Malus x domestica

Scientific Name

***Malus x domestica* Borkhausen.**

Synonyms

Malus communis Poiret, *Malus dasyphylla* Borkh., *Malus dasyphylla* var. *domestic*a Koidz., *Malus domestica* subsp. *pumila* (Miller) Likhonos, *Malus niedzwetzkyana* Dieck ex Koehne, *Malus malus* (L.) Britton, nom. inval., *Malus pumila* auct., *Malus pumila* Mill., *Malus pumila* auct. var. *domestica* (Borkh.) C. K. Schneid., *Malus sylvestris* auct., *Malus sylvestris* Mill. subsp. *mitis* (Wallr.) Mansf., *Malus sylvestris* var. *domestica* (Borkh.) Mansf., *Malus sylvestris* auct. var. *domestica* (Borkh.) Mansf., *Pyrus malus* L., *Pyrus malus* var. *pumila* Henry.

Family

Rosaceae

Common/English Names

Apple, Apple Tree

Vernacular Names

Arabic: Tuffahh;
Brazil: Maça, Maçanzeira, Maceira, Macieira;
China: Ping Guo;
Czech: Jabloň Domácí;
Danish: Abild, Æble, Æbletræ (Tree), Almindelig Æble;
Dutch: Appel, Vruchtappel;
Eastonian: Aed-Õunapuu;
Finnish: Omena, Paratiisiomena, Tarhaomenapuu
French: Pomme, Pommier, Pommier Commun;
Gaelic: Aabhail;
German: Apfel, Apfelbaum, Echter Apfelbaum, Kultur-Apfel;
Hungarian: Alma, Nemes Alma(Fa);
Icelandic: Eplatré, Garðepli;
India: Seb (Hindu), Badara, Mushtinanan, Seba, Seva (Sanskrit), Applepazham (Tamil);
Indonesia: Epal;
Italian: Mela, Melo, Melo Commune, Pomo;
Japanese: Ringo, Seiyou Ringo;
Korean: Sagwanamu;
Malaysia: Epal;
Norwegian: Apal;
Philippines: Mansanas;
Polish: Jabłoń Domowa;
Portuguese: Macieira;
Russian: Iabloko, Iablonia;
Serbian: Jabuka;

T.K. Lim, *Edible Medicinal And Non-Medicinal Plants: Volume 4, Fruits*,
DOI 10.1007/978-94-007-4053-2_49, © Springer Science+Business Media B.V. 2012

Slovaščina: Jablana, Žlahtna Jablana;
Slovencina: Jabloň Domáca;
Sorbic: Jablušina;
Spanish: Manzana, Manzano;
Swedish: Äpple, Äppel, Äppelträd;
Thai: Aeppen, Aoppoen;
Turkish: Elma;
Vietnamese: Pom.

Origin/Distribution

Recent genomic studies by Velasco et al. (2010) identified the progenitor of the cultivated apple as *M. sieversii*. This species was found in the IIi Valley, on the northern slopes of the Tien Shan mountains at the border of northwest China and Kazakhstan. Leaves taken from trees in this area were analyzed for DNA composition, which showed them all to belong to the species *M. sieversii*, with some genetic sequences common to *Malus domestica.* However, another chloroplast DNA analysis found that *Malus sylvestris* had also contributed to the genome of *M. domestica* (Coart et al. 2006). A closer relationship than presently accepted was found between *M. sylvestris* and *M. domestica* at the cytoplasmic level, with the detection of eight chloroplast haplotypes shared by both species. Hybridization between *M. sylvestris* and *M. domestica* was also apparent at the local level with sharing of rare haplotypes among local cultivars and sympatric wild trees. Indications of the use of wild *Malus* genotypes in the (local) cultivation process of *M. domestica* and cytoplasmic introgression of chloroplast haplotypes into *M. sylvestris* from the domesticated apple were found. Only one of the *M. sieversii* trees studied displayed one of the three main chloroplast haplotypes shared by *M. sylvestris* and *M. domestica*. Thus the origin of the domestic apple is still unresolved. There are more than 7,500 known cultivars of apples, resulting in a diverse range of desired characteristics.

Agroecology

Apples are best adapted to the cool temperate areas from about 35–50° latitude. Apples thrives best in cool temperate climates with high light intensity, warm (not hot) days and cool nights. Apples require about 1,000–1,600 hours of chilling (7.2°C) to break dormancy. Wood and buds are hardy to −40°C but open flowers and developing fruitlets are damage by brief exposure to −2°C or less.

In the tropics, apples can be grown in cool areas in the high elevation of 800–1,200 m where temperatures hovers from 16 to 27°C, rainfall 1,600–3,200 mm, relative humidity 75–85% and sunshine more than 50% duration.

Apples can be grown in a wide variety of soils but does best in deep, fertile, well-drained, loamy soils with pH 6–7.

Edible Plant Parts and Uses

Apples are widely eaten fresh and are often eaten baked or stewed. Apples are also dried and eaten or reconstituted by soaked in water, alcohol or some other liquid, for subsequent use. Apples can be canned or juice. Apple juice has surpassed orange juice consumption by children in the USA. Apples are milled to produce apple cider (non-alcoholic sweet beverage) and filtered for apple juice. Apple juice can be fermented to process cider, ciderkin (weak alcoholic cider) and vinegar, Distillation of apple juice affords various alcoholic beverages such as apfelwein (apple wine), applejack (strong alcoholic beverage) and Calvados (apple brandy). Apples are widely used in pies, pastries, cakes, jams, sauces, apple butter, apple jellies, meat dishes. In the United Kingdom, traditional toffee apples made by coating apples in hot toffee are relished, and candy apples and caramel apples in USA. Fruit pectins and apple seed oil are also produced.

Botany

The tree is small and deciduous, reaching 5–12 m tall, with a broad, often densely twiggy crown. Branchlets brown, tomentose when young, glabrous when old. Stipules caducous and lanceolate. Leaves, alternate, simple, ovate, or broadly elliptic 5–11 cm × 3–6 cm, both surfaces densely puberulous when young, adaxially glabrecent, pinnately veined, apex acute, base broadly cuneate or rounded, margin serrated on 2–5 cm petiole (Plates 1, 2 and 3). Flowers in 3–7 flowered corymb at the apices of branchlets, 3–4 cm across, pedicel tomentose; bracts linear-lanceolate, caducous. Flower – hypanthium tomentose; sepals lanceolate-deltoid, longer than hypanthium, tomentose; petals 5 white with tinge of pink, obovate, base shortly clawed, apex rounded; stamens 20, unequal; ovary 5-loculed with 2 ovules per locule, style 5 tomentose at the base (Plate 1). Pome subglobose, obovoid to ellipsod, variable size and colour, 5–10 cm diameter, pale green, yellow, pink to red, impressed at the base, sepals persistent and fruting pedicel short and thickened (Plates 3, 4, 5, 6, 7 and 8). Seeds small and black-brown.

Plate 1 Apple blossoms

Plate 2 Immature apples

Plate 3 Maturing apples and leaves

Plate 4 Red Delicious apple

Plate 5 Indonesian cultivar ‘Anna’

Plate 6 Granny Smith

Plate 7 Indonesian cultivar 'Mana Lagi'

Nutritive/Medicinal Properties

Fruit Nutrients

The nutrient composition of raw apples (*Malus domestica*) with skin based on analytical data (per 100 g edible portion) for red delicious, golden delicious, gala, granny smith, and fuji varieties was reported as: water 85.56 g, energy 52 kcal (218 kJ), protein 0.26 g, total lipid (fat) 0.17 g, ash 0.19 g, carbohydrate13.81 g, total dietary fibre 2.4 g, total sugars 10.39 g, sucrose 2.07 g glucose (dextrose) 2.43 g, fructose 5.90 g, starch 0.05 g, Ca 6 mg, Fe 0.12 mg, Mg 5 mg, P 11 mg, K 107 mg, Na 1 mg, Zn 0.04 mg, Cu 0.027 mg, Mn 0.035 mg, F 3.3 μg, vitamin C 4.6 mg, thiamin 0.017 mg, riboflavin 0.026 mg, niacin 0.091 mg, pantothenic acid 0.061 mg, vitamin B-6 0.041 mg, total folate 3 μg, total choline 3.4 mg, betaine 0.1 mg, vitamin A54 IU, vitamin A 3 μg RAE, β-carotene 27 μg, β-cryptoxanthin 11 μg, lutein + zeaxanthin 29 μg, vitamin E (α-tocopherol) 0.18 mg, vitamin K (phylloquinone) 2.2 μg, total saturated fatty acids 0.028 g, 14:0 (myristic acid) 0.001 g, 16:0 (palmitic acid) 0.024 g, 18:0 (stearic acid) 0.003 g, total monounsaturated fatty acids 0.007 g, 18:1 undifferentiated (oleic) 0.007 g, total polyunsaturated fatty acids 0.051 g, 18:2 undifferentiated (linoleic acid) 0.043 g, 18:3 undifferentiated (linolenic acid) 0.009 g,

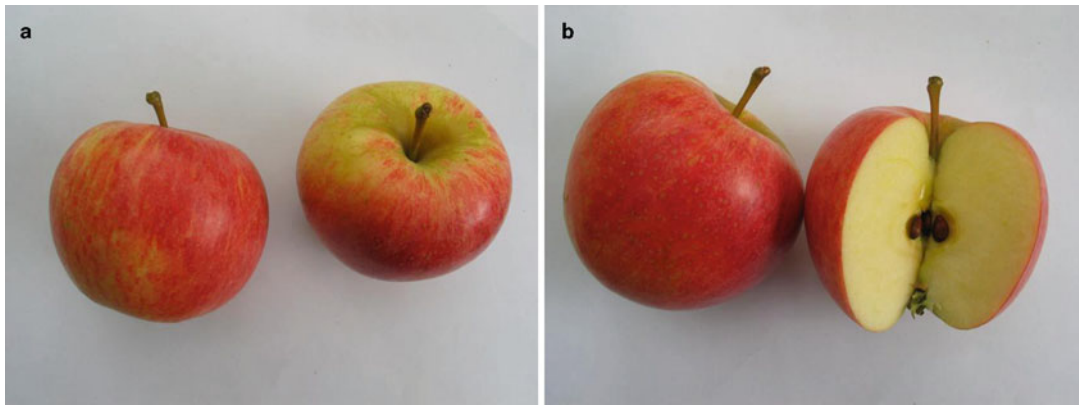

Plate 8 (**a**) Gala apple whole; (**b**) sliced

phytosterols 12 mg, tryptophan 0.001 g, threonine 0.006 g, isoleucine 0.006 g, leucine 0.013 g, lysine 0.012 g, methionine 0.001 g, cystine 0.001 g, phenylalanine 0.006 g, tyrosine 0.001 g, valine 0.012 g, arginine 0.006 g, histidine 0.005 g, alanine 0.011 g, aspartic acid 0.070 g, glutamic acid 0. 025 g, glycine 0.009 g, proline 0.006 g, and serine 0.010 g (USDA 2011).

Fruit Volatile Compounds

Over 300 volatile compounds had been reported associated with the aroma profile of apples (Dixon and Hewett 2000). These compounds included alcohols, aldehydes, carboxylic esters, ketones, ethers, acids, bases, acetals, and hydrocarbons (Dimick and Hoskin 1983). Compounds in the volatile profile of apples were reported to be dominated by esters (78–92%) and alcohols (6–16%) (Paillard 1990). The most abundant compounds were even numbered carbon chains including combinations of acetic, butanoic, and hexanoic acids with ethyl, butyl, and hexyl alcohols (Paillard 1990). The important aroma volatile compounds reported include: aldehydes:- acetaldehyde, trans-2-hexenal (Flath et al. 1967), hexanal (Paillard 1990); alcohols:- ethanol (Teranishi et al. 1987), propan-1-ol, butan-1-ol, heaxa-1-ol, (Flath et al. 1967), 2 methyl butan-1-ol (Buttery et al. 1973); esters:- ethyl-2-methyl butanoate (Flath et al. 1967), propyl acetate (Takeoka et al. 1996), ethyl acetate, butyl acetate, pentyl acetate, hexyl acetate, ethyl butanoate, ethyl-2-methyl butanoate, ethyl propionate, ethyl pentanoate, ethyl hexanoate (Teranishi et al. 1987; Takeoka et al. 1996); propyl butanoate, 2 methyl butyl acetate (Teranishi et al. 1987). Dixon and Hewett (2000) reported that hypoxic treatment of fresh fruit could induce significant increases in volatile concentrations that could be used in production of high quality essences from apple juice. In addition the use of hypoxia to enhance volatile concentrations may be a beneficial side effect when such treatments are used for disinfestations purposes. It is possible that given equal efficacy, hypoxia could be either preferred or used as an adjunct to heat treatments to eradicate insects.

Other Fruit Phytochemicals

Main structural classes of apple constituents include hydroxycinnamic acids, dihydrochalcones, flavonols (quercetin glycosides), catechins and oligomeric procyanidins, as well as triterpenoids in apple peel and anthocyanins in red apples (Gerhauser 2008). The phenolic compound profile in apples varies with varieties. The highest levels of phenolic compounds were found in the peel of four apple varieties (Golden and Red Delicious, Granny Smith and Green Reineta) (Escarpa and Gonzalez 1998). High levels of catechins and flavonol glycosides, especially rutin, were found in apple peels. Chlorogenic acid was the major compound in the pulp for all apple varieties studied except for Granny Smith. Significant quantitative differences between the apple varieties were also found, the Golden Delicious variety showing the lowest content of phenolic compounds and Green Reineta variety the highest. Studies in Poland found the Champion apple variety to be the best source of phenolic acids and epicatechin compared to the Jonica variety (Malik et al. 2009). Chlorogenic predominated in the Champion variety whereas in the Jonica variety, chlorogenic and homovanilic acids were dominant. The highest concentration of chlorogenic acid was detected in the pulp of Jonica variety around the cities of Puławy and Lublin, whereas homovanilic acid was the highest in the other samples collected from the vicinity of Stryjno and Góry Markuszowskie. Among the Jonica and Champion varieties of apples collected from various orchards in the vicinity of Lublin, the highest content of epicatechin (13,12 mg/kg) was found in the pulps of Champions variety collected in Puławy. Studies reported the following phenolic compound in 14 French apple varieties: monomeric catechins, proanthocyanidins, hydroxycinnamic acids, and dihydrochalcones (Sanoner et al. 1999). Depending on the variety, the total polyphenol concentration varied from 1 to 7 g/kg of fresh cortex. Cider varieties generally showed a higher polyphenol concentration than the dessert apple Golden Delicious, bitter varieties had the highest concentration. For all varieties, procyanidins were the domiant group, mainly

constituted of (−)-epicatechin units with a small proportion of (+)-catechin as a terminal unit. Of the apple polyphenols, procyanidins were found to bind with cell wall material, leading to decreased levels of polyphenols found in apple juices (Renard et al. 2001). Hydroxycinnamic acids and (−)-epicatechin did not bind to cell walls.

The air-dried and freeze-dried apple (Rome Beauty) peels had the highest total phenolic, flavonoid, and anthocyanin contents (Wolfe and Liu 2003). On a fresh weight basis, the total phenolic and flavonoid contents of these samples were similar to those of the fresh apple peels. Freeze-dried peels had a lower water activity than air-dried peels on a fresh weight basis. The total phenolic content of apple peel powder was 3,342 mg gallic acid equivalents/100 g dried peels, the flavonoid content was 2,299 mg catechin equivalents/100 g dried peels, and the anthocyanin content was 169.7 mg cyanidin 3-glucoside equivalents/100 g dried peels. These phytochemical contents were a significantly higher than those of the fresh apple peels if calculated on a fresh weight basis. Apple peel extracts had higher total soluble phenolic content and related antioxidant capacity than pulp extracts (Barbosa et al. 2010). Quercetin derivatives, protocatechuic acid, chlorogenic acid, and p-coumaric acid were detected, and the amount varied significantly between aqueous and ethanolic extracts. Compared with apple pulps, peels were found to be richer in phenolics (Chinnici et al. 2004). Flavonols, flavanols, procyanidins, dihydrochalcones, and hydroxycinnamates were the identified phenolic classes in apple peel tissue, and the most abundant compounds were epicatechin, procyanidin B2, and phloridzin (Chinnici et al. 2004). Pulps were poorer in phytochemicals. Their major phenolics were procyanidins and hydroxycinnamates. Flavonols in amounts <20 mg/kg fresh weight (fw) were also found. In both peels and pulps, integrated production samples were richer in polyphenols. Among the 14 compounds identified, only phloridzin had a tendency to appear higher in organic peels. Apples also contain soluble polysaccharides. The yield of soluble polysaccharides in peeled apples was found to range from 0.43% to 0.88%, with molecular weight ranging 223–848 kDa (Ker et al. 2010). All belonged to peptidoglycans. Among the 14 amino acids found, seven were essential amino acids. Additionally, 50% of apple samples consisted of glucoarabinan, 37.5% comprising taloarabinan and the remaining 12.5% containing alloglucan. Further, the soluble polysaccharides consisted of a huge amount of myo-inositol (>5.61%) and uronic acid (>11.7%). Talose, allose and fucose were found for the first time in the soluble polysaccharides of apples. The most abundant phenolic compounds found in Annurca apple peel ethanol extract were rutin, epicatechin, dicaffeoylquinic acid, and caffeic acid; these compounds constituted 27.43%, 24.93%, 16.14%, and 15.3% of the total phenols, respectively (Fratianni et al. 2011).

Apple peels were found to contain hypophasic carotenoids mainly composed of violaxanthin, zeaxanthin and lutein and epiphasic carotenoids composed of a high content of β,β-carotene and β-cryptoxanthin (Molnár et al. 2005). Seven additional carotenoids were isolated from apple peels: (all-E)-luteoxanthin, (all-E)-neoxanthin, (9'Z)-neoxanthin, (all-E)-antheraxanthin, (all-E)-violaxanthin, (9Z)-violaxanthin and (all-E)-lutein (Molnár et al. 2010).

Organic acids found in apple peels included: glyoxylic, isocitric, malic, quinic, shikimic, glyceric, α-oxoglutaric, pyruvic; and in apple pulp: pyruvic, malic, quinic, shikimic, citramalic, glyceric, and α-oxoglutaric (Salunkhe and Kadam 1995).

Apple Juice Chemicals

Delage et al. (1991) found the following phenolic compounds chlorogenic acid, *p*-coumaric acid, protocatechuic acid, (+)-catechin, (−)-epicatechin, phloridzin and di-, tri- and tetrameric procyanidins in apple juice. Phenolic and furfural compounds found in apple juice comprised chlorogenic and coumaroylquinic acids and phloridzin as the major phenolic components and caffeic, *p*-coumaric, ferulic, gallic and protocatechuic acids, and catechin as the minor

phenolics; and 5-hydroxymethyl-2-furaldehyde and 2-furaldehyde (Kermasha et al. 1995). Organic acids found in apple juice included: malic, quinic, succinic, lactic, glucoronic, citramalic, mucic acids (Salunkhe and Kadam 1995).

Apple Pomace Chemicals

The predominant phenolic compounds in apple pomace were phloridzin, chlorogenic acid and quercetin glycosides (Schieber et al. 2003). While the polyphenolics recovered from apple pomace may be used as natural antioxidants or as functional food ingredients, extended fields of application may be obtained for decolorised, refined apple pectins. Six high-purified polyphenols were identified in apple pomace: chlorogenic acid, quercetin-3-glucoside/quercetin-3-glacaside, quercetin-3-xyloside, phloridzin, quercetin-3-arabinoside and quercetin-3-rhamnoside (Cao et al. 2009). HPLC analysis indicated that the major polyphenols of apple pomace consisted of chlorogenic acid, caffeic acid, syrigin, procyanidin B2, (−)-epicatechin, cinnamic acid, coumaric acid, phlorizin and quercetin, of which procyanidin B2 had the highest content of 219.4 mg/kg (Bai et al. 2010). The actual yield of polyphenols was 62.68 mg gallic acid equivalent per 100 g dry apple pomace.

Apple Seed Oil

Oil content extracted from apple seeds ranged from 20.69 to 24.32 g/100 g (Tian et al. 2010). The protein, fibre and ash contents were found to be 38.85–49.55, 3.92–4.32 and 4.31–5.20 g/100 g, respectively. The extracted oils exhibited an iodine value of 94.14–101.15 g I/100 g oil; refractive index (40°C) was 1.465–1.466; density (25°C) was 0.902–0.903 mg/ml; saponification value was 179.01–197.25 mg KOH/g oil; and the acid value was 4.036–4.323 mg KOH/g oil. The apple seed oils consisted mainly of linoleic acid (50.7–51.4 g/100 g) and oleic acid (37.49–38.55 g/100 g). Other prominent fatty acids were palmitic acid (6.51–6.60 g/100 g), stearic acid (1.75–1.96 g/100 g) and arachidic acid (1.49–1.54 g/100 g).

Leaf Phytochemicals

In apple, the dihydrochalcone phloridzin (phloretin 2′-O-glucoside) was found to be dominant representing more than 90% of the soluble phenolics in the leaves (Gosch et al. 2009). Apple leaves were found to contain flavonoids dihydrochalcones such as phloridzin, sieboldin and trilobatin (Dugé de Bernonville et al. 2010).

Scientific studies suggested that apples and apple products possessed a wide range of biological activities that include antioxidant, antiproliferative, anti-diabetic, anti-inflammatory, lipid oxidation inhibition, and cholesterol lowering activities which may contribute to health beneficial effects against cardiovascular disease, asthma and pulmonary dysfunction, diabetes, obesity, and cancer (Boyer and Lui 2004).

Antioxidant Activity

Apples were reported to contain a variety of phytochemicals, including quercetin, catechin, phloridzin and chlorogenic acid, all potent antioxidants (Boyer and Lui 2004). Eberhardt et al. (2000) reported that 100 g of fresh apples had an antioxidant activity equivalent to 1,500 mg of vitamin C. All the apple polyphenols epicatechin, its dimer (procyanidin B2), trimer, tetramer and oligomer, quercetin glycosides, chlorogenic acid, phloridzin and 3-hydroxy-phloridzin displayed strong antioxidant activities (Lu and Foo 2000). Their DPPH-scavenging activities were 2–3 times and superoxide anion radical-scavenging activities were 10–30 times better than those of the antioxidant vitamins C and E. Sun et al. (2002) found that cranberry had the highest total antioxidant activity (177.0 μmol of vitamin C equiv/g of fruit), followed by apple, red grape, strawberry, peach, lemon, pear, banana, orange, grapefruit, and pineapple. Results of studies indicated that flavonoids such as quercetin,

epicatechin, and procyanidin B(2) rather than vitamin C contributed significantly to the total antioxidant activity of apples (Lee et al. 2003). They found that the average concentrations of major phenolics and vitamin C in six apple cultivars were as follows (mg/100 g of fresh weight of apples): quercetin glycosides, 13.20; procyanidin B(2), 9.35; chlorogenic acid, 9.02; epicatechin, 8.65; phloretin glycosides, 5.59; vitamin C, 12.80. A highly linear relationship ($R^2 > 0.97$) was attained between concentrations and total antioxidant capacity of phenolics and vitamin C. Relative vitamin C equivalent antioxidant capacity (VCEAC) values of these compounds were in the order quercetin (3.06) > epicatechin (2.67) > procyanidin B(2) (2.36) > phloretin (1.63) > vitamin C (1.00) > chlorogenic acid (0.97). In another study, the estimated contribution of major phenolics and vitamin C to the total antioxidant capacity of 100 g of fresh apples was as follows: quercetin (40.39 VCEAC) > epicatechin (23.10) > procyanidin B(2) (22.07) > vitamin C (12.80) > phloretin (9.11) > chlorogenic acid (8.75). Processing was found to impact on the bioactivity of apple products (van der Sluis et al. 2002). Raw juice obtained by pulping and straight pressing or after pulp enzyming had an antioxidant activity that was only 10% and 3%, respectively, of the activity of the fresh apples. The levels of flavonoids and chlorogenic acid in the juice were reduced to between 50% (chlorogenic acid) and 3% (catechins). Most of the antioxidants were retained in the pomace rather than being transferred into the juice. In apple juice, 45% of the total measured antioxidant activity could be ascribed to the analyzed antioxidants. For three apple cultivars tested (Elstar, Golden Delicious, and Jonagold), the processing methods had similar effects.

Integrated apple peels gave the highest total antioxidant capacities (TAC) (18.56 mM/kg fw), followed by organic peels (TAC = 14.96), integrated pulps (TAC = 7.12), and organic pulps (TAC = 6.28) (Chinnici et al. 2004). In peels, the top contributors to the antioxidant activity were found to be flavonols, flavanols, and procyanidins, which accounted for about 90% of the total calculated activity whereas in pulps, the TAC was primarily derived from flavanols (monomers and polymers) together with hydroxycinnamates. A good correlation between the sum of polyphenols and the radical scavenging activities was found. Among the single classes of compounds, procyanidins (in peels and pulps) and flavonols (in peels) were statistically correlated to the TAC. The apple peel (Rome Beauty) powder had a total antioxidant activity of 1,251 μmol vitamin C equivalent/g, similar to fresh Rome Beauty peels on a fresh weight basis (Wolfe and Liu 2003). One gram of powder had an antioxidant activity equivalent to 220 mg of vitamin C. Apple peel powder may be used in a various food products to add phytochemicals and promote good health. In four varieties of apples (Rome Beauty, Idared, Cortland, and Golden Delicious) commonly used in apple sauce production, the total phenolic and flavonoid contents were highest in the peels, followed by the flesh + peel and the flesh (Wolfe et al. 2003). Idared and Rome Beauty apple peels had the highest total phenolic contents (588.9 and 500.2 mg of gallic acid equivalent/100 g of peels, respectively). Rome Beauty and Idared peels had highest flavonoids (306.1 and 303.2 mg of catechin equivalent/100 g of peels, respectively). Idared apple peels had the most anthocyanins, with 26.8 mg of cyanidin 3-glucoside equivalent/100 g of peels. The peels all had significantly higher total antioxidant activities than the flesh + peel and flesh of the apple varieties examined. Idared peels had the greatest antioxidant activity (312.2 μmol of vitamin C equivalent/g of peels). In separate study, apple peel and pulp were found to have significantly higher antioxidant potentials than in pear peel and pulp as measured by 1,1-diphenyl-2-picrylhydrazyl (DPPH), β-carotene bleaching (β-carotene), and nitric oxide inhibition radical scavenging (NO) assays (Leontowicz et al. 2003). The ethanol extract of apple peels exhibited the strongest inhibition of lipid peroxidation as a function of its concentration and was comparable to the antioxidant activity of butylated hydroxyanisole. The polyphenols, phenolic acids, and flavonoids contributed to the antioxidant potential which correlated well with polyphenols and flavonoids. The correlation coefficients between

polyphenols and antioxidant activities by DPPH, β-carotene, and NO were as follows: 0.9207, 0.9350, and 0.9453. In contrast, the correlation coefficient between the content of dietary fiber and the antioxidant activities test was low. The content of all studied indices in apple and pear peel was significantly higher than in peeled fruits. Diets supplemented with fruit peels exercised a significantly higher positive influence on plasma lipid levels and on plasma antioxidant capacity of rats than diets with fruit pulps.

In-vitro studies found apple skin extracts to be effective inhibitors of oxidation of polyunsaturated fatty acid in a model system (Huber and Rupasinghe 2009). The antioxidant capacity measured by Folin-Ciocalteu ranged from 16.2 to 34.1 mg GAE/100 g DW, ferric reducing antioxidant power varied from 1.3 to 3.3 g TE/100 g DW, oxygen radical absorbance capacity ranged from 5.2 to 14.2 g TE/100 g DW, and percent inhibition of oxidation of methyl linolenate from 73.8% to 97.2% among the apple genotypes. The total phenolic concentrations of methanolic extracts of skins of the apple genotypes varied from 150 to 700 mg/100 g DW. The test for 2,2-diphenyl-1-picryl-hydrazyl free radical-scavenging activity showed that the ethanol extract of annurca apple peel rich in polyphenols (rutin, epicatechin, dicaffeoylquinic acid, and caffeic acid) possessed an impressive antioxidant capacity (50% effective concentration of 2.50 μg/g of product) (Fratianni et al. 2011).

Honeycrisp and Red Delicious apple varieties had the highest total phenolic contents and a significant correlation with antioxidant capacity ($R^2 = 0.91$) (Barbosa et al. 2010). Quercetin-rich apple peel extract and apple pomace were found to effectively reduced ROS (reactive oxygen species)-DNA damage in Caco-2 cells (with the former being more potent), whereas apple juice was only moderately effective (Bellion et al. 2010). Glutathione peroxidise activity was reduced by all the extracts in the following order apple juice > apple pomace > apple peel. Direct antioxidant activity decreased in the order apple juice > apple peel > apple pomace. The data suggested that apple phenolics at low, nutritionally relevant concentrations may protect intestinal cells from ROS-induced DNA damage, mediated by cellular defense mechanisms rather than by antioxidant activity.

During long-term cold storage (120 days at 1°C) as well as during an additional 7 day storage of fruits at 16°C, total phenols, total antioxidant activity (TAA), and radical scavenging activity (RSA) in the peel of two apple cultivars (Jonagold and S'ampion) increased considerably, irrespective of the storage conditions (Leja et al. 2003). A slight decrease in anthocyanins was observed in apples stored in air, while the controlled atmosphere treatment (2% CO_2/2% O_2) did not cause any significant changes.

Results of a study suggested that the two farming systems (organic/conventional) did not result in differences in the bioavailability of apple polyphenols in humans (Stracke et al. 2010). In a randomized cross-over short term intervention study of six men after 1 kg intake of apples phloretin and coumaric acid plasma concentrations increased significantly in both intervention groups, without differences between the two farming systems. In a double-blind, randomized long term intervention study of 43 healthy individuals, consumption of organically or conventionally grown apples did not result in increasing polyphenol concentrations in plasma and urine compared to the control group suggesting no accumulation of apple polyphenols or degradation products in humans.

Apple polyphenols have beneficial bioactive effects such as antioxidant activity in-vivo, but can also exert prooxidative effects in-vitro (Bellion et al. 2009). From their findings they cautioned that the generation of hydrogen peroxide in-vitro by polyphenols had to be taken into consideration when interpreting results of such cell culture experiments. However they maintained that high polyphenol concentrations, favoring substantial H_2O_2 formation, were not expected to occur in-vivo, even under conditions of high end nutritional uptake.

The dihydrochalcone phloridzin from apple leaves exhibited high antioxidant activity in the oxygen radical absorbance capacity (ORAC) assay, and sieboldin in young leaves had high 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity (Dugé de Bernonville et al. 2010).

Inhibition of Lipid Oxidation/ Hypolipidemic Activities

Six commercial apple juices and extracts of the peel (RP), flesh (RF) and whole fresh Red Delicious apples (RW), tested at 5 μM gallic acid equivalents (GAE), all inhibited low density lipoprotein oxidation (Pearson et al. 1999). The inhibition by the juices ranged from 9% to 34%, and inhibition by RF, RW and RP was 21%, 34% and 38%, respectively. The phenolic composition of six commercial apple juices, and of the peel (RP), flesh (RF) and whole fresh Red Delicious apples (RW), was found to comprise several classes of phenolic compounds: cinnamates, anthocyanins, flavan-3-ols and flavonols. Phloridzin and hydroxy methyl furfural were also detected. The profile of total phenolic concentration in the apple juices was: hydroxy methyl furfural, 4–30%; phloridzin, 22–36%; cinnamates, 25–36%; anthocyanins, n.d.; flavan-3-ols, 8–27%; and flavonols, 2–10%. The phenolic profile of the Red Delicious apple extracts differed from those of the juices. The profile of phenolic classes in fresh apple extracts was: hydroxy methyl furfural, n.d.; phloridzin, 11–17%; cinnamates, 3–27%; anthocyanins, n.d.–42%; flavan-3-ols, 31–54%; and flavonols, 1–10%. Liver microsomal lipid peroxidation was decreased in rats pretreated with apple juice by 52–87% when compared to animals given toxicants N-nitrosodiethylamine (NDEA) or carbon tetrachloride alone (Kujawska et al. 2011). Pretreatment with juice protected antioxidant enzymes: catalase, glutathione peroxidase and glutathione reductase but not superoxide dismutase. The plasma activity of paraoxonase 1 was reduced by both toxicants and was increased by 23% in the apple/carbon tetrachloride group. A rise in plasma protein carbonyls caused by the xenobiotics was reduced by 20% only in apple/NDEA-treated rats. Also, in this group of animals, a 9% decrease in DNA damage in blood leukocytes was observed.

Soluble polysaccharides of apples comprising all peptidoglycans and also a huge amount of myo-inositol (>5.61%) and uronic acid (>11.7%), may play a synergistic role in the hypolipidemic effect (Ker et al. 2010). The biological value of soluble polysaccharides was attributable to the differential effect of soluble polysaccharides and the synergistic effect exerted by its unique soluble polysaccharides profile, high myo-inositol and uronic acid contents.

Cardiovascular/Antiatherosclerotic/ Antihypercholesterolemic Activities

Leontowicz et al. (2002) found that diets with apples and to a lesser extent with peaches and pears improved lipid metabolism and increased the plasma antioxidant potential especially in rats fed with added cholesterol. The total polyphenols of peeled fruits and fruit peels of apples were higher than in pears or peaches. Caffeic, p-coumaric and ferulic acids and the total radical-trapping antioxidative potential (TRAP) values in peeled apples and their peels were significantly higher than in peaches and pears. Dietary fibre were similar in all three fruits. They concluded that the higher content of biologically active compounds and the better results in rats makes apple preferable for dietary prevention of atherosclerosis and other diseases. The content of all studied indices in peels was significantly higher than peeled fruits. A good correlation between the total polyphenols and the TRAP values was found in all fruits. Aprikian et al. (2002) found that a moderate supply of dessert apples elicited interesting effects on lipid and peroxidation parameters. When cholesterol fed rats were supplemented with lyophilized apples (15%), there was a significant drop in plasma cholesterol and liver cholesterols and an increase in high-density lipoproteins (HDL) giving. Furthermore, they found that cholesterol excretion increased in the faeces of rats fed apples, suggesting reduced cholesterol absorption. Concomitantly apple supplementation gave higher FRAP (ferric reducing antioxidant power) plasma levels than controls together with a reduced malondialdehyde excretion in urine. In another study, Aprikian et al. (2003) found that combined apple pectin and high polyphenol freeze-dried apple lowered plasma and liver cholesterol, triglycerides, and apparent cholesterol absorption to a much greater

extent than either apple pectin alone or apple phenolic fraction alone in rats. Their study suggested a beneficial interaction between fruit fibre and polyphenolic components on large intestine fermentations and lipid metabolism and also supports the benefits of eating whole fruits as opposed to dietary supplements.

Studies showed that consumption of apple, pear or orange juice increased total plasma antioxidant capacity, total cholesterol, high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol in non-smokers (Alvarez-Parrilla et al. 2010). In smokers, fruit/juice supplementation decreased total cholesterol without inducing increase in total antioxidant capacity. Prospective epidemiological studies had reported that a higher fruit and vegetable intake is associated with a lower risk of coronary heart disease. Hansen et al. (2010) found in a median follow-up of 7.7 years of the Diet, Cancer and Health cohort study in 1993–1997, 1,075 incident acute coronary syndrome (ACS) cases were identified among 53 383 men and women, aged 50–64 years. They found an inverse association for apple intake with ACS. This association was also seen among women, albeit borderline significant. Their results supported previously observed inverse associations between fresh fruit intake, particularly apples, and ACS risk.

Apple juice (5 and 10 ml) significantly decreased total cholesterol, total glyceride, C-reactive protein, fibrinogen, factor VII levels, atherosclerotic lesions in the right and left coronary arteries and increased nitrite and nitrate in rabbits compared to those fed a cholesterolemic diet (Setorki et al. 2009). Ten ml but not 5 ml apple juice significantly reduced LDL-C and increased HDL-C. No significant difference was found between 5 and 10 ml apple juice groups with regard to C-reactive protein P, nitrite, nitrate, fibrinogen, factor VII, total glyceride, HDL-C and total cholesterol concentrations. The anti atherosclerotic effect of apple juice was attributed to its antioxidant and antiinflammatory properties.

Apple procyanidins exerted a potent vasorelaxation effect in 1.0 μM phenylephrine-contractive rat thoracic aorta (Matsui et al. 2009). The procyanidin-induced vasorelaxation was found to be associated with NO-cGMP pathway in combination with hyperpolarization due to multiple activation of Ca(2+)-dependent and -independent K(+) channels.

Anticancer Activity

Apple extracts and it phytochemicals, especially oligomeric procyanidins, had been shown to influence multiple mechanisms relevant for cancer prevention in in-vitro studies (Gerhauser 2008). These include antimutagenic activity, modulation of carcinogen metabolism, antioxidant activity, antiinflammatory mechanisms, modulation of signal transduction pathways, antiproliferative and apoptosis-inducing activity, as well as novel mechanisms on epigenetic events and innate immunity. Apple products had been shown to prevent skin, mammary and colon carcinogenesis in animal models. Epidemiological observations indicated that regular consumption of one or more apples a day may reduce the risk for lung and colon cancer (Boyer and Lui 2004; Gerhauser 2008).

Several in-vitro studies had shown apples to have antiproliferative activity. Cranberry showed the highest in-vitro inhibitory effect on proliferation of HepG(2) human liver-cancer cells followed by lemon, apple, strawberry, red grape, banana, grapefruit, and peach (Sun et al. 2002). Eberhardt et al. (2000) found that whole-apple extracts inhibited the growth of Caco-2 colon cancer cells and Hep G2 liver cancer cells in-vitro in a dose-dependent manner. They proposed that the unique combination of phytochemicals in the apples were responsible for inhibiting the growth of tumour cells. The antiproliferative activity of apples was found to vary with apple varieties (Liu et al. 2001). At a dose of 50 mg/ml, Fuji apple extracts inhibited Hep G2 human liver cancer cell proliferation by 39% and Red Delicious extracts inhibited cell proliferation by 57%. Northern Spy apples had no effect on cell proliferation. They found that total phenolic and flavonoid content was positively related to antioxidant activity and inhibition of cell proliferation. Wolfe et al. (2003) found that apple peels

(Rome Beauty, Idared, Cortland, and Golden Delicious varieties) were more effective in inhibiting the growth of HepG(2) human liver cancer cells than whole apple or apple flesh. Rome Beauty apple peels showed the most bioactivity, inhibiting cell proliferation by 50% at the low concentration of 12.4 mg of peels/ml. The freeze-dried apple peels of Rome Beauty exerted a strong antiproliferative effect on HepG(2) liver cancer cells with a median effective dose (EC_{50} of 1.88 mg/ml) (Wolfe and Liu 2003). This was lower than the EC_{50} exhibited by the fresh apple peels.

The results of studies by Ding et al. (2004) showed that an extract from fresh apple peel may inhibit tumour promoter-induced carcinogenesis and associated cell signalling and suggested that the chemopreventive effects of fresh apple may be through its antioxidant properties by blocking reactive oxygen species-mediated AP-1-MAPK activation. Oral administration of apple peel extracts decreased the number of nonmalignant and malignant skin tumours per mouse induced by 12-O-tetradecanolyphorbol −13-acetate (TPA) in 7,12-dimethylbenz(a)anthracene-initiated mouse skin. This inhibitory effect appeared to be mediated by the inhibition of ERKs and JNK activity. ESR analysis indicated that apple extract strongly scavenged hydroxyl (OH) and superoxide O_2^- radicals. Reagan-Shaw et al. (2010) found that apple (gala) peel extract exhibited potent antiproliferative effects. The peel extract elicited a significant decrease in growth and clonogenic survival of human prostate carcinoma CWR22Rnu1 and DU145 cells and breast carcinoma Mcf-7 and Mcf-7:Her18 cells. The peel extract treatment caused a marked concentration-dependent decrease in the protein levels of proliferative cell nuclear antigen, a marker for proliferation and generated a marked increase in maspin, a tumour suppressor protein that negatively regulates cell invasion, metastasis, and angiogenesis.

The study of Lapidot et al. (2002) suggested that apple antioxidants did not directly inhibit tumour cell proliferation, but instead they indirectly inhibit cell proliferation by generating H_2O_2 in reaction with the cell culture media. However, studies by Liu and Sun (2003) demonstrated that apple extracts did not generate H_2O_2 formation in WME, DMEM, or DMEM/Ham F12 media, and H_2O_2 addition to culture medium did not inhibit Hep G2 cell proliferation or Caco-2 colon cancer cell proliferation. Additionally, the addition of catalase did not obstruct the antiproliferative activity of apple extracts.

Hypophasic carotenoids of apple peel mainly composed of violaxanthin, zeaxanthin and lutein showed slightly higher cytotoxic activity against three human tumour cell lines (squamous cell carcinoma HSC-2, HSC-3, submandibular gland carcinoma HSG) and human promyelocytic leukemic HL-60 cells than against three normal human oral cells (gingival fibroblast HGF, pulp cell HPC, periodontal ligament fibroblast HPLF), suggesting a tumour-specific cytotoxic activity and displayed much higher multidrug resistance -reversing activity than (±)-verapamil (Molnár et al. 2005).

Liu et al. (2005) found whole apple extracts prevented mammary cancer in a rat model in a dose-dependent manner at doses comparable to human consumption of one, three, and six apples a day. In further studies they isolated 13 triterpenoids from apple peels; most of the triterpenoids showed high potential anticancer activities against human HepG2 liver cancer cells, MCF-7 breast cancer cells, and Caco-2 colon cancer cells (He and Liu 2007). Among the compounds isolated, 2α-hydroxyursolic acid, 2α-hydroxy-3β-{[(2E)-3-phenyl-1-oxo-2-propenyl]oxy}olean-12-en-28-oic acid, and 3β-trans-p-coumaroyloxy-2α-hydroxyolean-12-en-28-oic acid showed higher antiproliferative activity toward HepG2 cancer cells. Ursolic acid, 2α-hydroxyursolic acid, and 3β-trans-p-coumaroyloxy-2α-hydroxyolean-12-en-28-oic acid exhibited higher antiproliferative activity against MCF-7 cancer cells. All triterpenoids tested showed antiproliferative activity against Caco-2 cancer cells, especially 2α-hydroxyursolic acid, maslinic acid, 2α-hydroxy-3β-{[(2E)-3-phenyl-1-oxo-2-propenyl]oxy}olean-12-en-28-oic acid, and 3β-trans-p-coumaroyloxy-2α-hydroxyolean-12-en-28-oic acid, which displayed much higher antiproliferative activities. The results showed the triterpenoids isolated from apple peels may

be partially responsible for the anticancer activities of whole apples. He and Liu (2008) isolated 29 compounds, including triterpenoids, flavonoids, organic acids and plant sterols which showed antiproliferative and antioxidant activities from Red Delicious apple peels. On the basis of the yields of isolated flavonoids, the major flavonoids in apple peels were quercetin-3-O-β-D-glucopyranoside (82.6%), then quercetin-3-O-β-D-galactopyranoside (17.1%), followed by trace amounts of quercetin (0.2%), (−)-catechin, (−)-epicatechin, and quercetin-3-O-α-L-arabinofuranoside. Among the compounds isolated, quercetin and quercetin-3-O-β-D-glucopyranoside showed potent antiproliferative activities against HepG2 and MCF-7 cells, with EC_{50} values of 40.9 and 49.2 μM to HepG2 cells and 137.5 and 23.9 μM to MCF-7 cells, respectively. Six flavonoids (18–23) and three phenolic compounds (10, 11, and 14) showed potent antioxidant activities. Caffeic acid (10), quercetin (18), and quercetin-3-O-β-D-arabinofuranoside (21) showed higher antioxidant activity, with EC_{50} values of <10 μM. Most tested flavonoids and phenolic compounds had high antioxidant activity when compared to ascorbic acid and might be responsible for the antioxidant activities of apples. Apple phytochemical extracts significantly inhibited human breast cancer MCF-7 and MDA-MB-231 cell proliferation at concentrations of 10–80 mg/ml (Sun and Liu 2008). The apple extracts were found to significantly induced G1 arrest in MCF-7 cells in a dose-dependent manner at concentrations. At concentrations of 15, 30, and 50 mg/ml, apple extracts caused a greater increase in the G1/S ratio in MDA-MB-231 cells when compared with MCF-7 cells. Cyclin D1 and Cdk4 proteins, the two major G1/S transit regulators, decreased in a dose-dependent manner after exposure to apple extracts. The results suggested that the antiproliferative activities of apple phytochemical extracts toward human breast cancer cells might be due to the modulation effects on cell cycle machinery. In further studies, Liu et al. (2009) showed that fresh apples potently and dose-dependently suppressed 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary cancers in rats. Tumour multiplicity and proportions of adenocarcinoma masses decreased with increasing apple extracts. The expression of proliferating cell nuclear antigen (PCNA), cyclin D1, and Bcl-2 decreased, and Bax expression and apoptosis increased with increasing apple extracts. The antiproliferative activity of MCF-7 human breast cancer exerted by apple extract and quercetin 3-β-d-glucoside (Q3G) was twofold to fourfold greater than apple extract and Q3G alone, indicating a synergistic effect in antiproliferative activity (Yang and Liu 2009).

Polyphenol-enriched apple juice extracts were fractionated to identify components with cancer chemopreventive potential (Zessner et al. 2008). Regression analyses indicated that 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging potential correlated with the sum of low molecular weight (LMW) antioxidants (such as chlorogenic acid, flavan-3-ols, and flavonols) and procyanidins, whereas peroxyl radicals were more effectively scavenged by LMW compounds than by procyanidins. Quercetin aglycone was identified as a potent Cyp1A inhibitor, whereas phloretin and (−)-epicatechin were the most potent cyclooxygenase 1 (Cox-1) inhibitors. Aromatase and Cyp1A inhibitory potential and cytotoxicity toward HCT116 colon cancer cells increased with increasing content in procyanidins. Hypermethylation of the promoter of hMLH1 colon cancer gene and subsequent microsatellite instability had been reported to occur in approximately 12% of sporadic colorectal cancers (CRC) (Fini et al. 2007). Annurca apple polyphenol extract was found to have potent demethylating activity through the inhibition of DNA methyltransferase proteins. The authors maintained that the lack of toxicity in Annurca extracts makes them excellent candidates for the chemoprevention of colorectal cancers.

Pinova and Braeburn apple pomace extracts showed potent antiproliferative activity against cervix epithelioid carcinoma (HeLa) and colon adenocarcinoma (HT-29) human cancer cell lines (Cetkovic et al. 2011). HeLa cells were found more sensitive than HT-29 cells to the extracts. The relationship between radical scavenging activities and phenolic contents or flavonol

glycosides ($R^2 \geq 0.80$) was high, but there were no significant correlations between the total phenolic contents or individual phenolic compounds and the antiproliferative activity.

An oligogalactan composed of five galacturonic acids from apple pectin exhibited protective efficacy against intestinal toxicities and carcinogenesis in a mouse model of colitis-associated colon cancer induced by 1,2-dimethylhydrazine and dextran sodium sulphate (Liu et al. 2010). The apple oligogalactan (AOG) decreased the elevated levels of TLR4 and tumour necrosis factor-α (TNF-α) induced by inflammation in-vivo in this model system. In in-vitro studies, AOG alone only slightly increased the levels of protein expression and messenger RNA of TLR4, phosphorylation of IκBα and production of TNF-α in HT-29 cells. However, AOG significantly decreased the elevation of all the biomarkers induced by lipopolysaccharide (LPS) when it was combined with LPS. AOG was active against inflammation and carcinogenesis through targeting LPS/TLR4/NF-κB pathway. The results indicated that the apple oligogalactan AOG may be useful for treatment of colitis and prevention of carcinogenesis.

Apple extract rich in flavonoids were found to inhibit proliferation of HT29 human colon cancer cells and modulate expression of genes involved in the biotransformation of xenobiotics (Veeriah et al. 2006). Treatment of preneoplastic cells derived from colon adenoma (LT97) with apple fruit extract induced expression of 30 and 46 genes expressed over cut-off in Superarray and custom array, respectively (Veeriah et al. 2008). Of 87 genes spotted on both arrays, 4 genes (CYP3A7, CYP4F3, CHST7, GSTT2) were regulated with similar directional changes. Expression of selected phase II genes (GSTP1, GSTT2, GSTA4, UGT1A1, UGT2B7), regulated on either array were also confirmed. The enzyme activities of glutathione S-transferases and UDP-glucuronosyltransferases were altered by treatment of LT97 cells with apple extract. The observed altered gene expression patterns in LT97 cells, resulting from apple extract treatment, suggested a possible protection of the cells against some toxicological insults. Studies demonstrated that induction of the phase II gene glutathione S-transferase T2 (GSTT2) by apple polyphenols protected colon epithelial cells against cumene hydroperoxide-induced genotoxic damage (Petermann et al. 2009; Miene et al. 2009). Apple extract was found to enhance expression of glutathione S-transferases (e.g., GSTT2) in human colon adenoma cells (LT97). Storage of apple extract caused changes in phenolic composition along with loss of activity regarding GSTT2 induction and amplified growth inhibition. Apple extract was also found to protect against oxidatively induced DNA damage.

Epidemiologic studies suggested an inverse correlation between apple consumption and colon cancer risk (Koch et al. 2009). In rat studies they found that under the cancer promoting condition of obesity, apple juice did not show cancer-preventive bioactivity.

A Polish case-control study of 592 incident cases of colorectal cancer and a comparison group of 765 patients without colorectal cancer found that the adjusted risk of colorectal cancer inversely correlated with daily number of apple servings (Jedrychowski et al. 2010). The reduced risk of colorectal cancer of border significance level was already observed at the consumption of at least one apple a day, but at the intake of more than one apple a day the risk was reduced by about 50%. Neither the consumption of vegetables nor other fruits displayed beneficial effects on the risk of colorectal cancer. The observed protective effect of apple consumption on colorectal risk may result from their rich content of flavonoid and other polyphenols, which can inhibit cancer onset and cell proliferation.

Studies by Lhoste et al. (2010) found that using a model of human microbiota-associated rats (HMA), fed a human-type diet and injected with 1–2,dimethylhydrazine (DMH), aberrant crypt foci numbers and multiplicity induced by DMH were not reduced by apple proanthocyanidin-rich extract at 0.001% and 0.01% in drinking water. They maintained that the modulating role of human gut microbiota should be taken into account in colon carcinogenesis models and in using proanthocyanidin extracts as dietary supplements for humans.

Antiviral Activity

Methanolic and acetonic extracts of apple pomace were able to inhibit both herpes simplex virus HSV-1 and HSV-2 replication in Vero cells by more than 50%, at non-cytotoxic concentrations (Suárez et al. 2010). Selectivity indexes (SI) ranged from 9.5 to 12.2. Acetone extraction yielded the higher amounts of phenolic compounds. Among the polyphenols analysed, quercetin glycosides were the most important family, followed by dihydrochalcones.

Antimicrobial Activity

Apple seed oil was found to be almost completely active against bacteria but not mildews, with inhibitory concentration (MIC) ranging from 0.3 to 0.6 mg/ml (Tian et al. 2010). The observed biological properties showed that the oil had a good potential for use in the food industry and pharmacy. Annurca apple peel ethanol extract exhibited antimicrobial activity against *Bacillus cereus* and *Escherichia coli* serotype O157:H7 (Fratianni et al. 2011). No activity was observed against the probiotic lactobacilli tested or against *Staphylococcus aureus*. The apple peel extracts also displayed antiquorum sensing activity tested by using the microorganism *Chromobacterium violaceum*. The results indicated the potential of apple peel extract for treating some microbial infections through cell growth inhibition or quorum sensing antagonism, thereby validating the health benefits of apples.

Antihyperglycaemic Activity

In a randomised study of hypercholesterolemic, overweight, non-smoking Brazilian women (aged 30–50 years), placed on a diet consisting of 55% of energy from carbohydrate, 15% from protein, and 30% from fat, dietary supplementation of apples or pear s resulted in a significantly greater decrease of blood glucose compared to those supplemented with oat cookies (De Oliviera et al. 2003). However, the glucose:insulin ratio was not statistically different from baseline to follow-up.

Aqueous apple pulp extracts exhibited high α-amylase and α-glucosidase inhibitory activities (Barbosa et al. 2010). However, the peel extracts had the highest α-glucosidase inhibitory activity along with low α-amylase inhibitory activity. No correlation between α-amylase inhibitory activity and total phenolic content was observed. However, positive correlations between α-glucosidase inhibitory activity and total phenolics in aqueous ($r=0.50$) and ethanolic ($r=0.70$) extracts were observed. Native fructose, FructiLight extracted from apple was found to improve glucose tolerance in mice (Dray et al. 2009). FructiLight, had a very low impact on glycemic and insulin response during acute treatment compared to other sugars based on glycemic index and exhibited beneficial properties when administrated for long term treatment. As with two other sugars extracted from apple (FructiSweetApple and FructiSweet67), FructiLight exposure during 21 weeks in beverage promoted an enhancement of glucose tolerance compared to glucose treatment without affecting food intake and weight. Nishigaki et al. (2010) showed that fresh apple extract treatment at 100 or 250 μg of human umbilical vein endothelial cells (HUVEC) exposed to glycated protein (GFBS) either alone or combined with iron chelate, significantly decreased the level of lipid peroxidation and returned the levels of antioxidants cytochrome c reductase and glutathione S-transferase to near normal in a dose-dependent manner. The extracts recovered viability of HUVEC damaged by GFBS-iron treatment in a concentration-dependent manner. The findings suggested a protective effect of apple extract on HUVEC against glycated protein/iron chelate-induced toxicity, which suggested that apple extract could exert a beneficial effect by preventing diabetic angiopathies. The dihydrochalcone sieboldin from apple leaves exhibited ability to prevent oxidative-dependent formation of advanced glycation end-products (AGEs) and phenylephrine-induced vasocontraction of isolated rat mesenteric arteries, provided interesting information concerning a potential use of sieboldin as

a therapeutic (Dugé de Bernonville et al. 2010) The results also confirmed the bioactivity of dihydrochalcones as functional antioxidants in the resistance of apple leaves to oxidative stress.

Anti-asthmatic Activity

A study in United Kingdom involving a survey of 607 individuals with asthma and 864 individuals without asthma found that apple consumption and wine intake was inversely related to severity of asthma indicating a protective effect of flavonoids (Shaheen et al. 2001). Intake of dietary selenium was also negatively associated with asthma. In a study involving 1,601 adults in Australia, apple and pear intake was found to be associated with a decreased risk of asthma and a decrease in bronchial hyper-reactivity, but total fruit and vegetable intake was not associated with asthma risk or severity (Woods et al. 2003). Specific antioxidants, such as vitamin E, vitamin C, retinol, and β-carotene, were not associated with asthma or bronchial hypersensitivity.

A study of over 13,000 adults in the Netherlands found that apples had a beneficial effect on incidence of chronic obstructive pulmonary disease (Tabak et al. 2001). Apple, pear and catechin intake was positively associated with pulmonary function and negatively associated with chronic obstructive pulmonary disease but not tea (also rich in catechin). Smoking was strongly associated with chronic obstructive pulmonary disease, independent of dietary effects. A prospective cohort study of 2,512 Welshmen aged 45–59 also found a strong positive association between lung function and the number of apples eaten per week (Butland et al. 2001). Good lung function, indicated by high maximum FEV (forced expiratory volume in 1 s), was associated with high intakes of vitamin C, vitamin E, β-carotene, citrus fruit, apples, and the frequent consumption of fruit juices/squashes. However, the association with citrus fruit and fruit juice/squash lost significance after adjustment for smoking. Apple consumption remained positively correlated with lung function after taking into account possible confounders such as smoking, body mass index, social class, and exercise.

Anxiolytic Activity

Studies showed that aged rats fed with the annurca apple enriched diet showed a significant decrease in the anxiety level (Viggiano et al. 2006). The aged rats improved in the ability to sustain long-term potentiation P, reaching the level of the young rats superoxide dismutase (SOD) activity was increased in the aged rats fed with the standard diet whereas SOD activity in the hippocampus of the aged rats treated with annurca apple was at the level of the young animals. The results suggested that a diet rich in annurca apple could have an important role in health-care during aging.

Hepatoprotective Activity

Apple polyphenols were found to have significant protective effect against acute hepatotoxicity induced by CCl(4) in mice, which may be due to its free radical scavenging effect, inhibition of lipid peroxidation, and its ability to increase antioxidant activity (Yang et al. 2010). Apple polyphenols significantly prevented the increase in serum alanine aminotransferase and aspartate aminotransferase levels in acute liver injury induced by CCl(4) and produced a marked amelioration in the histopathological hepatic lesions coupled to weight loss. Apple polyphenols reduced malondialdehyde formation and enhanced superoxide dismutase activity and GSH (reduced glutathione) concentration in the hepatic homogenate in apple polyphenolic-treated groups compared with the CCl(4)-intoxicated group. Apple polyphenols also exhibited antioxidant effects on FeSO(4)-L-Cys-induced lipid peroxidation in rat liver homogenate and DPPH free radical scavenging activity in-vitro.

Gastroprotective Activity

Apple extracts prevented exogenous damage to human gastric epithelial cells in-vitro induced by xanthine-xanthine oxidase or indomethacin and to

the rat gastric mucosa in-vivo (Graziani et al. 2005). The apple extracts caused a fourfold increase in intracellular antioxidant activity, prevented its decrease induced by xanthine-xanthine oxidase, counteracted xanthine-xanthine oxidase induced lipid peroxidation, and decreased indomethacin injury to the rat gastric mucosa by 40%. This effect appeared to be associated with the antioxidant activity of apple phenolic compounds such as catechin or chlorogenic acid (the main phenolic components of apple extracts) which were equally effective as apple extracts in preventing oxidative injury to gastric cells. The findings suggested that a diet rich in apple antioxidants might exert a beneficial effect in the prevention of gastric diseases related to generation of reactive oxygen species. Apple peel extract (60% of total polyphenols; 58% of flavonoids; 30% of flavan-3-ols and procyanidins) displayed an inhibiting effect on the multiplication of two *Helicobacter pylori* strains with a minimum inhibitory concentration (MIC) value of 112.5 μg gallic acid equivalent (GAE)/ml (Pastene et al. 2009). The apple peel extract inhibited the respiratory burst of neutrophils induced by *H. pylori*, phorbol myristate acetate (PMA), and formyl-methionyl-leucyl-phenylalanine (fMLP) in concentration-dependent manner. The result suggested that apple peel polyphenols had an attenuating effect on the damage to gastric mucosa caused by neutrophil generated reactive oxygen species and, particularly, when *H. pylori* displayed its evasion mechanisms. In-vitro studies showed that apple peel polyphenol-rich extract significantly prevented vacuolating *H. pylori* toxin (VacA) induced vacuolation in HeLa cells with an IC_{50} value of 390 μg of gallic acid equivalents (GAE)/ml (Pastene et al. 2010). The extract also displayed an in-vitro antiadhesive effect against *Helicobacter pylori*. In-vivo studies in mice found a significant inhibition with a 20–60% reduction of *H. pylori* attachment at concentrations between 0.250 and 5 mg of GAE/ml. Orally administered apple peel polyphenols also showed an antiinflammatory effect on *H. pylori*-associated gastritis, lowering malondialdehyde levels and gastritis scores. In Caco-2 cells, apple peel polyphenol extract prevented deleterious mitochondrial oxidative and cell viability alterations induced by indometacin possibly through its ability to scavenge reactive oxygen species (Carrasco-Pozo et al. 2010). The extract was found to actively scavenge O_2^-, hydroxyl and peroxyl radicals. Such free radical-scavenging activity of the extract suggested that its ability to protect mitochondria and prevent the oxidative and lytic damage induced by indometacin conventional antiinflammatory agent, arose from its potent antioxidant capacity.

Hypophasic carotenoids, violaxanthin, zeaxanthin and lutein of Golden delicious apple peel showed potent anti-*H. pylori* activity (MIC (50) = 36 μg/ml), comparable to metronidazole (MIC_{50} = 45 μg/ml) (Molnár et al. 2005). The MIC_{50} values of anti-*H. pylori* activity of (all-E)-luteoxanthin, (all-E)-neoxanthin and (9′Z)-neoxanthin were 7.9, 11 and 27 μg/mL, respectively (Molnár et al. 2010). Other carotenoids and, β-carotene did not exhibit potent anti-*H. pylori* activity (MIC_{50} > 100 μg/ml).

Antiinflammatory Activity

Apple extract powders from three different manufacturers showed similar, but clearly different, antiinflammatory activities, and had substantially different total phenolic contents, and different chemical compositions (Lauren et al. 2009). The most active fractions were those that contained epicatechin, catechin with phloridzin and quercetin glycosides, or those that contained procyanidin polymers. In-vitro studies showed that apple juice extract significantly inhibited the expression of NF-κB regulated proinflammatory genes (TNF-α, IL-1β, CXCL9, CXCL10), inflammatory relevant enzymes (COX-2, CYP3A4), and transcription factors (STAT1, IRF1) in LPS/IFN-γ stimulated MonoMac6 cells without significant effects on the expression of house-keeping genes. (Jung et al. 2009). The bioactive constituents procyanidin B(1), procyanidin B(2), and phloretin were responsible for the antiinflammatory activity and may serve as transcription-based inhibitors of proinflammatory gene expression. Studies showed that administration of Marie Ménard

apples, rich in polyphenols and used at present only in the manufacturing of cider, ameliorated colon inflammation in transgenic rats developing spontaneous intestinal inflammation, suggesting the possible use of these and other apple varieties to control inflammation in inflammatory bowel diseased patients (Castagnini et al. 2009). Rats fed Marie Ménard apples had reduced myeloperoxidase activity and reduced cyclooxygenase-2 and inducible NO synthase gene expression in the colon mucosa and significantly less diarrhoea, compared with control rats. A down-regulation of the pathways of prostaglandin synthesis, mitogen-activated protein kinase (MAPK) signalling and TNFα-NF-κB was observed in Marie Ménard-fed rats.

Cognitive/Behavioral Activity

Studies demonstrated that apple juice concentrate prevented the increase in oxidative damage to brain tissue and decline in cognitive (maze) performance observed when transgenic mice lacking apolipoprotein E (ApoE−/−) were maintained on a vitamin-deficient diet and challenged with excess iron (included in the diet as a pro-oxidant) (Tchantchou et al. 2005). Further they found dietary supplementation with apple juice concentrate alleviated the compensatory increase in glutathione synthase transcription and activity that accompanied dietary- and genetically-induced oxidative stress (Tchantchou et al. 2004). Their findings provided further evidence that the antioxidant potential of apple juice concentrate could compensate for dietary and genetic deficiencies that otherwise promoted neurodegeneration. They demonstrated that apple juice concentrate, administered ad libitum in drinking water, could compensate for the increased reactive oxygen species and decline in cognitive performance in maze trials observed when normal and transgenic mice lacking apolipoprotein E were deprived of folate and vitamin E (Rogers et al. 2004). Additionally, they demonstrated that this protective effect was not derived from the sugar content of the concentrate. They also demonstrated that apple juice concentrate administered in drinking water, maintained acetylcholine levels that otherwise declined when adult and aged mice were maintained on the vitamin-deficient, oxidative stress-promoting diet (Chan et al. 2006). The findings presented a likely mechanism by which consumption of antioxidant-rich foods such as apples could prevent the decline in cognitive performance that accompanied dietary and genetic deficiencies and aging.

Apple juice was found to alleviate the neurotoxic consequences of exposure of cultured neuronal cells to amyloid-β (Ortiz and Shea 2004). Apple juice prevented the increased generation of reactive oxygen species (ROS) normally induced by Abeta treatment and prevented Abeta-induced calcium influx and apoptosis. The results suggested that the antioxidant potential of apple products can prevent Abeta-induced oxidative damage that contributes to the decline in cognitive performance during normal aging and in neurodegenerative conditions such as Alzheimer's disease. Chan and Shea (2009) demonstrated that dietary deficiency in folate and vitamin E, coupled pro-oxidant stress induced by dietary iron, increased amyloid-β (Abeta) levels in normal adult mice. This increase was potentiated by apolipoprotein E (ApoE) deficiency as shown by treatment of transgenic mice homozygously lacking murine ApoE. Dietary supplementation with apple juice concentrate in drinking water alleviated the increase in Abeta for both mouse genotypes. More recent studies indicated that supplementation with apple juice concentrate can compensate for genetic as well as dietary insufficiency in folate in a murine model of genetic folate compromise (Chan et al. 2011). MTHFR+/− mice deficient in methylene tetrahydrofolate reductase activity exhibited significantly impaired cognitive performance in standard reward-based T maze and the non-reward-based Y maze tests as compared to MTHFR+/+ when maintained on the complete diet; supplementation with apple juice concentrate improved the performance of MTHFR+/− to the level observed for MTHFR+/+ mice. MTHFR+/+ and +/− demonstrated virtually identical neuromuscular performance in the standard paw grip endurance test when maintained on the complete diet, and displayed similar, non-significant declines in performance when maintained on the deficient diet. Supplementation of either diet with apple juice

concentrate dramatically improved the performance of both genotypes.

In an open-label clinical study of 21 institutionalized individuals with moderate-to-severe Alzheimer's disease, consumption of apple juice daily for a month did not improve cognitive activities but attenuated behavioral and psychotic symptoms associated with dementia (Remington et al. 2010).

Anti-toxin Activity

Crude polyphenol extract from immature apples dose-dependently inhibited cholera toxin catalyzed ADP-ribosylation of agmatine (Saito et al. 2002). Additionally the extract reduced cholera toxin induced fluid accumulation two diarrhea models for in vivo mice. On fractionation the FAP3 and FAP4 fractions, which possessed highly polymerized catechin compounds, strongly inhibited the ADP-ribosylation, indicating that the polymerized structure of catechin was responsible for the inhibitory effect of the crude extract. FAP2, which contained compounds with monomeric, dimeric, and trimeric catechins, inhibited the ADP-ribosylation only partially, but significantly. FAP1, which contained non-catechin polyphenols, did not significantly inhibit the CT-catalyzed ADP-ribosylation of agmatine. In another study, dilutions of freshly prepared apple juices and Apple Poly (a commercial apple polyphenol preparation) inhibited the biological activity of staphylococcal enterotoxin A (SEA) produced by *Staphylococcus aureus*, without any significant cytotoxic effect on the spleen cells (Rasooly et al. 2010). Additional studies with antibody-coated immunomagnetic beads bearing specific antibodies against the toxin revealed that SEA added to apple juice appeared to be largely irreversibly bound to the juice constituents.

Probiotic Effect

Studies in rats showed that a 4-week consumption of apple pectin (7% in the diet) increased the population of butyrate-glucuronidase and β-glucuronidase producing Clostridiales, and decreased the population of specific species within the Bacteroidetes group in the rat gut (Licht et al. 2010). Similar changes were not found by consumption of whole apples, apple juice, purée or pomace. Shinohara et al. (2010) found in a study of eight healthy adult humans that apple consumption improved intestinal environment and apple pectin was one of the effective bioactive component. Ingestion of apples was found to increase the faecal population of *Bifidobacterium* and *Lactobacillus* and also *Streptococcus* and *Enterococcus*. The lecithinase-positive clostridia, including *Clostridium perfringens*, Enterobacteriaceae and *Pseudomonas* tended to decrease. Several isolates of *Bifidobacterium, Lactobacillus, Enterococcus*, and the *Bacteroides fragilis* group utilized apple pectin, most isolates of *Escherichia coli, Collinsela aerofaciense, Eubacterium limosum*, and *Clostridium perfringens* could not. Additionally, the concentrations of faecal acetic acid tended to increase on apple intake, while faecal ammonia and sulphide tended to decrease on apple intake.

Bioavailability of Apple Phytochemicals

Studies involving ten healthy ileostomy subjects showed that oligomeric procyanidins, D-(−)-quinic acid and 5-caffeoylquinic acid reaching the ileostomy bags were considerably higher after apple smoothie consumption than after the consumption of cloudy apple juice or cider (Hagl et al. 2011). The results suggested that the food matrix might affect the colonic availability of polyphenols, and apple smoothies could be more effective in the prevention of chronic colon diseases than both cloudy apple juice and apple cider.

Allergy Problem

Consumption of apples can provoke severe allergic reactions, in susceptible individuals, due to the presence of the allergen Mal d 3, a nonspecific lipid transfer protein, found largely in the fruit skin (Sancho et al. 2006). The scientists found that pre- and postharvest treatments (i.e., storage) could modify the allergen load in

apple peel, the highest levels being found in overly mature and freshly harvested fruits. During storage, levels of Mal d 3 decreased in all cultivars (cvs. Cox, Jonagored, and Gala), the rate of overall decrease being greatest under controlled atmosphere conditions. A separate study of 22 Spanish patients with oral allergy syndrome after apple ingestion found that the ten apple varieties tested differed in the antigenic and allergenic profiles and the content of the allergen Mal d 3 (Carnés et al. 2006). Another allerge, Mal d 2 a thaumatin-like protein and important allergen of apple fruits was found to be associated with IgE-mediated symptoms in apple allergic individuals (Krebitz et al. 2003). Purified recombinant Mal d 2 displayed the ability to bind IgE from apple-allergic individuals equivalent to natural Mal d 2. In addition, the recombinant thaumatin-like Mal d 2 exhibited antifungal activity against *Fusarium oxysporum* and *Penicillium expansum*, implying a function in plant defence against fungal pathogens.

Traditional Medicinal Uses

Raw apples are eaten for indigestion and for constipation and is said to be good for gout. Apples have been found useful in acute and chronic dysentery among children.

Other Uses

Dried apple pomace was found to be a cost-effective and good feed adjunct for broiler chicks (Zaffar et al. 2005).

Comments

China is the leading producer of apples followed by the United States.

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