 4-sided pyramid attached at the apex with the square base facing away from the attachment.

Obpyriform Inversely pyriform, resembling a pear which is attached at the narrower end. *Cf.* pyriform.

Obspathulate Inversely spathulate; resembling a spoon but attached at the broadest end. *Cf.* spathulate.

Obtriangular Inversely triangular; triangular but attached at the apex. *Cf.* triangular.

Obtrullate Inversely trullate; resembling a trowel blade with the broadest axis above the middle. *Cf.* trullate.

Obtuse With a blunt or rounded tip, the converging edges separated by an angle greater than 90°.

Ochraceous A dull yellow colour.

Ocreate Having a tube-like covering around some stems, formed of the united stipules; sheathed.

-oid Suffix denoting a 3-dimensional shape, e.g. spheroid.

Oleaginous Oily.

Oligotrophic Lacking in plant nutrients and having a large amount of dissolved oxygen throughout.

Operculum A lid or cover that becomes detached at maturity by abscission, e.g. in *Eucalyptus*, also a cap or lid covering the bud and formed by fusion or cohesion of sepals and/or petals. *Adj.* operculate.

Opposite Describing leaves or other organs which are borne at the same level but on opposite sides of the stem. *Cf.* alternate.

Orbicular Of circular outline, disc like.

Order A taxonomic rank between class and family used in the classification of organisms, i.e. a group of families believed to be closely related.

Orifice An opening or aperture.

Organosols Soils not regularly inundated by marine waters and containing a specific thickness of organic materials within the upper part of the profile.

Orth. Var. Orthographic variant, i.e. an incorrect alternate spelling of a name.

Ovary The female part of the pistil of a flower which contains the ovules (immature seeds).

Ovate Egg shaped, usually with reference to two dimensions.

Ovoid Egg shaped, usually with reference to three dimensions.

Ovule The young, immature seed in the ovary which becomes a seed after fertilization. *Adj.* ovular.

Ovulode A sterile reduced ovule borne on the placenta, commonly occurring in Myrtaceae.

Oxisols Refer to ferralsols.

Pachymorphic Describes the short, thick, rhizomes of clumping bamboos with short, thick and solid internode (except the bud-bearing internodes, which are more elongated). *Cf.* sympodial.

Palate (Botany) A raised appendage on the lower lip of a corolla which partially or completely closes the throat.

Palea The upper of the two membranous bracts of a grass floret, usually enclosing the lodicules, stamens and ovary. *Pl.* paleae; *Adj.* paleal; *Cf.* lemma.

Paleate Having glumes.

Palm Heart Refers to soft, tender inner core and growing bud of certain palm trees which are eaten as vegetables. Also called heart of palm, palmito, burglar's thigh, chonta or swamp cabbage.

Palmate Describing a leaf which is divided into several lobes or leaflets which arise from the same point. *Adj.* palmately.

Palmito See Palm Heart.

Palustrial Paludal, swampy, marshy.

Palustrine Marshy, swampy.

Palustrine Herb Vegetation that is rooted below water but grows above the surface in wetland system.

Panduriform Fiddle shaped, usually with reference to two dimensions.

Panicle A compound, indeterminate, racemose inflorescence in which the main axis bears lateral racemes or spikes. *Adj.* paniculate.

Pantropical Distributed throughout the tropics.

Papilionaceous Butterfly like; said of the pea flower or flowers of Papilionaceae; flowers which are zygomorphic with imbricate petals, one broad upper one, two narrower lateral ones and two narrower lower ones.

Papilla A small, superficial protuberance on the surface of an organ being an outgrowth of one epidermal cell. *Pl.* papillae; *Adj.* papillose.

Papillate Having papillae.

Papillose Covered with papillae.

Pappus A tuft (or ring) of hairs, bristles or scales borne above the ovary and outside the corolla as in Asteraceae often persisting as a tuft of hairs on a fruit. *Adj.* pappose.

Papyraceous Resembling parchment of paper.

Parenchyma Undifferentiated plant tissue composed of more or less uniform cells.

Parietal Describes the attachment of ovules to the outer walls of the ovaries.

Paripinnate Pinnate with an even number of leaflets and without a terminal leaflet. *Cf.* imparipinnate.

-partite Divided almost to the base into segments, the number of segments written as a prefix.

Patelliform Shaped like a limpet shell; cap shaped and without whorls.

Patent Diverging from the axis almost at right angles.

Peat Is an accumulation of partially decayed vegetation matter.

Pectin A group of water-soluble colloidal carbohydrates of high molecular weight found in certain ripe fruits.

Pectinate Pinnatifid with narrow segments resembling the teeth of a comb.

Pedicel The stalk of the flower or stalk of a spikelet in Poaceae. *Adj.* pedicellate.

Pedicellate Having pedicel.

Peduncle A stalk supporting an inflorescence. *Adj.* pedunculate

Pellucid Allowing the passage of light; transparent or translucent.

Pellucid Dotted Copiously dotted with immersed, pellucid, resinous glands.

Peltate With the petiole attached to the lower surface of the leaf blade.

Pendant Hanging down.

Pendulous Drooping, as of ovules.

Penniveined or Penni-nerved Pinnately veined.

Pentamerous In five parts.

Perennial A plant that completes it life cycle or lives for more than 2 years. *Cf.* annual, biennial.

Perfoliate A leaf with the basal lobes united around, and apparently pierced by, the stem.

Pergamentaceous Parchment like.

Perianth The two outer floral whorls of the Angiosperm flower; commonly used when the calyx and the corolla are not readily distinguishable (as in monocotyledons).

Pericarp (Botany) The wall of a ripened ovary; fruit wall composed of the exocarp, mesocarp and endocarp.

Persistent Remaining attached; not falling off. *Cf.* caduceus.

Petal Free segment of the corolla. *Adj.* petaline; *Cf.* lobe.

Petiolar Relating to the petiole.

Petiolate Having petiole.

Petiole Leafstalk. *Adj.* petiolate.

Petiolulate Supported by its own petiolule.

Petiolule The stalk of a leaflet in a compound leaf. *Adj.* petiolulate.

pH Is a measure of the acidity or basicity of a solution. It is defined as the cologarithm of the activity of dissolved hydrogen ions (H+).

Phenology The study of periodic plant life cycle events as influenced by seasonal and interannual variations in climate.

Phyllary A bract of the involucre of a composite plant, term for one of the scale-like bracts beneath the flower head in Asteraceae.

Phylloclade A flattened, photosynthetic branch or stem that resembles or performs the function of a leaf, with the true leaves represented by scales.

Phyllode A petiole that function as a leaf. *Adj.* phyllodineous; *Cf.* cladode.

Phyllopodia Refers to the reduced, scale-like leaves found on the outermost portion of the corm where they seem to persist longer than typical sporophylls as in the fern Isoetes.

Phytoremediation Describes the treatment of environmental problems (bioremediation) through the use of plants which mitigate the environmental problem without the need to excavate the contaminant material and dispose of it elsewhere.

Pileus (Botany) Cap of mushroom.

Piliferous (Botany) Bearing or producing hairs, as of an organ with the apex having long, hair-like extensions.

Pilose Covered with fine soft hairs.

Pinna A primary division of the blade of a compound leaf or frond. *Pl.* pinnae.

Pinnate Bearing leaflets on each side of a central axis of a compound leaf; divided into pinnae.

Pinnatifid, Pinnatilobed A pinnate leaf parted approximately halfway to midrib; when divided to almost to the midrib described as deeply pinnatifid or pinnatisect.

Pinnatisect Lobed or divided almost to the midrib.

Pinnule A leaflet of a bipinnate compound leaf.

Pistil Female part of the flower comprising the ovary, style and stigma.

Pistillate Having one or more pistils; having pistils but no stamens.

Placenta The region within the ovary to which ovules are attached. *Pl.* placentae.

Placentation The arrangement of the placentae and ovules in the ovary.

Plano- A prefix meaning level or flat.

Pleonanthic Refer to palms in which the stem does not die after flowering.

Plicate Folded like a fan.

Plumose Feather like, with fine hairs arising laterally from a central axis; feathery.

Pneumatophore Modified root which allows gaseous exchange in mud-dwelling shrubs, e.g. mangroves.

Pod A dry 1 to many-seeded dehiscent fruit, as applied to the fruit of Fabaceae, i.e. Caesalpiniaceae, Mimosaceae and Papilionaceae.

Podzol, Podsolic Soil Any of a group of acidic, zonal soils having a leached, light-coloured, grey and ashy appearance. Also called spodosol.

Pollen Cone Male cone or microstrobilus or pollen cone is structurally similar across all conifers, extending out from a central axis are microsporophylls (modified leaves). Under each microsporophyll is one or several microsporangia (pollen sacs).

Pollinia The paired, waxy pollen masses of flowers of orchids and milkweeds.

Polyandrous (Botany) Having an indefinite number of stamens.

Polyembryonic Seed Seeds contain many embryos, most of which are asexual (nucellar) in origin and genetically identical to the maternal parent.

Polygamous With unisexual and bisexual flowers on the same or on different individuals of the same species.

Polymorphic With different morphological variants.

Polypetalous (Botany) Having a corolla composed of distinct, separable petals.

Pome A fleshy fruit where the succulent tissues are developed from the receptacle.

Pore A tiny opening.

Premorse Abruptly truncated, as though bitten or broken off as of a leaf.

Procumbent Trailing or spreading along the ground but not rooting at the nodes, referring to stems. *Cf.* ascending, decumbent, erect.

Pro Hyb. Latin, as a hybrid.

Pro Parte Latin, in part.

Pro Parte Majore Latin, for the greater part.

Pro Parte Minore Latin, for a small part.

Pro Sp. Latin, as a species.

Pro Subsp. Latin, as a subspecies.

Pro Syn. Latin, as a synonym.

Prophyll A plant structure that resembles a leaf.

Prostrate Lying flat on the ground.

Protandrous Relating to a flower in which the anthers release their pollen before the stigma of the same flower becomes receptive.

Proximal End of any structure closest to the point of attachment. *Cf.* distal.

Pruinose Having a thick, waxy, powdery coating or bloom.

Pseudocarp A false fruit, largely made up of tissue that is not derived from the ovary but from floral parts such as the receptacle and calyx.

Pseudostem The false, herbaceous stem of a banana plant composed of overlapping leaf bases.

Pteridophyte A vascular plant which reproduces by spores; the ferns and fern allies.

Puberulent Covered with minute hairs or very fine down; finely pubescent.

Puberulous Covered with a minute down.

Pubescent Covered with short, soft hairs.

Pulvinate Having a swelling, pulvinus at the base as a leafstalk.

Pulvinus Swelling at the base of leafstalk.

Pulviniform Swelling or bulging.

Punctate Marked with translucent dots or glands.

Punctiform Marked by or composed of points or dots.

Punctulate Marked with minute dots; a diminutive of punctate.

Purpurascent Purple or becoming purple.

Pusticulate Characterized by small pustules.

Pyrene The stone or pit of a drupe, consisting of the hardened endocarp and seed.

Pyriform Pear shaped, a 3-dimensional shape; attached at the broader end. *Cf.* obpyriform.

Pyxidium Seed capsule having a circular lid (operculum) which falls off to release the seed.

Raceme An indeterminate inflorescence with a simple, elongated axis and pedicellate flowers, youngest at the top. *Adj.* racemose.

Rachilla The main axis of a grass spikelet.

Rachis The main axis of the spike or other inflorescence of grasses or a compound leaf.

Radiate Arranged around a common centre; as of an inflorescence of Asteraceae with marginal, female or neuter, ligulate ray-florets and central, perfect or functionally male, tubular, disc florets. *Cf.* disciform, discoid.

Radical Arising from the root or its crown or the part of a plant embryo that develops into a root.

Ray The marginal portion of the inflorescence of Asteraceae and Apiaceae when distinct from the disc. Also, the spreading branches of a compound umbel.

Receptacle The region at the end of a pedicel or on an axis which bears one or more flowers. *Adj.* receptacular.

Recurved Curved downwards or backwards.

Reflexed Bent or turned downward.

Regosol Soil that is young and undeveloped, characterized by medium to fine-textured unconsolidated parent material that maybe alluvial in origin and lacks a significant horizon layer formation.

Reniform Kidney shaped in outline.

Repand With slightly undulate margin.

Replicate Folded back, as in some corolla lobes.

Resinous Producing sticky resin.

Resupinate Twisted through 180°.

Reticulate Having the appearance of a network.

Retrorse Bent or directed downwards or backwards. *Cf.* antrorse.

Retuse With a very blunt and slightly notched apex. *Cf.* emarginated.

Revolute With the margins inrolled on the lower (abaxial) surface.

Rhizine A root-like filament or hair growing from the stems of mosses or on lichens.

Rhizoid Root-like filaments in a moss, fern, fungus, etc. that attach the plant to the substratum.

Rhizome A prostrate or underground stem consisting of a series of nodes and internodes with adventitious roots and which generally grows horizontally.

Rhizophore A stilt-like outgrowth of the stem which branches into roots on contact with the substrate.

Rhombic Shaped like a rhombus.

Rhomboid Shaped like a rhombus.

Rib A distinct vein or linear marking, often raised as a linear ridge.

Riparian Along the river margins, interface between land and a stream.

Rosette A tuft of leaves or other organs arranged spirally like petals in a rose, ranging in form from a hemispherical tuft to a flat whorl. *Adj.* rosetted, rosulate.

Rostrate Beaked; the apex tapered into a slender, usually obtuse point.

Rostrum A beak-like extension.

Rosulate Having a rosette.

Rotate Wheel shaped; refers to a corolla with a very short tube and a broad upper part which is flared at right angles to the tube. *Cf.* salverform.

Rotundate Rounded, especially at the end or ends.

Rugae Refers to a series of ridges produced by folding of the wall of an organ.

Rugose Deeply wrinkled.

Rugulose Finely wrinkled.

Ruminate Animal, chew repeatedly over an extended period.

Ruminate Endosperm Uneven endosperm surface that is often highly enlarged by ingrowths or infoldings of the surrounding tissue. Cf. homogenous endosperm.

Rz Value Is a numerical reference to the mesh/emulsion equalization on the screen.

Saccate Pouched.

Sagittate Shaped like an arrow head.

Saline Soils Soils that contain excessive levels of salts that reduce plant growth and vigour by altering water uptake and causing ion-specific toxicities or imbalances.

Salinity Is characterized by high electrical conductivities and low sodium ion concentrations compared to calcium and magnesium.

Salverform Applies to a gamopetalous corolla having a slender tube and an abruptly expanded limb.

Samara An indehiscent, winged, dry fruit.

Sand A naturally occurring granular material composed of finely divided rock and mineral particles range in diameter from 0.0625 μm to 2 mm. *Adj.* sandy

Saponins Are plant glycosides with a distinctive foaming characteristic. They are found in many plants, but get their name from the soapwort plant (*Saponaria)*.

Saprophytic Living on and deriving nourishment from dead organic matter.

Sapwood Outer woody layer of the tree just adjacent to and below the bark.

Sarcotesta Outermost fleshy covering of Cycad seeds below which is the sclerotesta.

Scabrid Scurfy, covered with surface abrasions, irregular projections or delicate scales.

Scabrous Rough to the touch because of scattered rough hairs.
Scale Dry bract or leaf.
Scandent Refer to plants, climbing.
Scape Erect flowering stem, usually leafless, rising from the crown or roots of a plant. *Adj.* scapose.
Scapigerous With a scape.
Scarious Dry, thin and membranous.
Schizocarp A dry fruit which splits into llongitudinally multiple parts called mericarps or cocci. *Adj.* schizocarpous.
Sclerotesta The innermost fleshy coating of cycad seeds, usually located directly below the sarcotesta.
Scorpoid Refers to a cymose inflorescence in which the main axis appears to coil.
Scutellum (Botany) Any of various parts shaped like a shield.
Secondary Venation Arrangement of the lateral veins arising from the midrib in the leaf lamina.
Secund With the flowers all turned in the same direction.
Sedge A plant of the family Apiaceae, Cyperaceae.
Segmented Constricted into divisions.
Seminal Root Or seed root originate from the scutellar node located within the seed embryo and are composed of the radicle and lateral seminal roots.
Senescence Refers to the biological changes which take place in plants as they age.
Sepal Free segment of the calyx. *Adj.* sepaline.
Septum A partition or cross wall. *Pl.* septa; *Adj.* septate.
Seriate Arranged in rows.
Sericeous Silky; covered with close-pressed, fine, straight silky hairs.
Serrate Toothed like a saw; with regular, asymmetric teeth pointing forward.
Serrated Toothed margin.
Serratures Serrated margin.
Serrulate With minute teeth on the margin.
Sessile Without a stalk.
Seta A bristle or stiff hair. *Pl.* setae; *Adj.* setose, setaceous.
Setaceous Bristlelike.
Setate With bristles.
Setiform Bristle shaped.
Setulose With minute bristles.
Sheathing Clasping or enveloping the stem.
Shrub A woody plant usually less than 5 m high and many branched without a distinct main stem except at ground level.
Silicula A broad, dry, usually dehiscent fruit derived from two or more carpels which usually dehisce along two sutures. *Cf.* siliqua.
Siliqua A silicula which is at least twice as long as broad.
Silt Is soil or rock derived granular material of a grain size between sand and clay, grain particles ranging from 0.004 to 0.06 mm in diameter. *Adj.* silty.
Simple Refer to a leaf or other structure that is not divided into parts. *Cf.* compound.
Sinuate With deep wavy margin.
Sinuous Wavy.
Sinus An opening or groove, occuring between the bases of two petals.
Sodicity Is characterized by low electrical conductivities and high sodium ion concentrations compared to calcium and magnesium.
Sodic Soils Contains high levels of sodium salts that affect soil structure, inhibits water movement and causes poor germination and crop establishment and plant toxicity.
Soil pH Is a measure of the acidity or basicity of the soil. See pH.
Solitary Usually refers to flowers which are borne singly and not grouped into an inflorescence or clustered.
Sorocarp Fruiting body formed by some cellular slime moulds and has both stalk and spore mass.
Sorophore Stalk bearing the sorocarp.
Sorosis Fleshy multiple fruit formed from flowers that are crowded together on a fleshy stem, e.g. pineapple and mulberry.
Sorus A discrete aggregate of sporangia in ferns. *Pl.* sori
Spadix Fleshy spike-like inflorescence with an unbranched, usually thickened axis and small embedded flowers often surrounded by a spathe. *Pl.* spadices.
Spathe A large bract ensheathing an inflorescence or its peduncle. *Adj.* spathaceous.
Spatheate Like or with a spathe.
Spathulate Spatula or spoon shaped; broad at the tip and narrowed towards the base.

Spicate Borne in or forming a spike.

Spiculate Spikelet bearing.

Spike An unbranched, indeterminate inflorescence with sessile flowers or spiklets. *Adj.* spicate, spiciform.

Spikelet A small or secondary spike characteristics of the grasses and sedges and generally composed of 2 glumes and one or more florets. Also applied to the small spike-like inflorescence or inflorescence units commonly found in Apiaceae.

Spine A stiff, sharp, pointed structure, formed by modification of a plant organ. *Adj.* spinose.

Spinescent Ending in a spine; modified to form a spine.

Spinulate Covered with small spines.

Spinulose With small spines over the surface.

Spodosol see Podsol.

Sporidia Asexual spores of smut fungi.

Sporangium A spore-bearing structure found in ferns, fern allies and gymnosperms. *Pl.* sporangia; *Adj.* sporangial.

Sporocarp A stalked specialized fruiting structure formed from modified sporophylls, containing sporangia or spores as found in ferns and fern allies.

Sporophore A spore-bearing structure, especially in fungi.

Sporophyll A leaf or bract which bears or subtends sporangia in the fern allies, ferns and gymnosperms.

Sporophyte The spore-producing phase in the life cycle of a plant that exhibits alternation of generations.

Spreading Bending or spreading outwards and horizontally.

Spur A tubular or saclike extension of the corolla or calyx of a flower.

Squama Structure shaped like a fish scale. *Pl.* squamae.

Squamous Covered in scales.

Squarrose Having rough or spreading scale-like processes.

Stamen The male part of a flower, consisting typically of a stalk (filament) and a pollen-bearing portion (anther). *Adj.* staminal, staminate .

Staminate Unisexual flower-bearing stamens but no functional pistils.

Staminode A sterile or abortive stamen, often reduced in size and lacking anther. *Adj.* staminodial.

Standard Refers to the adaxial petal in the flower of Papilionaceae. Cf. keel, wing.

Starch A polysaccharide carbohydrate consisting of a large number of glucose units joined together by glycosidic bonds α–1–4 linkages.

Stellate Star shaped, applies to hairs.

Stem The main axis of a plant, developed from the plumule of the embryo and typically bearing leaves.

Sterile Lacking any functional sexual parts which are capable of fertilization and seed production.

Stigma The sticky receptive tip of an ovary with or without a style which is receptive to pollen.

Stilt Root A supporting root arising from the stem some distance above the ground as in some mangroves, sometimes also known as a prop root.

Stipe A stalk that support some other structure like the frond, ovary or fruit.

Stipel Secondary stipule at the base of a leaflet. *Pl.* stipellae. *Adj.* stipellate.

Stipitate Having a stalk or stipe, usually of an ovary or fruit.

Stipulated Having stipules.

Stipule Small leaflike, scale-like or bristlelike appendages at the base of the leaf or on the petiole. *adj.* stipulate.

Stolon A horizontal, creeping stem rooting at the nodes and giving rise to another plant at its tip.

Stoloniferous Bearing stolon or stolons.

Stoma A pore in the epidermis of the leaf or stem for gaseous exchange. *Pl*. stomata.

Stone The hard endocarp of a drupe, containing the seed or seeds.

Stramineous Chaffy; straw liked.

Striae Parallel longitudinal lines or ridges. *Adj.* striate.

Striate Marked with fine longitudinal parallel lines or ridges.

Strigose Bearing stiff, straight, closely appressed hair; often the hairs have swollen bases.

Strobilus A cone-like structure formed from sporophylls or sporangiophores. *Pl.* strobili

Strophile An appendage at the hilum of certain plant seeds.

Strophiolate Furnished with a strophile or caruncle.

Style The part of the pistil between the stigma and ovary.

Sub- A prefix meaning nearly or almost, as in subglobose or subequal.

Subcarnose Nearly fleshy.

Subfamily Taxonomic rank between the family and tribe.

Subglobose Nearly spherical in shape.

Subretuse Faintly notched at the apex.

Subsessile Nearly stalkless or sessile.

Subshrub Intermediate between a herb and shrub.

Subspecies A taxonomic rank subordinate to species.

Substrate Surface on which a plant or organism grows or attached to.

Subtend Attached below something.

Subulate Narrow and tapering gradually to a fine point, awl shaped.

Succulent Fleshy, juicy, soft in texture and usually thickened.

Suckers Young plants sprouting from the underground roots of a parent plant and appearing around the base of the parent plant.

Suffrutescent Stem Stem woody at the base.

Sulcate Grooved longitudinally with deep furrows.

Sulcus A groove or depression running along the internodes of culms or branches.

Superior Refers to the ovary is free and mostly above the level of insertion of the sepals and petals. *Cf.* inferior.

Suture Line of dehiscence.

Swidden Slash and burn or shifting cultivation.

Syconium A type of pseudocarp formed from a hollow receptacle with small flowers attached to the inner wall. After fertilization the ovaries of the female flowers develop into one-seeded achenes, e.g. fig.

Symbiosis Describes close and often long-term mutualistic and beneficial interactions between different organisms.

Sympetalous Having petals united.

Sympodial Refers to a specialized lateral growth pattern in which the apical meristem is terminated. *Cf.* monopodial.

Synangium An organ composed of united sporangia, divided internally into cells, each containing spores. *Pl.* synangia.

Syncarp An aggregate or multiple fruit formed from two or more united carpels with a single style. *Adj.* syncarpous.

Syncarpous Carpels fused forming a compound pistil.

Synteny Presence of two or more genetic loci on the same chromosome.

Tannins Group of plant-derived phenolic compounds.

Taxon The taxonomic group of plants of any rank, e.g. a family, genus, species or any infraspecific category. *Pl.* taxa.

Tendril A slender, threadlike organ formed from a modified stem, leaf or leaflet which, by coiling around objects, supports a climbing plant.

Tepal A segment of the perianth in a flower in which all the perianth segments are similar in appearance and are not differentiated into calyx and corolla; a sepal or petal.

Tetrasporangium A sporangium containing four haploid spores as found in some algae.

Terete Having a circular shape when cross-sectioned or a cylindrical shape that tapers at each end.

Terminal At the apex or distal end.

Ternate In threes as of leaf with three leaflets.

Testa A seed coat, outer integument of a seed.

Thallus Plant body of algae, fungi and other lower organisms.

Thyrse A dense, panicle-like inflorescence, as of the lilac, in which the lateral branches terminate in cymes.

Tomentose Refers to plant hairs that are bent and matted forming a woolly coating.

Tomentellose Mildly tomentose.

Torus Receptacle of a flower.

Transpiration Evaporation of water from the plant through leaf and stem pores.

Tree That has many secondary branches supported clear of the ground on a single main stem or trunk.

Triangular Shaped like a triangle, three angled and three sided.

Tribe A category intermediate in rank between subfamily and genus.

Trichome A hair-like outgrowth of the epidermis.

Trichotomous Divided almost equally into three parts or elements.

Tridentate Three toothed or three pronged.

Trifid Divided or cleft into three parts or lobes.
Trifoliate Having three leaves.
Trifoliolate A leaf having three leaflets.
Trifurcate Having three forks or branches.
Trigonous Obtusely three angled; triangular in cross-section with plane faces.
Tripartite Consisting of three parts.
Tripinnate Relating to leaves, pinnately divided three times with pinnate pinnules.
Tripliveined Main laterals arising above base of lamina.
Triploid Describing a nucleus or cell that has three times (3*n*) the haploid number (*n*) of chromosomes.
Triveined Main laterals arising at the base of lamina.
Triquetrous Three edged; acutely three angled.
Trullate With the widest axis below the middle and with straight margins; ovate but margins straight and angled below middle, trowel shaped, angular ovate.
Truncate With an abruptly transverse end as if cut off.
Tuber A stem, usually underground, enlarged as a storage organ and with minute scale-like leaves and buds. *Adj.* tuberous.
Tubercle A wart-like protuberance. *Adj.* tuberculate.
Tuberculate Bearing tubercles; covered with warty lumps.
Tuberization Formation of tubers in the soil.
Tuft A densely packed cluster arising from an axis. *Adj.* tufted.
Turbinate Having the shape of a top; cone shaped, with the apex downward, inversely conic.
Turgid Distended by water or other liquid.
Turion The tender young, scaly shoot such as asparagus, developed from an underground bud without branches or leaves.
Turnery Articles made by the process of turning.
Twining Winding spirally.
Ultisols Mineral soils with no calcareous material, have less than 10 % weatherable minerals in the extreme top layer of soil and with less the 35 % base saturation throughout the soil.
Umbel An inflorescence of pedicellate flowers of almost equal length arising from one point on top of the peduncle. *Adj.* umbellate.
Umbellet A secondary umbel of a compound umbel. *Cf.* umbellule.
Umbellule A secondary umbel of a compound umbel. *Cf.* umbellet.
Uncinate Bent at the end like a hook; unciform.
Undershrub Subshrub; a small, usually sparsely branched woody shrub less than 1 m high. *Cf.* shrub.
Undulate With an edge/margin or edges wavy in a vertical plane; may vary from weakly to strongly undulate or crisped. *Cf.* crisped.
Unifoliolate A compound leaf which has been reduced to a single, usually terminal leaflet.
Uniform With one form, e.g. having stamens of a similar length or having one kind of leaf. *Cf.* dimorphic.
Uniseriate Arranged in one row or at one level.
Unisexual With one sex only, either bearing the anthers with pollen, or an ovary with ovules, referring to a flower, inflorescence or individual plant. *Cf.* bisexual.
Urceolate Shaped like a jug, urn or pitcher.
Utricle A small bladdery pericarp.
Valvate Meeting without overlapping, as of sepals or petals in bud. *Cf.* imbricate.
Valve One of the sections or portions into which a capsule separates when ripe.
Variant Any definable individual or group of individuals which may or may not be regarded as representing a formal taxon after examination.
Variegate, Variegated Diverse in colour or marked with irregular patches of different colours, blotched.
Variety A taxonomic rank below that of subspecies.
Vein (Botany) A strand of vascular bundle tissue.
Veinlets Small veins.
Velum A flap of tissue covering the sporangium in the fern, Isoetes.
Velutinous Having the surface covered with a fine and dense silky pubescence of short fine hairs; velvety. *Cf.* sericeous
Venation Distribution or arrangement of veins in a leaf.
Veneer Thin sheet of wood.
Ventral (Botany) Facing the central axis, opposed to dorsal.

Vernation The arrangement of young leaves or fronds in a bud or at a stem apex. *Cf.* circinate.

Verrucose Warty.

Verticil A circular arrangement, as of flowers, leaves, or hairs, growing about a central point; a whorl.

Verticillaster False whorl composed of a pair of opposite cymes as in Lamiaceae.

Verticillate Whorled, arranged in one or more whorls.

Vertisol A soil with a high content of expansive montmorillonite clay that forms deep cracks in drier seasons or years.

Vertosols Soils that both contain more than 35 % clay and possess deep cracks wider than 5 mm during most years.

Vesicle A small bladdery sac or cavity filled with air or fluid. *Adj.* vesicular.

Vestigial The remaining trace or remnant of an organ which seemingly lost all or most of its original function in a species through evolution.

Vestiture Covering; the type of hairiness, scaliness or other covering commonly found on the external parts of plants. *Cf.* indumentums.

Vibratile Capable of to-and-fro motion.

Villose Covered with long, fine, soft hairs, finer than in pilose.

Villous Covered with soft, shaggy unmatted hairs.

Vine A climbing or trailing plant.

Violaxanthin Is a natural xanthophyll pigment with an orange colour found in a variety of plants like pansies.

Viscid Sticky, being of a consistency that resists flow.

Viviparous Describes seeds or fruit which sprout before they fall from the parent plant.

Whorl A ringlike arrangement of leaves, sepals, stamens or other organs around an axis.

Winged Having a flat, often membranous expansion or flange, e.g. on a seed, stem or one of the two lateral petals of a Papilionaceous flower or one of the petal-like sepals of Polygalaceae. *Cf.* keel, standard.

Xanthophylls Are yellow, carotenoid pigments found in plants. They are oxidized derivatives of carotenes.

Xeromorphic Plant with special modified structure to help the plant to adapt to dry conditions.

Xerophyte A plant which naturally grows in dry regions and is often structurally modified to withstand dry conditions.

Zygomorphic Having only one plane of symmetry, usually the vertical plane, referring to a flower, calyx or corolla. *Cf.* actinomorphic.

Zygote The fist cell formed by the union of two gametes in sexual reproduction. *Adj.* zygotic.

Common Name Index

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