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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