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Review

Flavanones, chalcones and dihydrochalcones – nature, occurrence and dietary burden

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Abstract: This paper reviews the occurrence in foods of flavanones, chalcones and dihydrochalcones. The major dietary sources of flavanones and dihydrochalcones are citrus fruits and apples respectively. These compounds may make a greater contribution to the total daily intake of flavonoids than the more extensively studied flavonols. There are no data for plasma or tissue levels, but both endogenous and gut flora metabolites of both classes of compound are found in urine. For these reasons, these compounds deserve greater attention in epidemiological studies.

Keywords: absorption; apples; beer; burden; chalcones; cider; citrus; dihydrochalcones; eriodictyol; flavanones; flavanonols; fruit juices; hesperidin; hops; licorice; metabolism; naringenin; narirutin; neohesperidin; phloretin; phloridzin; prenylflavanones; retrochalcones

INTRODUCTION

Flavanones, flavanonols, chalcones, retrochalcones and dihydrochalcones (DHCs) are biochemically related compounds of restricted occurrence. For this reason, they are described as minor flavonoids despite sometimes being present in foods at a dietarily significant concentration. Flavanones and flavanonols have a saturated C-ring. Chalcones and retrochalcones are unsaturated and, along with dihydrochalcones, have an open structure and a carbon skeleton numbered in a way different from other flavonoids (Fig 1).

Flavanones can be easily converted to isomeric chalcones in alkaline media (or *vice versa* in acidic media) provided that there is a hydroxyl substituent at position 2′ (or 6′) of the chalcone. Such chalcones may be transformed spontaneously during extraction procedures, and both transformations might be expected as these substances pass through the gastrointestinal tract. Retrochalcones also can cyclise[1] in a manner similar to the anthocyanin-derived chalcones (qv). Naturally occurring flavanones usually have the 2*S* configuration, but racemisation can occur during extraction. In contrast, plant flavanonols are usually 2*R*:3*R*, but a few are known with 2*S*:3*S* or 2*R*:3*S* stereochemistry.[2]

The flavanones are less soluble than the chalcones, tend to separate first in fractional crystallisation and are easily precipitated at low pH, especially if solutions are chilled or frozen. These precipitates remain insoluble in water, methanol, ethanol or acetone (and mixtures thereof). Heating, or preferably the use of strong solvents such as dimethyl sulphoxide, dimethyl sulphoxide/methanol mixtures (1:1) or dimethylformamide, is essential to ensure efficient recovery of the precipitate. These physical phenomena are of analytical and technological significance as discussed below.

OCCURRENCE AND TRANSFORMATION DURING PROCESSING

Flavanones occur as glycosides, usually rutinosides (6-*O*-α-L-rhamnosyl-D-glucosides) and neohesperido-

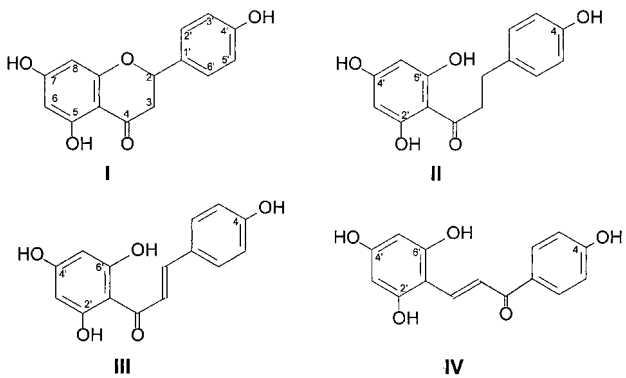

Figure 1. Structures and numbering systems for flavanones, dihydrochalcones, chalcones and retrochalcones: I, naringenin (flavanone); II, phloretin (dihydrochalcone); III, isosalipurpurin (chalcone); IV, retrochalcone.

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Table 1. Flavanones characteristic of common citrus fruits

Flavanone	Sweet orange (Citrus sinensis)	Sour orange (Citrus aurantium)	Lemon (Citrus limon)	Grapefruit (Citrus paradisi)	Lime (Citrus aurantifolia)	Mandarin (Citrus reticulata)
Eriocitrin	–	–	++	–		–
Narirutin	+	–	–	++		++
Hesperidin	+++	–	+++	Trace	+++	+++
Naringin	–	+++	–	+++		–
Neohesperidin	–	++	–	Trace		–

–, absent.
+, ++, +++, present in progressively greater amounts.

sides (2-*O*-α-L-rhamnosyl-D-glucosides) attached at position 7. They are characterisitc compounds of citrus fruit (Table 1). Lemon, lime, mandarin (tangerine) and sweet orange are dominated by rutinosides (mainly hesperetin). Grapefruit and sour (bitter) orange are dominated by neohesperidosides, mainly naringenin in the former but similar amounts of naringenin, neoeriodictyol and neohesperetin in the latter. Equivalent data are also available for many other citrus species and hybrids. The chromatographic profiles of the intact glycosides can be used for identifying the botanical origin of the fruit and products such as juices, preserves and honey, and as a monitor of adulteration.[3–6] Flavanone glucosides are comparatively rare but are found in some species of *Mentha* used as culinary herbs (0.3–3.3 g kg^{-1} dry weight (DW)) (where they occur as 7-glucosides)[7] and as minor components of grapefruit, lemon and sweet orange (where they occur as 4′-glucosides).[3,6] Hesperidin and the aglycones naringenin, eriodictyol and hesperitin have been reported in the herbal tea (Honeybush tea) prepared from the legume *Cyclopia intermedia*,[8] but quantitative data were not available. Naringenin and eriodictyol have been reported in potato.[9]

Moraceae, Leguminosae, Asteraceae and Cannabinaceae (including the hop, *Humulus lupulus*) are characterised by their contents of prenyl-flavonoids (isopentenyl-flavonoids) that occur as aglycones. Prenyl-flavanones (6- and 8-prenyl-naringenin, 6-geranyl-naringenin and 8-prenyl-isoxanthohumol) and prenyl-chalcones (xanthohumol and desmethyl-xanthohumol) are found in hops, hop-containing beers and hop-containing herbal teas.[10] The profiles varied, and total flavanone/chalcone content ranged from undetectable up to 4 mg l^{-1} in beers sold in the USA.

Flavanone 7-rutinosides are generally tasteless, but flavanone 7-neohesperidosides, eg neohesperidin, naringin, etc, are intensely bitter and are responsible for the characteristic taste of bitter orange and grapefruit. The bitter flavanone glycosides can be transformed into the corresponding dihydrochalcone glycosides by treatment with alkali, followed by hydrogenation. Neohesperidin dihydrochalcone is an intense, non-cariogenic and hypocaloric sweetener that has been accepted by the EU and the FDA as a food additive. It may be used as a sweetener in a wide range of foods (non-alcoholic drinks, desserts and confectionery) at concentrations in the range 10–400 mg kg^{-1} (or mg l^{-1}),[11] or as a flavour modifier at concentrations of up to 5 mg kg^{-1}.[12]

Citrus fruits and associated products are a major dietary source of flavanones, which are present both in juices and in tissues that are ingested when eating the peeled fresh fruit (albedo, segments and membranes). However, the distribution is very non-uniform, with much higher concentrations in the solid tissues compared with the juice. For example, the naringin content of grapefruit juice was reported as 295–377 mg l^{-1}, whereas the albedo, back membrane and side membranes of the fruit contained 13–16, 18–27 and 11.5–17.6 g kg^{-1} respectively, tending to be higher towards the centre of the fruit.[5] Citrus peels (albedo + flavedo) are also particularly rich, with grapefruit peel containing naringin (1–16 g kg^{-1} fresh weight (FW)), sour orange peel containing neohesperidin (0.7–31 g kg^{-1} FW) and sweet orange peel containing hesperidin (4.6–12.8 g kg^{-1}).[13] Dry orange peel may contain hesperidin at concentrations up to 70 g kg^{-1}.

These quantitative data for flavanones indicate that citrus fruit and products could make a significant contribution to total dietary flavonoids, but in order to properly assess this contribution, the following factors must be considered.

Citrus peel is clearly the richest tissue, but with the exception of certain preserves (marmalades), candied peel and other products containing peel, the flavedo is little consumed. The albedo is also frequently discarded, but the efficiency with which this can be done varies markedly with cultivar. There are orange cultivars, for example 'Clementines', where the segments are readily detached from the peel and little albedo remains to be ingested. In contrast, cultivars such as 'Navel' can only be peeled with a knife and much more albedo remains on the fruit segments, so the flavanone intake is higher when this cultivar is eaten.

The amount of albedo ingested from other citrus fruits such as lemon or grapefruit is much smaller. Lemons are only ingested as diluted juices, and in grapefruit the albedo is not eaten at all owing to the large content of the intensely bitter flavanone neohesperidosides.

Because of the tendency for flavanones (especially hesperidin) to precipitate and the need for extracts or

Table 2. Hesperidin content of Navel orange juices submitted to different technological treatments (Tomás-Barberán FA, unpublished)

	Hesperidin content			
Treatment	Soluble ($mg l^{-1}$)	Haze ($mg l^{-1}$)	Soluble (%)	Haze (%)
Hand-squeezed (fresh)	528	42	93	7
Unpasteurised	191	171	53	47
Pasteurised	166	205	45	55
Concentrated (after dilution)	169	179	48	52

juices to be clarified before analysis, it is essential that precipitated flavanones are resolubilised with strong solvents if reliable data for composition and burden are to be obtained. Such precipitates form not only during the extraction of material for analysis but also during commercial handling and processing of citrus fruit. For example, when grapefruit were peeled, cut and stored refrigerated (4 °C, 7 days), an apparent decrease in the content of naringin from 600 to 400 $mg kg^{-1}$ was reported.[14] It has been suggested that this may actually have been caused by crystallisation of naringin near the surface of the peeled fruit and failure of the extraction method to recover it. White crystals were apparent under the segmental membrane by day 7, and samples that were heated to solubilise naringin prior to analysis contained consistently higher levels (800 $mg kg^{-1}$) than the unheated samples (<600 $mg kg^{-1}$).

Flavanone precipitation can be readily seen in fresh-cut oranges after refrigerated storage and in satsuma orange segments canned in syrup, and these losses can be substantial. In fresh juices (Table 2) prepared from hand-squeezed 'Navel' oranges, 93% of the flavanones (hesperidin and narirutin) are in solution and only 7% are detected in the haze (recovered by centrifugation and extraction of the pellet with DMSO). However, this proportion increases on storage, especially at low temperatures, with approximately half the hesperidin and narirutin becoming insoluble (Tomás-Barberán FA, unpublished). Most of this insoluble material may be consumed, and if the analytical methodology does not take account of it, intake could be seriously underestimated. Optimisation of methodology is discussed in Ref 6.

The production of fresh single-strength and concentrated orange juices leaves a residue of pulp that may be extracted with water to produce pulp-wash. Pulp-wash, which has appreciably higher concentrations of hesperidin and narirutin than the juice, can be used in drink manufacture, but its use to adulterate fresh juice is prohibited in many countries.[15] Citrus composition varies with place of cultivation, rootstock, cultivar and maturity in addition to the factors discussed above. Some published data for citrus juices and pulp-wash obtained by reliable methods are summarised in Table 3.

As mentioned above, native chalcone glycosides tend to transform to flavanone glycosides during extraction. Chalcones *per se* are therefore of restricted occurrence in foods. Naringenin chalcone is present in tomato skin and may be present in juice, paste and ketchup. Acid hydrolysis, as is used prior to HPLC in many routine analyses for dietary flavonoids, converts the chalcone to the corresponding flavanone (naringenin), which is naturally present only in trace amounts (2–15 $mg kg^{-1}$) in the tomato.[16–18] The naringenin chalcone content of tomato skin in post-climacteric fruits is 64 $mg kg^{-1}$ FW (80 times higher than that of the pulp), but in tomato ketchup, naringenin chalcone is transformed to naringenin, and the chalcone is only present in trace amounts.[17,19]

Mixtures of retrochalcones (eg echinatin, licochalcones A and B) along with isomeric flavanones and chalcones (eg liquiritigenin and isoliquiritigenin) have been reported in licorice (liquorice) root (*Glycyrrhiza* spp) and some licorice-based traditional medicines and therefore might be found in confectionery containing such root extracts, but quantitative data have not been located.[20–24] Mixtures of prenyl-chalcones (eg xanthohumol, desmethylxanthohumol) occur with isomeric prenyl-flavanones (isoxanthohumol and 8-prenyl-naringenin respectively) in hops and beer.[8] Flavanone–chalcone mixtures (eg cerasinone, cerasin) have also been reported in *Prunus* spp, but it is not clear whether they occur in edible tissues.[25]

Dihydrochalcones (DHCs) are characteristic of apples and derived products (apple juice, cider, pomace, etc). Phloretin 2′-glucoside (phloridzin), phloretin 2′(2″-xylosyl-glucoside) and 3-hydroxyphloridzin have been idntified unequivocally[26] and some investigators have reported phloretin 2′(2″-xylosyl-galactoside).[27] Their analysis has been suggested as a suitable technique for monitoring the adulteration of these products. The phloridzin content of apples can vary greatly depending on the cultivar.[27–29] They are present in the skin, pulp and especially the seeds, where they may account for up to 60% of the total phenols content compared with less than 3% of the phenols in the epidermis and parenchyma zones.[30] Kemerrien, a French variety of cider apple, contained 169 $mg kg^{-1}$ phloridzin, of which 67 mg was present in the core, 46 mg in the parenchyma and 24 mg in the epidermis. Some English cider apples can contain as much as 190 $mg kg^{-1}$, whereas cultivar Verde Doncella contains less than 0.1 $mg kg^{-1}$.[31] The phloridzin content of most cultivars ranges between 5 and 10 $mg kg^{-1}$, but phloretin 2′(2″-xylosyl-glucoside) has been reported in the flesh at 10–30 $mg kg^{-1}$.[27] The skin is some 5–10 times richer than the flesh, and apple pomace is appreciably richer than either (1.42 $g kg^{-1}$ and 170 $mg kg^{-1}$ respectively), accompanied by 270 $mg kg^{-1}$ 3-hydroxyphloridzin.[26]

When eating an apple, the seeds and core of the fruit

Table 3. Flavanone content of citrus juices

	Flavanones ($mg\,l^{-1}$)							
Juice type	*Hesperidin*	*Neohesperidin*	*Narirutin*	*Eriocitrin*	*Naringin*	*Total bitter*	*Grand total*	*Reference*
Sweet orange	487–584							64
Valencia	215–227							64
Hand-squeezed	235–407		30–84					65
Unpasteurised	122–260		18–65					66
Fresh, hand-squeezed, various cultivars	122–254		18–65					67
Unpasteurised	166–226							Tomás-Barberán FA, unpublished
Hand-squeezed, Navel	528		Trace					Tomás-Barberán FA, unpublished
Fresh, hand-squeezed Brazilian, various cultivars	104–537		16–80					15
Frozen concentrate, Brazilian, after dilution to 12° Brix	531–690		62–84					15
Frozen concentrated pulp-wash, Brazilian, after dilution to 12° Brix	1089–1200		154–239					15
Lemon								
Hand-squeezed	84–196			47–94				65
Grapefruit								
Hand-squeezed			33–161		113–481			65
Various cultivars			23–124		73–419			67
					295–377			5
Pumelo					40–144			67
Grapefruit × pumelo hybrids						440–495	500–1000	69
Sour orange		97–209			133–362			67
Mandarin	80–191		150–249					67

are usually discarded and thus some of the apple dihydrochalcones are not ingested. If fruits are eaten peeled, then more of the DHCs are removed with the peel and the DHC intake is smaller. Further data for apple products are summarised in Table 4.

Whole apple fruits are processed industrially to produce juices and ciders, and therefore the contribution of these processed products to the intake of DHCs can be higher than that of the fresh apples. It has been shown that fruit bruising can cause browning and a reduction of between 20 and 40% in the content of dihydrochalcones.

Juices produced in a laboratory from single-variety cider apples contained between 3 and $20\,mg\,l^{-1}$ phloridzin, whereas a commercially pressed juice contained $26\,mg\,l^{-1}$. A similar quantity of a second, incompletely characterised DHC was also present in the commercial cider apple juice.[32] In juices prepared from some Spanish varieties of cider apple the content of phloretin 2-xyloglucoside ($26–36\,mg\,l^{-1}$) exceeds

Table 4. Content of dihydrochalcones in apple juices and other apple products. Values are $mg\,l^{-1}$ (juices) or $mg\,kg^{-1}$ (jams, etc)

	Content ($mg\,l^{-1}$ or $mg\,kg^{-1}$ as appropriate)			
Commodity and method of preparation	*Phloretin-2′-xyloglucoside*	*Phloridzin*	*Total DHC*	*Reference*
Juice (domestic extractor)	4.0	4.4	8.4	35
Juice (experimental)	27–33	13–18	40–51	36
Juice (experimental)	3.8	5.4	9.2	70
Juice (commercial)	2.1–2.3	2.7–3.3	4.8–5.6	70
Jam (commercial)	1.7	2.3	4.0	70
Compote (commercial)	5.2	9.1	14.3	70
Jelly (commercial)	0.4	1.0	1.4	70
Juice (domestic extractor)	5	4	9	34
Juice commercial clear	34	38	72	34
Juice commercial cloudy	27	12	39	34
Mash commercial	53	33	86	34
Nectar commercial	17	12	29	34
Juice (domestic)	14–38	83–196	97–223	31

that of phloridzin (12–20 mg l^{-1}).[29,33] The content of DHCs in clear or cloudy commercial apple juices can be 5–10 times higher than in juices obtained with a domestic juice extractor.[34] This occurs because the industrial process extracts whole apples (including seeds, core and peels) and uses thermal treatments that inactivate the enzymes (polyphenoloxidases) that directly or indirectly degrade dihydrochalcones in home-made juices.

Juice clarification with commercial (impure) pectinases always decreased the DHC content dramatically (by 90%). The corresponding aglycone (phloretin) seemed less stable or more easily degraded by the environment and oxidative enzymes. Surprisingly, pasteurisation (105 °C, 45 min) led to a greater DHC loss than sterilisation (120 °C, 20 s), probably because of greater inactivation of oxidative enzymes at the higher temperature.[35] Clarification of apple juices by filtration also generally decreases the phloridzin content, but the decrease is less for extended filtration times because of reduced retention on the filters.[36]

As discussed above, neohesperidin dihydrochalcone may be added to a wide range of foods, but data on its actual usage have not been traced.

DIETARY BURDEN

Flavanonols and retrochalcones (with the possible exception of those derived from anthocyanins (qv)) have not been reported at significant levels in foods or beverages and will not be considered further in this section. The intake of flavanones, chalcones and dihydrochalcones has been ignored in many recent epidemiological studies concerned with flavonoids in European diets, for example Refs 37–39, but a Japanese study recorded a mean daily intake of 0.3 mg eriodictyol in women.[40]

However, while the analytical data presented above indicate that for some people in Europe the consumption of these so-called minor flavonoids will be very low or zero, it is clear that for others the intake could be substantial. For example, an individual drinking orange juice (250 ml) will have a daily flavanone intake (as aglycones) in the range 25–60 mg. For those eating the flesh of a whole orange (200 g) this intake could be as high as 125–375 mg, although dependent on the cultivar and amount of albedo ingested. Regular consumers of heavily hopped beers might consume significant amounts of prenyl-flavanones and chalcones, but appropriate analytical data are not available. The main sources of DHCs will undoubtedly be apple juice or cider, where 250 ml might supply some 1–5 mg as phloretin. In contrast, a dessert apple (100 g) will probably supply less than 1 mg, and further small amounts may be obtained from jams and similar products. According to Lindley,[12] the main uses for neohesperidin dihydrochalcone in 1996 were in animal feed and certain pharmaceutical preparations, which would not constitute a significant burden for many people. It was anticipated that usage in foods would increase, but it has not been possible to locate any quantitative data for this review. The only significant source of chalcones will be tomatoes consumed with skin, where 100 g might supply up to 0.7 mg, or a little more for the smallest cultivars where the proportion of skin is greater.

It is clear, therefore, that regular consumers of citrus products might consume quantities of these so-called minor flavonoids considerably greater than their consumption of flavonols and flavones which previous studies suggest rarely exceed some 30–40 mg day^{-1} (as aglycones).[41–43]

ABSORPTION AND METABOLISM

The absorption and metabolism of flavanones have been investigated by several groups[44,45] and the early studies have been reviewed by DeEds[46] and Scheline.[47] Flavanone neohesperidosides and rutinosides are not absorbed *per se*, but the aglycones released by the gut microflora are absorbed and may be excreted as glucuronides. Whether the corresponding glucosides would be absorbed in the duodenum (as occurs for quercetin glucosides) is unknown at present, but cell-free extracts of human small intestine are able to hydrolyse naringenin 7-glucoside.[48]

Volunteers who consumed grapefruit juice containing some 200 mg naringin excreted some 30 mg naringenin glucuronide daily.[45] Volunteers (aged 25–87 years) given single oral doses of naringin (500 mg) or hesperidin (500 mg) excreted naringenin or hesperetin glucuronides within 3 h of administration and for 38 h thereafter. Cumulative urinary recovery was less than 5% for each compound tested. After multiple doses of mixed citrus juices the glucuronides were detected in urine within 6 h of the first dose and for 24 h after the fifth and final dose. Urinary recovery of naringenin was about 7%, but about 24% for hesperitin. When juice or fruit was given, four additional mono- or dimethylated flavanones were observed in urine. It is thought that these had originated in the fruit, but the possibility that some methylation arises through human metabolism, as has been observed for flavanols and flavonols, cannot be excluded.

Flavanone aglycones can be degraded by human and rat intestinal microflora to yield a range of simple phenols (resorcinol, pyrogallol, phloroglucinol), phenolic acids (4-hydroxybenzoic, 2,4,6-trihydroxybenzoic, 4-hydroxyphenylacetic, 2,4-dihydroxyphenylacetic, 3,4-dihydroxyphenylpropionic, 4-hydroxyphenylpropionic, 3-hydroxy-4-methoxyphenylhydracrylic) and 2,4-dihydroxyacetophenone.[47,49,50]

Certain flavanones (predominantly 2S enantiomers) have been identified in the urine of volunteers taking certain Chinese herbal medicines that do not themselves contain such compounds. It has been suggested that these are gut microflora metabolites of flavones.[51–53]

In rats, approximately half of the intragastric dose of phloretin, the DHC aglycone of phloridzin, was excreted in the urine, mainly within 2 days. Small amounts of phloretin were found, but most of the metabolites were degradation products. The latter included phloroglucinol and, in larger amounts, phloretic acid (4-hydroxyphenylpropionic acid) and related metabolites formed by its dehydrogenation, β-oxidation and glycine conjugation. Phloroglucinol, administered in similar experiments, was rapidly (90% within 24 h) excreted in the urine, either unchanged or as conjugates (glucuronide/sulphate). Incubation of phloretin and its glucoside phloridzin with rat caecal micro-organisms resulted in the formation of phloroglucinol and phloretic acid.[54] In contrast, several other DHCs (not known to occur in foods) were excreted predominantly unchanged in the urine and faeces.[55] Phloridzin is subjected to biliary excretion, but the metabolites were not fully identified.[47]

When rats are given phloridzin (5 μM) by cannula, it inhibits uptake of glucose by the active glucose transporter (SGLTI) in the small intestine[56] and impairs resorption of glucose in the kidney, causing glucosuria. The observation of glucosuria led to claims that phloridzin is diabetogenic, but this is a misinterpretation since there is no evidence of an effect on the pancreas. Neohesperidin dihydrochalcone, the permitted sweetener, has been little studied (Renwick AG, pers commun). Early and otherwise unpublished work, cited by DeEds,[46] suggests that naringin and neohesperidin dihydrochalcones are metabolised differently by rats. Following a dose of naringin dihydrochalcone, rats excreted 3-hydroxyphenylpropionic acid and 3-hydroxycinnamic acid, but the aglycone was not detected. In contrast, the major metabolite produced from neohesperidin dihydrochalcone (0.5% of diet) was the aglycone, and 3-hydroxyphenylpropionic acid could not be detected, suggesting that it is not converted to phenolic acids by the gut microflora.

A study with male rats initiated with azoxymethane showed that hesperidin reduced the incidence and multiplicity of tumours in the large intestine and inhibited the development of aberrant crypt foci.[57] This observation is consistent with *in vitro* studies showing that various flavanone aglycones and some glycosides may protect against chemically induced carcinogenesis at low concentrations.[58,59] However, Habtemariam[60] showed that although eriodictyol inhibited tumour necrosis factor-alpha-induced cytotoxicity in murine fibroblasts, hesperetin had no effect and naringenin enhanced the cytotoxicity.

It has been reported that a flavanone-rich citrus extract in combination with ascorbic acid is an effective agent for decreasing lipids and for the inhibition of atherosclerosis in hamsters.[61] Eriocitrin, having a dihydroxy B-ring, is a potent free radical scavenger *in vitro*.[62] It has not been possible to trace data relating to the absorption and metabolism of prenyl-flavanones or prenyl-chalcones, but oestrogen-agonist activity has been reported in ovariectomised rats for 8-prenyl-naringenin at doses of 30 mg kg^{-1} body weight day^{-1} given subcutaneously for 2 weeks.[63] This compound was one order of magnitude more potent than genistein, and potency was not affected by the stereochemistry at C2. The 6-prenyl analogues, however, were inactive. The doses of 8-prenyl-naringenin used, coupled with the route of administration and the likely dietary burden, suggest that this effect is of no consequence in humans.

FUTURE RESEARCH REQUIREMENTS

The current data imply a variable but potentially substantial intake of citrus flavanones that would exceed by a considerable margin the intakes recorded for flavonols. Some consumers may also have significant intakes of phloretin derivatives, and still others of prenyl-flavanones and prenyl-chalcones. The actual burdens of these compounds should therefore be properly assessed and these data considered when seeking epidemiological associations between flavonoid consumption and disease incidence. There is a need for metabolic and pharmacokinetic data for the prenyl derivatives, which are likely to be appreciably more hydrophobic than the more extensively studied non-prenylated glycosides, and for neohesperidose dihydrochalcone. The lack of data for neohesperidose dihydrochalcone is remarkable in view of its status as a permitted food additive.

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