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Flavonoids in Food and Their Health Benefits

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Abstract. There has been increasing interest in the research of flavonoids from dietary sources, due to growing evidence of the versatile health benefits of flavonoids through epidemiological studies. As occurrence of flavonoids is directly associated with human daily dietary intake of antioxidants, it is important to evaluate flavonoid sources in food. Fruits and vegetables are the main dietary sources of flavonoids for humans, along with tea and wine. However, there is still difficulty in accurately measuring the daily intake of flavonoids because of the complexity of existence of flavonoids from various food sources, the diversity of dietary culture, and the occurrence of a large amount of flavonoids itself in nature. Nevertheless, research on the health aspects of flavonoids for humans is expanding rapidly. Many flavonoids are shown to have antioxidative activity, free-radical scavenging capacity, coronary heart disease prevention, and anticancer activity, while some flavonoids exhibit potential for anti–human immunodeficiency virus functions. As such research progresses, further achievements will undoubtedly lead to a new era of flavonoids in either foods or pharmaceutical supplements. Accordingly, an appropriate model for a precise assessment of intake of flavonoids needs to be developed.

Most recent research has focused on the health aspects of flavonoids from food sources for humans. This paper reviews the current advances in flavonoids in food, with emphasis on health aspects on the basis of the published literature, which may provide some guidance for researchers in further investigations and for industries in developing practical health agents.

Key words: Dietary source, Flavonoid, Health benefit, Intake, Level, Structure

Introduction

Flavonoids are plant pigments that are synthesized from phenylalanine [1] and generally display marvelous colors in the flowering parts of plants [2]. Flavonoids comprise a large group of polyphenolic compounds that are characterized by a benzo-*y*-pyrone structure, which is ubiquitous in vegetables and fruits. Besides their relevance in plants, flavonoids are important for human health because of their high pharmacological activities as radical scavengers [3]. Recent interest in these substances has been stimulated by the potential health benefits arising from the antioxidant activities of these polyphenolic compounds. As a dietary component, flavonoids are thought to have health-promoting properties due to their high antioxidant capacity in both in vivo and in vitro systems [3, 4]. The functionality in human health is supported by the ability of the flavonoids to induce human protective enzyme systems, and by a number of epidemiological studies suggesting protective effects against cardiovascular diseases, cancers, and other age-related diseases [3]. Some mechanisms have been proposed how flavonoids may help prevent steroid hormone-dependent cancers, but randomized clinical trials are still in progress. More research is needed to clarify the nature of the impact and interactions between these bioactive constituents and other dietary components, and to determine how efficient and practical it would be to reduce cancer risk and other human illness. Therefore, an overall review of the recent achievements in flavonoid research is imperative, with special reference to the progress in research in dietary occurrence and health aspects of flavonoids.

Chemical and Physical Properties of Flavonoids

The chemical nature of flavonoids depends on their structural class, degree of hydroxylation, other substitutions and conjugations, and degree of polymerization. They vary in the structure around the heterocyclic oxygen ring, but all have the characteristic C_6—C_3—C_6 carbon skeleton (Figure 1). In general, all flavonoids are derivatives of the 2-phenylchromone parent compound composed of three phenolic rings referred to as A, B, and C rings (Figure 2), all of which exhibit various levels of hydroxylation and methoxylation [2]. The biochemical activities of flavonoids and their metabolites depend on their chemical structure and the relative orientation of various moieties in the molecule.

Studies on flavonoids by UV spectrophotometry have revealed that most flavones and flavonols exhibit two major absorption bands: Band I (320–385 nm) represents the B ring absorption while Band II (250–285 nm) corresponds to the A ring absorption [3–7]. Functional groups attached to the flavonoid skeleton may cause a shift in absorption, such as from 367 nm in kaempferol (3,5,7,4′-hydroxyl groups), to 371 nm in quercetin (3,5,7,3′,4′-hydroxyl groups), and to 374 nm in myricetin (3,5,7,3′,4′,5′-hydroxyl groups) [3, 6]. The absence of a 3-hydroxyl group in flavones

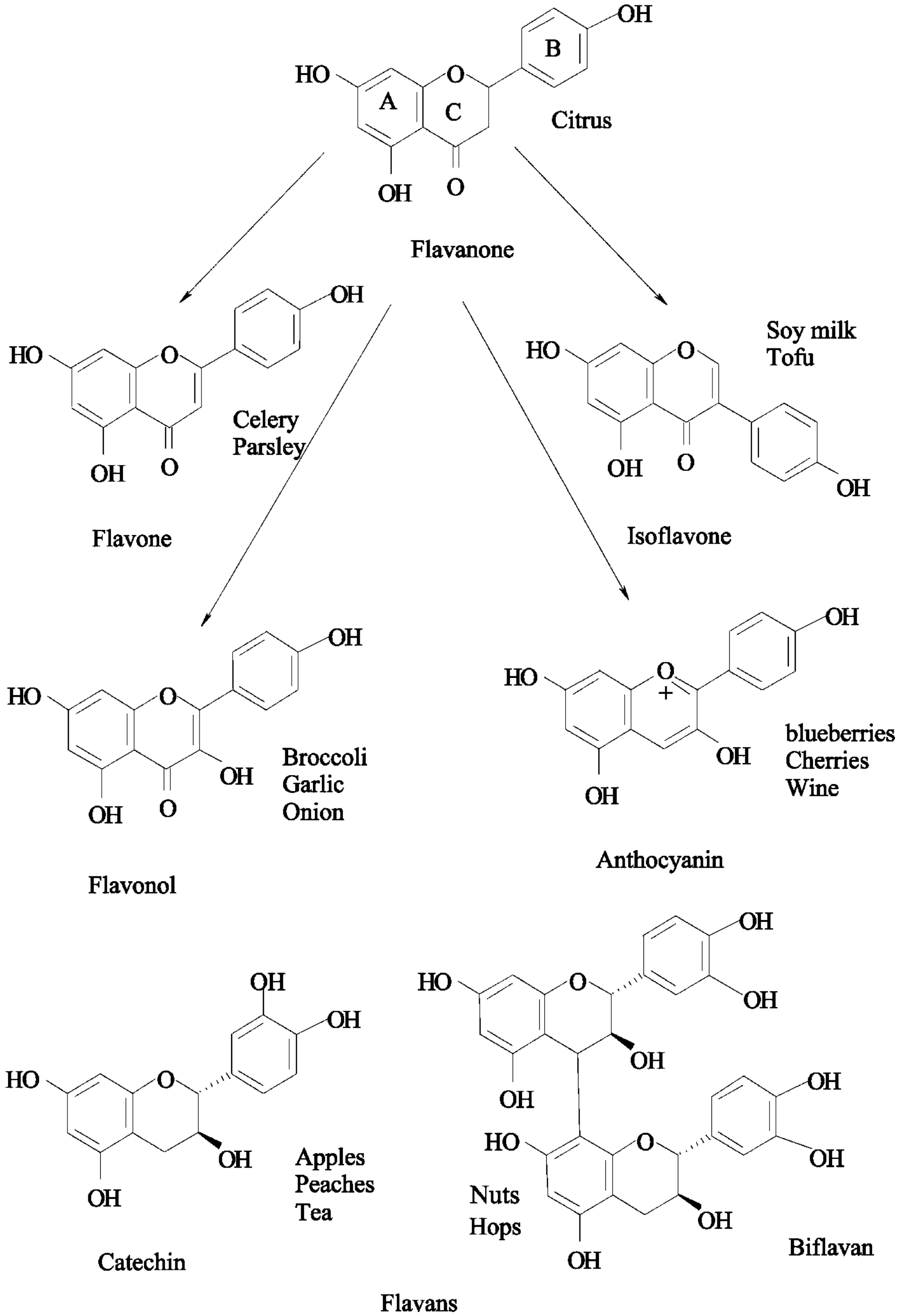
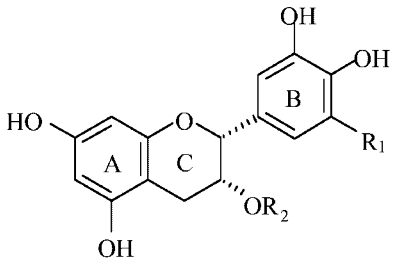


Figure 1. Structure and dietary occurrence of the main classes of flavonoids adapted from Peterson and Dwyer [4] (Arrows indicate biosynthetic path).

distinguishes them from flavonols. Thus, Band I always absorbs at a shorter wavelength by 20–30 nm, such as the 337 nm required for apigenin [4, 5, 8]. Flavanones have a saturated heterocyclic C ring, with no conjugation between the A and B rings, as determined by their UV spectral characteristics [4, 5]. Flavanones exhibit a very strong Band II absorption maximum between 270 and 295 nm, namely 288 nm (naringenin) and 285 nm (taxifolin) and only a shoulder for Band I at 326 and 327 nm. Band II appears as one peak (ca 270 nm) in compounds with a monosubstituted B ring, but as two peaks or one peak (ca 258 nm) with a shoulder (ca 272 nm) when a di-, tri-, or *o*-substituted B ring is present. As anthocyanins show distinctive Band I peaks in the 450–560-nm region due to hydroxyl cinnamoyl system of the B ring and Band II peaks in the 240–280-nm region due to the benzoyl system of the A ring [1], the colour of



Epicatechin (EC) $R_1 = R_2 = H$
Epicatechin gallate (ECG) $R_1 = H$, R_2 = gallate
Epigallocatechin (EGC) $R_1 = OH$, $R_2 = H$
Epigallocatechin gallate (EGCG) $R_1 = OH$, R_2 = gallate

Figure 2. Structures of EC, ECG, EGC, and EGCG.

the anthocyanins varies with the number and position of the hydroxyl groups [9].

Flavonoids are easily oxidized at the B ring, resulting in the opening of this ring at the oxygen atom [10]. The high chemical reactivity of flavonoids is expressed in the binding affinity to biological polymers and heavy metal ions, and the ability to catalyze electron transport and to scavenge free radicals [10]. The flavonoids are a group of phenolic compounds that share some common structural features and physicochemical properties, which are important in determining their biological effects. For example, anthocyanins in plants impart colour as pigments and ensure pollination, fertilization, and seed dispersal by animals [11]. Flavonoids can act as a light screen against damaging UV radiation in young leaves, antioxidants, enzyme inhibitors, and precursors of toxic substances, and provide resistance to pathogens. In addition, flavonoids may function as photosensitizing and energy-transfering compounds, and take part in the control of plant growth and development along with plant hormones [11]. Furthermore, these compounds have been implicated in defense against other plants, fungi, insects, and bacteria as regulators of interactions between beneficial fungi, herbivores, and insects, or as important constituents of animal diets, both nutritionally and medically [12, 13].

Natural Sources of Flavonoids

Flavonoids are the most common and widely distributed group of plant phenolic compounds, occurring virtually in all plant parts, particularly the photosynthesising plant cells. They are an integral part of both human and animal diets [1, 2]. Being plant phytochemicals, flavonoids cannot be synthesized by humans and animals [3]. Flavonoids found in animals are considered to originate from the plants that animals feed rather than being biosynthesized in situ. More than 5000 different plant-derived flavonoids have been isolated from various plants [3]. They are classified into at least 10 chemical groups. Flavanones, flavones, isoflavonoids, flavans (flavanols), anthocyanins, and flavonols are particularly common in the diet [3, 14, 15], as listed in Table 1. Flavonols are the most abundant flavonoids in foods, with quercetin, kaempferol, and myricetin being the three most common flavonols. Flavanones are mainly found in citrus fruits and flavones in celery. Catechins are present in large amounts in green and black teas, and in red wine, whereas anthocyanins are found in strawberries and other berries. Isoflavones are almost exclusively found in soy foods.

Flavonoids are a major coloring component of flowering plants, which are found in all plant foods [16]. Flavonoids in food are generally responsible for colour, taste, prevention of fat oxidation, and protection of vitamins and enzymes.

Table 1. Main subgroups of flavonoids, the individual compounds, and food sources

Subgroup	Color	Representative flavonoids	Food sources	Comment
Anthocyanins	Blue, red, violet	Cyanidin	Fruits and flowers	Natural dyes
Flavanols	Colorless	Catechins, gallocatechin, epicatechin, epigallocatechin gallate,	Apples, hops, tea, beer	Astringent taste
	Yellow	Procyanidin	Wine, fruit juice	
		Theaflavins	Black tea	
Flavanones	Colorless	Hesperidin	Citrus fruits	Bitter taste
	Pale	Naringenin, eriodictyol	Cumin, oranges, grapefruits,peppermint	
	Yellow	Neohesperidin		
Flavones	Pale yellow	Apigenin, chrysin, luteolin	Herbs, cereals, fruits, parsley, thyme	Bitter taste
		Diosmetin, luteolin	Vegetables, flowers	
Flavonols	Pale yellow	Isorhamnetin, kaempferol, quercetin, myricetin, rutin	Onions, cherries, apples, broccoli, kale, tomatoes, berries, tea, red wine, tartary buckwheat	
Flavanonols		Taxifolin	Limon, Aurantium	
Isoflavones	Colorless	Daizein, genistein, glycitein, formononetin	Legumes (e.g. soybeans)	

Flavonoid distribution in plants depends on several factors, including variation and the degree of light exposure. The formation of the higher oxidized flavonoids is accelerated by light. As coloring agents, flavanones occur predominantly in citrus fruits, isoflavonoids in legumes [17], and flavones mainly in herbs [18], while anthocyanins and catechins are found in teas, fruits, and vegetables [17, 18]. Any foods containing natural flavors and colorings or made from plants may contain flavonoids.

Large amounts of natural phenolic compounds are found in teas, fruits, and vegetables, while some amounts of polyphenols exist in red wine and coffee [19]. The flavonoids found in citrus fruits are flavanones, flavones, and flavonols [20], while genistein has been identified in citrus volatiles [21]. Fifteen anthocyanins and 10 flavonoids have been found in 34 French wines originating from six grape varieties and three growing areas [22]. Undoubtedly, it is expected that more food flavonoids from various plants will be identified in the near future.

Flavonoids in Foods

Level in Foods. Flavonoids found in the highest amounts in the human diet include the soy isoflavones (genistein, daidzein, biochanin A), flavonols (quercetin, myricetin, kaempferol), and the flavones (luteolin and apigenin) [23]. The levels of individual and total flavonoids in food are influenced by genetic factors such as species, environmental conditions such as light, ripeness, and postharvest treatments such as processing [14, 24, 25]. Although most fruits and some legumes contain catechins, the levels vary from 4.5 mg/kg in kiwifruit to 610 mg/kg in black chocolate [26]. Quercetin levels in the edible parts of vegetables are generally below 10 mg/kg [27, 28]. In black tea infusions, quercetin ranges from 10 to 25 mg/l, while kaempferol and myricetin vary from 7 to 17 mg/l and 2 to 5 mg/l, respectively. Tea is the only beverage that contains gallocatechin (GC), epigallocatechin (EGC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG), in addition to catechin and epicatechin (EC) [29]. Green tea has the highest level of phenolic compounds amongst foods, up to 35% of the dry matter [14]. Phenolic compounds are believed to influence wine flavour. Total phenolic content of wines is approximately 200 mg gallic acid equiv/L, but typical young red table wines have about 120 mg/l anthocyanins, 50 mg/l flavonols, 250 mg/l catechins, and 750 mg/l anthocyanogenic tannins [30].

The variations in the flavonoid levels may be used to differentiate food types. However, preparation and processing of food may decrease flavonoid levels depending on the methods used [31]. For example, in a recent study, orange juices were found to contain 81-200 mg/l soluble flavanones, while the content in the cloud was 206–644 mg/l [32], suggesting that the flavanones concentrated and presented in the cloud during processing and storage.

Dietary Intake. The flavonoid family of plant pigments comprises the most widely distributed group of secondary plant products ingested by humans. Accurate estimation of the average dietary intake of flavonoids is difficult, because of the wide varieties of available flavonoids and the extensive distribution in various plants, and also the diverse consumption of humans [33]. Thus, the measurement of dietary intake of flavonoids depends entirely on the criteria of survey, the method used, and the reference compounds selected for analysis. Bearing this in mind, the dietary intake of flavonoids has been estimated to vary from 100 to 1000 mg/day [15]. Although the dietary data on flavanones and dihydrochalcones are not yet available, these compounds may make a significant contribution to the daily intake of flavonoids.

Flavonoids are heat stable, but easily lost due to cooking and frying [34]. It is usually thought that flavonoids are absorbed by passive diffusion after the glycosylated flavonoids are converted to their aglycones. The colon microflora would play an important role in this conversion. The bioavailability of flavonoids is only partial, with the proportion of the ingested amount that is absorbed varying from 0.2 to 0.9% for tea catechins to 20% for quercetin and isoflavones [35, 36]. Thus, a large fraction remains unabsorbed and the gastrointestinal mucosa is exposed to particularly high concentrations of these compounds. After absorption, the flavonoids are conjugated in the liver by glucuronidation, sulfation, or methylation, or metabolized to smaller phenolic compounds [14]. The bioavailability of certain flavonoids differs markedly depending on the food source. For example, the absorption of quercetin from onions has been shown to be fourfold greater than from apples or tea [37].

Flavonoids and Health Benefits

Flavonoids are naturally occurring phenolic antioxidants that are present in the human diet. They contribute to the antioxidant properties of green vegetables, fruits, olive and soybean oils, red wine, chocolate, and teas. Some flavonoids have been reported to possess a variety of biological activities, including antiallergic, antiinflammatory, antiviral, antiproliferative, and anticarcinogenic activities, in addition to having effects on mammalian metabolism [38]. Flavonoids have received considerable attention because of their beneficial effects as antioxidants in the prevention of human diseases such as cancer and cardiovascular diseases, and some pathological disorders of gastric and duodenal ulcers, allergies, vascular fragility, and viral and bacterial infections [23]. Overall, flavonoids have so far been found to exhibit a wide spectrum of pharmacological properties, including antioxidative, antiallergic, antiinflammatory, antidiabetic, hepato- and gastro-protective, antiviral, and antineoplastic activities [23, 38].

General Benefits of Consumption

Food phenolic compounds, particularly flavonoids, are thought to play important roles in human health [17–19]. In vitro and animal studies have demonstrated that flavonoids have antioxidant and antimutagenic activities [15] and may reduce the risk of cardiovascular disease and stroke [24]. Isoflavonoids, such as phytoestrogens, have a wide range of hormonal and nonhormonal activities in animals or in vitro [39], suggesting potential human health benefits of diets rich in these compounds.

Flavonoids may act as antioxidants to inhibit free-radical mediated cytotoxicity and lipid peroxidation, as antiproliferative agents to inhibit tumor, growth or as weak estrogen agonists or antagonists to modulate endogenous hormone activity [40]. In these ways, flavonoids may confer protection against chronic diseases such as atherosclerosis and cancer and assist in the management of menopausal symptoms. Thus, flavonoids have been referred to as semiessential food components [41].

Early studies have uncovered some properties of tea polyphenols related to human health [42], including a capillary-strengthening property, an antioxidative property responsible for the radioprotective effect, and the antimicrobial property. Hara [43] showed that the habit of tea drinking could prevent cardiovascular diseases by increasing plasma antioxidant capacity in humans [24, 44]. Interestingly, tea polyphenols are rapidly absorbed after drinking with milk, and milk does not impair the bioavailability of polyphenols [45]. However, the underlying biochemistry requires further investigation.

Flavonoids have shown many biological properties that may account for cancer chemoprevention. In recent years, considerable attention has been paid to their abilities to inhibit the cell cycle, cell proliferation, and oxidative stress, and to induce detoxification enzymes, apoptosis, and activate the immune system [46]. Multiple mechanisms have been identified for the antineoplastic effects of flavonoids, including antioxidant, antiinflammatory, antiproliferative activities, inhibition of bioactivating enzymes and induction of detoxifying enzymes.

Antioxidant Activity

Flavonoids may protect against cancer and anticarcinogenesis through inhibition of oxidative damage. Flavonoids have been shown to have both antioxidant and pro-oxidant activities in vitro and in animal models. Flavonoids have been labeled as "high level" natural antioxidants on the basis of their abilities to scavenge free radicals and active oxygen species [47–49]. They contain conjugated ring structures and hydroxyl groups that have the potential to function as antioxidants in vitro or cell free systems by scavenging superoxide anion, singlet oxygen, lipid peroxyradicals, and stabilizing free radicals involved in oxidative processes through hydrogenation or complexing with oxidizing species [50, 51]. Clifford and Cuppett [2] divided the antioxidant mechanisms of flavonoids into free radical chain breaking, metal chelating, and singlet oxygen quenching, with the inhibition of enzymatic activity. Flavonoids including naringenin, hesperetin, and apigenin were also found to form pro-oxidant metabolites that oxidized NADH and glutathione upon oxidation by peroxidase/hydrogen peroxide. Flavonoids have been reported to chelate iron and copper and this may partly explain their antioxidant effects.

Bors et al. [52] suggested that the antioxidant mechanisms might include synergistic effects. The antioxidant activity of flavonoids usually increased with an increase in the number of hydroxyl groups and a decrease in glycosylation. EC and ECG (epicatechin and epicatechin gallate) with a vicinal diphenol structure in the B ring and a saturated C ring exhibit the strongest effects (Figure 2) [53]. EGCG (epigallocatechin gallate) with two triphenol components in its structure, one from the B ring and one from the gallate attachment (Figure 2), has been found to strongly and dose-dependently inhibit histamine release from rat basophilic leukemia cells [54]. However, Salah et al. [55] showed that the total antioxidative activity and the order of effectiveness of green tea polyphenols as radical scavengers is ECG > EGCG > EGC > gallic acid > EC = catechin. However, the oxidation of low density lipoproteins is inhibited by catechin, EC, ECG, and EGCG to a similar degree, not as much as in the presence of EGC or gallic acid. These results suggest that the triphenol structure plays an important role in the activities of tea polyphenols [56], but the action mechanism is still unclear.

Flavonoids are not only soluble in a water–alcohol mixture, but also have high solubility in fats and oils. Table 2 shows the antioxidant capacity, expressed as K_a/K_c, of compounds. Data shows that all compounds possess an antioxidant property in the hydrophilic environment, but in lipophilic environment, only some show an antioxidant property.

Metabolism and Clinical Effects

Flavonoids are absorbed by the gastrointestinal tracts of humans and animals, and are excreted either unchanged or as their metabolites in the urine and feces [3]. Colonic bacteria split the heterocyclic ring and degrade flavonoids to phenyl acids, which may be absorbed, conjugated, excreted,

Table 2. Antioxidant capacity of flavones, flavanol, and glycosylated flavonoids in hydrophilic and lipophilic environment [80]

Compounds	Antioxidant capacity in hydrophilic environment (K_a/K_c)	Antioxidant capacity in lipophilic environment (K_a/K_c)
Naringin−OH	2.41 ± 0.33	−1.53 ± 0.86
Narirutin−OH	2.46 ± 0.92	−0.80 ± 0.92
Naringenin−OH	2.73 ± 0.70	−1.88 ± 0.70
Didymin−OCH3	2.54 ± 0.35	0.21 ± 0.35
Isosakuratenin−OCH3	3.52 ± 0.25	0.62 ± 0.25
Neoheperidin−OH−OCH3	2.14 ± 0.10	0.69 ± 0.10
Hesperidin−OH−OCH3	2.81 ± 0.15	0.39 ± 0.15
Hesperetin−OH−OCH3	3.13 ± 0.20	0.36 ± 0.20
Neoericitrin−OH−OH	3.73 ± 0.34	−1.17 ± 0.74
Eridictyol−OH−OH	2.90 ± 0.39	−0.29 ± 0.06

or metabolized further by the bacteria [15]. Some flavonoid glycosides are rapidly deglycosylated by enzymes in human tissues, whereas others may remain unchanged. The rate and extent of deglycosylation depends on the structure of the flavonoid and the position/nature of the sugar substitutions [57]. Measurement of plasma and urine antioxidant power after ingestion of green tea has shown that absorption of antioxidants is rapid [58]. The antioxidants enter the systemic circulation soon after ingestion and cause a significant increase in plasma antioxidant status. Benzie et al. [58] and Feng [59] suggested that this increase might decrease oxidative damage to DNA and thus reduce the risk of cancer.

Various flavonoids (e.g. quercetin, apigenin, tea catechins) have also been shown to have antiinflammatory activity by inhibiting cycloxygenase-2 (COX2) and inducible nitric oxide synthase [60–61]. Flavonoids have profound effects on the functions of immune and inflammatory cells [62]. In animal studies, two EGCG methyl esters extracted from oolong tea significantly inhibited mice allergic reactions [63]. Gaby [64] suggested that quercetin might be of value in the treatment of asthma and be beneficial for diabetic and human immunodeficiency virus (HIV)-infected patients. A flavonoid known as baicalin was recently shown to possess antiinflammatory and anti-HIV-1 activities [65], by interfering with the interaction of the HIV-1 envelope proteins with chemokine coreceptors and blocking the HIV-1 entry to target cells. Thus, application of flavonoids may provide a means for industries in developing anti-HIV agents.

Protection against Heart Disease

A possible reason for the inferred protective effects of flavonoids against heart disease is their ability to prevent the oxidation of low density lipoproteins to an atherogenic form, although antiplatelet aggregation activity and vasodilatory properties are also reported [24, 66, 67]. Flavonoid intake may reduce the risk of death from coronary heart disease [68–72]. Differences in flavonoid intake in different countries may partly explain the differences in coronary heart disease mortality across populations [72].

The habitual intake of flavonoids from food sources such as tea may lead to a lower risk of atherosclerosis and coronary heart disease, and also protect against stroke [73–75]. This seems reasonable since tea pigments can reduce blood coagulability, increase fibrinolysis, prevent platelet adhesion and aggregation, and decrease the cholesterol content in aortic walls in vivo [76]. Green and black teas are able to protect against nitric oxide toxicity, which may be another reason for the beneficial effects observed with flavonoids [77]. In addition, consumption of quercetin may protect against cardiovascular disease [78] by reducing capillary fragility and inhibiting platelet aggregation [64]. Although the protective effect of flavonoids against heart disease exists, the use of the flavonoids as practical health agents is not currently practiced.

Cancer Prevention

Animal studies and epidemiological data indicate that dietary factors play an important role in the development of cancers. Fresh fruits and vegetables are rich in vitamins A, C, E, β-carotene, flavonoids, and other constituents that have been studied as cancer chemopreventive agents [18]. Numerous cell culture and animal models indicate potent anticarcinogenic activity by polyphenols that mediated through a range of mechanisms [24]. Dietary flavonoid intake has been reported to be inversely associated with the incidence of coronary artery disease, because flavonoids reduce the rate of formation of oxidized LDL and inhibit the growth of atherogenic plaques [79]. Flavonoids have been demonstrated to reduce carcinogenesis in animal models and to modulate enzymes implicated in the carcinogenic process. Their effects on the initiation and promotion stages of the carcinogenic process have been evaluated, and several mechanisms have been proposed, including influences on development and hormonal activities. The soy isoflavones genistein, daidzein, and biochanin A have all been used to determine effects on mammary carcinogenesis. The genistein could suppress the development of chemically induced mammary cancer without reproductive or endocrinological toxicities. Hesperidin, the major flavanone glycoside in orange juice, has been shown to inhibit chemically induced colon carcinogenesis, and double-strength orange juice slows down DMBA-induced mammary cancer in rats [38].

Antioxidant as an anticarcinogenic agent depends on its efficiency as an oxygen radical inactivator and inhibitor [80]. Diets rich in radical scavengers would reduce the cancer-promoting action of some radicals [81]. Some flavonoids can modify enzymes and bind carcinogens to DNA, thus exerting an anticarcinogenic effect [82]. Studies by Siess et al. [82] and Dragsted et al. [83] showed that a small dose of flavonoids, while ineffective alone, provided an effect when used in combination at the equivalent concentration. One case-control study used this new database [82] to look at 83 prostate cancer patients and 107 age-matched controls. They found that after adjustments for total calories, greater consumption of most phytoestrogens, including isoflavones and other flavonoids, had a slightly protective effect on prostate cancer risk. Moreover, genistein, daidzein, and coumestrol (a structurally related compound) showed the strongest protective associations.

Tea is a significant source of flavonoid antioxidants, with a suggested role in the prevention of cancer [84–88]. Polyphenols present in green tea show cancer chemopreventive effects against tumor initiation [89] and against promotion stages of multistage carcinogenesis in many animal tumor models [90–99]. Green tea may protect against cancer by causing cell cycle arrest and inducing apoptosis [100], while black tea can produce an inhibitory effect on tumor promotion [101].

The inhibiting effects of tea components may meaningfully reduce the risk of several important types of cancers in the world [102–105]. Histopathological examination revealed that both green and black teas were able to inhibit tumor cell proliferation in animal models [106, 107]. EGCG, EGC, and ECG inhibited soybean lipoxygenase, a carcinogen and tumor promoter, most effectively at lower doses [19]. Polyphenols from oolong and black teas have displayed strong inhibitory effects in human cancer cells [108]. However, more epidemiological data on the bioavailability, metabolism, and intracellular location of polyphenols is required before recommending increasing polyphenol intake for the prevention or treatment of human cancer.

Concluding Remarks

Flavonoids are generally nontoxic and manifest a diverse range of beneficial biological activities. Flavonoids are abundantly present in the human diet, e.g. in fruits, vegetables, and beverages such as tea and red wine. This group of compounds is being intensively investigated because of their health benefits. The role of dietary flavonoids in cancer prevention is widely discussed. There is much evidence that flavonoids have important effects in inhibiting carcinogenesis. Many mechanisms have been proposed on how flavonoids may help to prevent steroid-hormone-dependent cancers and several have been validated in vitro and in animal models. These include modulation of steroid hormones, inhibition of proliferation, and anticarcinogenic and antioxidative activities. Numerous in vitro and in vivo studies enable a variety of potential beneficial effects of flavonoids to be elucidated. More information on the health benefits of flavonoids has become evident and available through ongoing epidemiological studies. Recent research on the health benefits of flavonoids focused on the occurrences associated with dietary intake, theoretical studies (e.g. mechanisms of the functions of flavonoids to humans), incorporating and/or integrating data from basic research, and in vitro and in vivo investigations relating individual (or group of) flavonoids to specific health problems.

Fruits and vegetables are the main dietary sources of flavonoids for humans, with tea and wine being secondary sources. Antioxidative activities, scavenging (chelating) capacities, and interaction with enzyme systems are the principal mechanisms ascribed to the functions of flavonoids, while a diversity of clinical effects have been investigated or are on trials (e.g. anticancer and anti-HIV activities, prevention of coronary heart disease, and blood vessels disorders), with some encouraging results being achieved.

Research on flavonoids must also focus on the bioavailability of flavonoids and the objective measurement of oxidative damages in vivo. More research is needed to develop an authentic and convincing model or system for precisely assessing the human intake and metabolism of flavonoids, as well as their alleged heath benefits. It is also strongly recommended that specific research on a long-term basis be directed toward the direct utilization of flavonoids.

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