Bitter taste, phytonutrients, and the consumer: a review[1–3]

Adam Drewnowski and Carmen Gomez-Carneros

ABSTRACT Dietary phytonutrients found in vegetables and fruit appear to lower the risk of cancer and cardiovascular disease. Studies on the mechanisms of chemoprotection have focused on the biological activity of plant-based phenols and polyphenols, flavonoids, isoflavones, terpenes, and glucosinolates. Enhancing the phytonutrient content of plant foods through selective breeding or genetic improvement is a potent dietary option for disease prevention. However, most, if not all, of these bioactive compounds are bitter, acrid, or astringent and therefore aversive to the consumer. Some have long been viewed as plant-based toxins. As a result, the food industry routinely removes these compounds from plant foods through selective breeding and a variety of debittering processes. This poses a dilemma for the designers of functional foods because increasing the content of bitter phytonutrients for health may be wholly incompatible with consumer acceptance. Studies on phytonutrients and health ought to take sensory factors and food preferences into account. *Am J Clin Nutr* 2000;72:1424–35.

KEY WORDS Diet, phytonutrients, phenolic compounds, isoflavones, bitter compounds, astringent compounds, acrid compounds, sensory evaluation, debittering processes, functional foods, chemoprotection, cancer, cardiovascular disease, review

INTRODUCTION

Diets rich in vegetables and fruit have been linked with lower rates of cancer and coronary heart disease (1–5). Plant-based phenols, flavonoids, isoflavones, terpenes, glucosinolates, and other compounds that are present in the everyday diet are reported to have antioxidant and anticarcinogenic properties and a wide spectrum of tumor-blocking activities (1, 4, 6, 7). The search for the mechanisms of chemoprotection has focused on the biological activity of compounds found in cruciferous and green leafy vegetables, soybeans, citrus fruit, green tea, and red wine (3, 6, 8–11). These compounds, known as phytochemicals or phytonutrients (2), hold major promise in the creation of designer foods for the dietary prevention of chronic disease (12, 13).

Many people do not like to eat vegetables—and the feeling is mutual. Plants protect themselves against being eaten by secreting natural pesticides and other toxins (14–16). Plant-based phenols, flavonoids, isoflavones, terpenes, and glucosinolates are almost always bitter, acrid, or astringent (17–21). In addition to their bactericidal or biological activity (22), these substances may provide a defense against predators by making the plant unpalatable (17). Although potentially beneficial to human health in small doses, many such compounds are, in fact, toxic (14).

Sensitized to the bitter taste of plant alkaloids and other poisons, humans reject foods that are perceived to be excessively bitter (20, 23). This instinctive rejection of bitter taste may be immutable because it has long been crucial to survival (24, 25). The food industry routinely removes phenols and flavonoids, isoflavones, terpenes, and glucosinolates from plant foods through selective breeding and a variety of debittering processes (18–20, 26, 27). Many of the bioactive phytonutrients currently studied in the laboratory (2, 28, 29) have long been treated by industry and consumers alike as disposable bitter waste (20).

Consumer and marketing studies invariably showed that taste, as opposed to perceived nutrition or health value, is the key influence on food selection (30, 31). Yet, with some exceptions (17, 27, 32), studies on phytonutrients and health rarely considered the bitter taste of vegetables and other plant foods. Cancer researchers even proposed that heightened bitterness might be a positive feature, allowing consumers to select broccoli sprouts with the highest glucosinolate content (29, 33). This view contrasts with the food industry practice of measuring glucosinolate content merely as a way of predicting excessive bitterness of Brussels sprouts, a more pressing consumer concern (27). Whereas some scientists propose enhancing glucosinolates in broccoli sprouts for better health (29), the standard industry practice has been to remove glucosinolates from Brussels sprouts for better taste (27). When it comes to bitter phytonutrients, the demands of good taste and good health may be wholly incompatible.

Engineering plant foods with enhanced concentrations of chemopreventive phytonutrients is a promising new strategy for health promotion (12, 13). However, any meaningful discussion of phytonutrients and health ought to consider the bitter taste of these substances (2, 8, 34). Although present in very small amounts, antioxidant phytochemicals impart a perceptible bitter taste to foods. As documented below, some of these compounds are so aversive to the consumer (30, 35, 36)

[1] From the Nutritional Sciences Program, School of Public Health and Community Medicine, University of Washington, Seattle, and the Fred Hutchinson Cancer Research Center, Seattle.

[2] Supported by a grant from the National Cancer Institute (1 RO1 CA 61680).

[3] Reprints not available. Address correspondence to A Drewnowski, 305 Raitt Hall, Box 353410, University of Washington, Seattle, WA 98195. E mail: adamdrew@u.washington.edu.

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that they are selectively bred out of plants and routinely removed from processed foods (20, 26). Indeed, the low amounts of bitter plant compounds in the current diet largely reflect the achievements of the agricultural and food industries (26). The debittering of plant foods has long been a major sensory concern for food science (27).

BITTER TASTE AND FOOD REJECTION

Abnormal bitterness tends to be equated with dietary danger, and rightly so. Rancid fats, hydrolyzed proteins, plant-derived alkaloids, and other toxins generally have an unpleasant bitter taste (37). Microbial fermentation also results in bitter-tasting compounds (37). Bitterness has been reported in such diverse plant foods as potatoes and yams, beans and peas, cabbage and Brussels sprouts, cucumbers, pumpkins, zucchini and other squashes, lettuce, spinach, and kale (20). Given the wide distribution of plant-based bitter toxins, past efforts to develop less bitter cultivars of common plant foods may have been driven not so much by taste as by safety concerns (20).

Detection thresholds for bitter taste are extremely low (25, 38). Bitter compounds, including extremely toxic bitter poisons, are detected by humans in micromolar amounts. Although no direct relation between toxicity and bitter taste thresholds was observed (24), bitter quinine was detected at 25-μmol/L concentrations and bitter toxins were detected at even lower concentrations. In contrast, detection threshold for sucrose was on the order of 10 000 μmol/L (25). The bitter taste sensation was also more prolonged than were sweet, salty, or sour sensations (38).

The biology of bitter-taste perception is poorly understood. The long-term challenge has been to explain how so many structurally unrelated compounds can give rise to a uniform bitter taste. Among bitter-tasting compounds are amino acids and peptides, sulfimides (saccharin), ureas and thioureas [6-*n*-propylthiouracil (PROP) and phenylthiocarbamide (PTC)], esters and lactones, terpenoids, and phenols and polyphenols (39). The diverse chemical structures of these compounds has long suggested the existence of multiple bitter-taste receptors. McBurney (38) proposed that ≥3 different bitter-taste receptors exist, sensitive to quinine, urea, and to PTC or PROP, a related compound. Other studies (40, 41) suggested a common mechanism in the perception of sweet and bitter tastes, possibly linked to G proteins, given that small changes in chemical structure can alter the taste of a given substance from bitter to very sweet.

A very recent discovery of a novel family of bitter-taste receptors placed the number of gustducin-linked bitter taste receptors in humans as high as 40–80 (42, 43). These candidate taste receptors (T2Rs) are organized in the genome in clusters and are genetically linked to loci that influence bitter perception in humans and mice (42). T2Rs were expressed in all taste buds of circumvallate and foliate papillae and in the palate (43). Although T2Rs were rarely expressed in fungiform papillae, those fungiform taste buds that did express T2Rs usually had a full repertoire of different receptors, suggesting that each cell may be capable of recognizing multiple bitter tastants. This is consistent with the observation that humans are capable of recognizing diverse bitter substances but not always distinguishing among them (39). A complementary study (43) showed that a human bitter-taste receptor (hT^2R-4) responded only to denatonium and PROP, whereas a mouse receptor MT2R-5 responded only to bitter cycloheximide.

Genetic linkage studies in humans linked the ability to taste PROP with a locus at 5p15 (44). The ability to taste PTC and PROP, once thought to be transmitted as a dominant taster gene (45), may involve more than one locus. Genetic linkage studies suggested that PROP tasting may involve both a specific sensitivity to PROP and a more general bitter taste responsiveness (46). The early studies segregated PTC and PROP tasters from nontasters on the basis of their tasting of PTC or PROP crystals or the bimodal distribution of detection thresholds for PROP solutions (47). The wide variability of the tasters' responses led Bartoshuk (41) to propose the existence of PROP "supertasters." PROP supertasters, most of them women, were identified by the high ratio of perceived bitterness intensity of PROP to the perceived saltiness of sodium chloride solutions. On average, supertaster women had more fungiform papillae and a higher density of taste buds per papilla than did either medium tasters or nontasters of PROP (47).

Anthropologists have long thought that the protective value of this genetic polymorphism was to identify and reject bitter poisons (48). In sensory studies, PROP tasting was linked to a greater dislike of bitter PROP solutions (49, 50) and with reduced acceptance of some bitter foods (51). PROP tasters tended to dislike bitter caffeine and naringin solutions and bitter infusions of Japanese green tea (49–51). PROP tasters also gave lower acceptance ratings to coffee and grapefruit juice, cruciferous vegetables, and some salad greens (49). As a general rule, heightened perception of bitterness was the principal reason for food rejection.

BITTER PHENOLS AND TANNINS

Phenolic compounds are responsible for the bitterness and astringency of many foods and beverages (17, 52). There are ≥15 different classes of dietary phenolic compounds, ranging from simple phenolic molecules to polymers of high molecular weight. Flavonoids, the most important group, can be subdivided into 13 classes; >5000 compounds were described by 1990 (17). The flavonoid group includes flavanones, flavonols, flavones, isoflavones, flavans (catechins), and anthocyanins. High-molecular-weight (>500) polyphenols are also known as plant tannins (17). Whereas lower-molecular-weight phenolic compounds tend to be bitter, higher-molecular-weight polymers are more likely to be astringent (53). Astringency, defined as a drying or puckering mouth feel detectable throughout the oral cavity, may be due to a complexing reaction between dietary polyphenols and proteins of the mouth and saliva (53, 54).

Some bitter tasting phenolic compounds are shown in **Table 1.** Phenolic compounds act as natural pesticides (76), providing plants with resistance to pathogens, parasites, and predators (14, 77). Amounts of phenolic compounds in plant foods and the level of bitterness are influenced by genetic factors and by environmental conditions (8). The type of cultivar, germination, degree of ripeness, and processing and storage conditions can all influence the content of plant phenolics (17, 78). Bitter phenolics, such as quercetin, are the most common bitter compounds in immature apples and other fruit (17). Generally, higher concentrations of phenolic compounds are found in sprouts and seedlings than in the mature plant, consistent with the notion that plant phenolics provide a degree of protection against predation (59).

High-molecular-weight polyphenols or tannins have long been regarded as antinutrients because they interfere with protein absorption or reduce iron availability (17). Tannins are widely distributed in grains such as sorghum, millet and barley, peas, carobs, dry beans and legumes, fruit, tea, wine, and a variety of forage plants (8). Tan-

TABLE 1
Some bitter phytonutrients in common plant foods[1]

Phytonutrient class	Typical component	Taste quality	Food source	Amount present	Reference
Phenolic compounds					
Flavanones	Naringin	Bitter	Grapefruit, flavedo	2701–4319 mg/kg	55
			Grapefruit, albedo	1301–15 592 mg/kg	
			Grapefruit, pith	13 285–17 603 mg/kg	
			Grapefruit, seeds	295–2677 mg/kg	
			Immature grapefruit	97 920–144 120 mg/kg FW	56, 57
			Grapefruit juice	300–750 mg/L	56
			Oroblanco juice	346–489 mg/L	58
			Melogold juice	413–580 mg/L	58
Flavones	Tangeretin	Bitter	Orange fruit	0–30 mg/kg DW	59
			Orange juice	0.6 mg/L	
			Juice from concentrate	0.2–0.5 mg/L	60
	Nobiletin	Bitter	Orange fruit	14–112 mg/kg DW	59
			Orange juice	2.7–2.9 mg/L	
			Juice from concentrate	1.8–2.3 mg/L	60
	Sinensetin	Bitter	Orange fruit	14–46 mg/kg DW	59
			Orange juice (fresh)	0.1 mg/L	61–63
			Juice from concentrate (frozen)	0.5–2.9 mg/L	61, 62
			Juice from concentrate	1.7–1.8 mg/L	60
			Pure juice	2.7–2.9 mg/L	
Flavonols	Quercetin	Bitter	Grapefruit juice	4.9 mg/L	64
			Lemon juice	7.4 mg/L	64
			Endive	1.3 mg/kg FW	9
			Fresh hops	700 mg/kg FW	28
			Wine	4.1–16 mg/L	64
			Black tea infusion	10–25 mg/L	64
			Oolong tea infusion	13 mg/L	64
			Green tea infusion	14–23 mg/L	64
Flavans	Catechin	Bitter	Red wine	11.1 mg/L	65, 66
			Green tea infusion	13.0–19.1 mg/L	
			Oolong tea infusion	6.0–6.4 mg/L	
			Black tea infusion	9.2–15.6 mg/L	
	Epicatechin	Bitter	Red wine	7.7 mg/L	67
			Low-fat cocoa powder	940–2470 mg/kg	68
			Instant cocoa powder	180–320 mg/kg	68
			Green tea infusion	105.0–118.0 mg/L	65
			Oolong tea infusion	63.5–68.0 mg/L	65
			Black tea infusion	16.8–35.0 mg/L	65
	Epicatechin gallate	Bitter and astringent	Green tea infusion	152.2–223.0 mg/L	65
			Oolong tea infusion	182.8–227.2 mg/L	
			Black tea infusion	114.0–168.0 mg/L	
	Epigallocatechin	Bitter with sweet aftertaste	Green tea infusion	186.0–257.0 mg/L	65
			Oolong tea infusion	182.4–242.0 mg/L	
			Black tea infusion	17.0–50.0 mg/L	
	Epigallocatechin gallate	Bitter with sweet aftertaste	Green tea infusion	237.2–330.8 mg/L	65
			Oolong tea infusion	251.2–307.6 mg/L	
			Black tea infusion	96.8–110.8 mg/L	
Phenolic flavonoids	Catechin mono- and polymers MW < 500	Bitter	Red wine	1000–3500 mg/L	53, 54
			Rosé wine	200 mg/L	
	Catechin polymers MW > 500 (tannins)	Astringent	Red wine		53, 54
			Apple cider		
	Polyphenols	Astringent and bitter	Low-fat cocoa power	8380–31 000 mg/kg	68
			Instant cocoa powder	1370–4460 mg/kg	
Isoflavones	Genistein and daidzein	Bitter or astringent	Soybeans	24–40 mg/kg	69
			Toasted, defatted soy flakes	51 mg/kg	
			Textured soy protein	67 mg/kg	
			Breakfast patties	14 mg/kg	
			Tofu	29–78 mg/kg	
	Genistin	Astringent	Soy seeds	280–2780 mg/kg seed meal	70
	Daidzin			120–940 mg/kg seed meal	

(*Continued*)

TABLE 1 (*Continued*)

Phytonutrient class	Typical component	Taste quality	Food source	Amount present	Reference
Triterpenes					
Limonoid aglycones	Limonin	Bitter	Lemon juice	12.2 mg/L	56
			Orange juice	9.7 mg/L	
			Grapefruit juice	11.4 mg/L	
			Tangerine juice	34.7 mg/L	
			Grapefruit, flavedo	6.1–42 mg/kg	
			Grapefruit, albedo	11.6–65 mg/kg	
			Grapefruit, pith	103–525 mg/kg	
			Grapefruit, seeds	1188–1885 mg/kg	
	Nomilin	Bitter	Grapefruit juice	0.1–1.6 mg/L	58
			Oroblanco juice	0.4–0.8 mg/L	
			Melogold juice	0.9–1.8 mg/L	
	Limonin glucoside	Tasteless	Grapefruit juice	102–135 mg/L	58, 71
			Lemon juice	54 mg/L	
Organosulfur compounds					
Glucosinolates	Sinigrin	Bitter	Cabbage	70–410 mg/kg	27, 72–74
			Brussels sprouts	110–1560 mg/kg FW	
			Cauliflower	10–630 mg/kg	
			Turnip or swede	0–100 mg/kg	
			Calabrese	0–10 mg/kg	
			Broccoli	0–16 μmol/kg FW	72
			Collards	625–1973 μmol/kg FW	72
			Kale	0–287 μmol/kg FW	72
			Mustard greens	6930–7790 μmol/kg FW	72
	Progoitrin	Bitter	Brussels sprouts	100–1000 mg/kg FW	18, 19, 27, 73, 74
			Cabbage	10–80 mg/kg	
			Cauliflower	0–140 mg/kg	
			Turnip or swede	90–830 mg/kg	
			Calabrese	0–82 mg/kg	
	Glucobrassicin	Bitter	Brussels sprouts	220–1110 mg/kg FW	73
Hydrolysis product of glucosinolates	Goitrin 5-vinyl-2-oxazolidine thione	Bitter	Aqueous extract of Brussels sprouts	89–280 mg/kg	27
			Cabbage, pith	2.9–19 mg/kg	75
			Cabbage, cambial cortex	6.9–18 mg/kg	
			Cabbage, leaf	0–5.4 mg/kg	
Isothiocyanates	Allyl-isothiocyanate	Acrid mustard oils; pungent or lachrymatory	Cabbage, pith	14–42 mg/kg	75
			Cabbage, cambial cortex	45–146 mg/kg	
			Cabbage, leaf	2–8 mg/kg	
	3-Methyl-sulfinylpropyl isothiocyanate	Acrid mustard oils	Cabbage, pith	4–52 mg/kg	75
			Cabbage, cambial cortex	28–175 mg/kg	
			Cabbage, leaf	17–85 mg/kg	
	Benzyl isothiocyanate	Acrid mustard oils; garlic-like	Cabbage, cambial cortex	1.2–3.4 mg/kg	75
			Cabbage, leaf	0.4–1.3 mg/kg	
	4-Methylsulfinyl butyl isothiocyanate	Acrid mustard oils	Cabbage, pith	0–36 mg/kg	75
			Cabbage, cambial cortex	0–59 mg/kg	
			Cabbage, leaf	3–63 mg/kg	
	Phenylethyl isothiocyanate	Acrid, irritant, or lachrymatory	Cabbage, pith	0.3–3.5 mg/kg	75
			Cabbage, cambial cortex	15–33 mg/kg	
			Cabbage, leaf	1.6–1.9 mg/kg	

[1] MW, molecular weight; DW, dry weight; FW, fresh weight.

nins complex with proteins, starches, and digestive enzymes and are thought to reduce the nutritional value of foods (8).

BITTER FLAVONOIDS IN CITRUS FRUIT

Flavonoids in citrus fruit include flavanones (naringin), flavones (nobiletin), and flavonols (quercetin). Polymethoxylated flavones (tangeretin and nobiletin) are concentrated in the skin of unripe fruit and are the constituents of bitter citrus oils (79). Bitter flavonoids may act through bactericidal activity or by making the plant unpalatable (17). Some flavonoids are very bitter whereas others are not, depending on the type of the glycoside chain. Naringin, a flavanone neohesperidoside, and neohesperidin are very bitter, whereas hesperidin is tasteless. On the other hand, neohesperidin dihydrochalcone is intensely sweet. Naringin concentrations are highest in young leaves and in the pulp (albedo) of immature fruit (59). Although typical concentrations of naringin in grapefruit juice are ≈400 mg/L , problems with early-season grapefruit juice can raise naringin concentrations to a less acceptable 1200 mg/L (80). Blending of juices means that bitterness affects even more of the crop.

Limonin, a triterpene, is responsible for the so-called delayed bitterness of citrus juices. A tasteless limonin precursor,

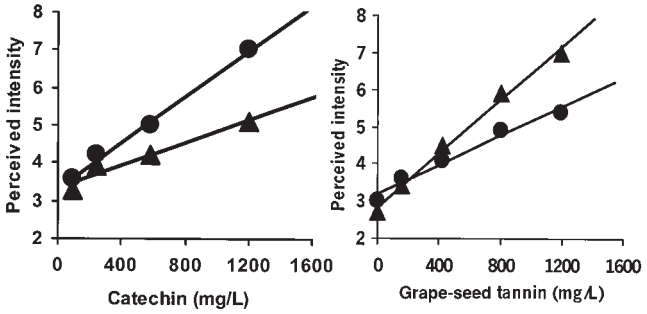

FIGURE 1. Mean intensity ratings for bitterness (●) and astringency (▲) as a function of concentration. Adapted from reference 89, with permission.

released when fruit tissue is damaged, is gradually converted to limonin, resulting in bitterness. Bitterness due to flavonoids and limonoids poses a major problem for the citrus industry. As described below, a wide variety of patented techniques have been developed to remove or adsorb excess naringin and limonin from citrus juices (56, 81).

BITTER PHENOLIC COMPOUNDS IN TEA AND CHOCOLATE

Phenolic compounds, including catechin and epicatechin (pentahydroxylated flavans), also occur in tea (65, 82). A typical green tea polyphenol is epigallocatechin gallate (32). Epicatechin is generally more bitter than is catechin (66). Japanese green tea has higher concentrations of catechins and epigallocatechin than do either fermented black or semifermented oolong tea and is also the most bitter. Bitterness of tea is generally ascribed to the combination of catechins, saponin, caffeine, and amino acids (82). Depending on molecular weight, catechins can be bitter or astringent, whereas saponins are often described as acrid (32).

Recent studies suggested that the bitter taste of chocolate may also be due to catechins, present in higher amounts in bitter than in milk chocolate (83). Fermented cocoa contains epicatechin, polyphenols, and anthocyanins (84). Anthocyanins are glycoside forms of anthocyanidins, with a sugar moiety attached. Catechins in cocoa have been described variously as bitter with a sweet aftertaste or as bitter and astringent (85). Fermentation of cocoa beans leads to polymerization of catechins and to complexing with proteins. Optimal sensory response to fermented cocoa (85) was associated with limited amounts of polyphenols (maximum of 58 mg/g), tannins (31 mg/g), and epicatechin (3 mg/g). The presence of catechins in chocolate advances our understanding of its bitter taste, which was thought previously to be caused by caffeine, theobromine, and the interaction of theobromine (a methylxanthine) and diketopiperazines during roasting (20). Whereas the taste of theobromine is described as bitter and metallic, diketopiperazines are associated with the flavor of roasted malt.

BITTER PHENOLIC COMPOUNDS IN RED WINE

Phenolic compounds in wine range from low-molecular-weight catechins to high-molecular-weight tannins (86–88). As shown in **Figure 1**, perceived bitterness and astringency increased as a linear function of concentration for catechin and for grape-seed tannin (89). Flavonoid monomers such as catechin and epicatechin were rated as more bitter than astringent (90). At higher molecular weights, catechin polymers became progessively more astringent. Thus, wine polyphenols with molecular weights >500, such as grape-seed tannin, were more astringent than bitter (91). As is often the case, sensory studies used 5-point category scales and were based on a limited number of respondents (90).

A sensory study of catechins in red wine and in a model system similar in composition to a dry table wine (66) showed that epicatechin was significantly more bitter and astringent than was catechin. Ratings of bitterness and astringency were associated with perceived mouth drying and with mouth roughening, especially at higher concentrations (66).

The concentrations of catechins used were within the range found in wine. The usual amount of grape phenolics is ≈2–4 mg/g grape. However, phenols in wine are largely derived not from juice but from grape skins (30%) and seeds (70%). Skins and seeds remain in contact with fermenting grape juice from 24 to 36 h for rosé wines and from 4 to 21 d for red wines. Phenolic content of red wines can thus reach 1000–3.500 mg/L, depending on processing conditions (43, 54, 86). The bitterness of phenolics is reduced by sucrose and is substantially enhanced by ethanol (53, 54)

BITTER ISOFLAVONES IN SOYBEANS

Genistin, a bitter and astringent isoflavone glucoside (92), is thought to be responsible for the objectionable taste of soy protein (70, 93). Isoflavones are associated with the protein fraction in soybeans (69), soy isolates, and texturized soy protein (94, 95). Hexane-defatted soy flours, soy concentrates, and isolates all have an undesirable bitter taste and an undesirable flavor—"beaniness" (92, 93, 96). L-Phenylalanine and phenolic acids (syringic) in soy products have also been described as phenol-like, bitter, astringent, or sour. Enzyme or acid-based hydrolysis of soy proteins produces additional bitter soy peptides and bitter hydroxy fatty acids. Soy flours are reported to have an astringent aftertaste and a chalky mouth feel (97).

Bitter isoflavone glucosides, genistin and daidzin, are hydrolyzed during fermentation to bitter isoflavone aglycones, genistein and daidzein. Genistein and daidzein are said to be responsible for the objectionable taste of soy milk. Their concentrations increase during soaking of soybeans, the first step of soy milk manufacturing. They also impart the characteristic taste to the secondary products miso, soybean paste, and soy sauce (69). As shown in **Figure 2**, the objectionable aftertaste of soy milk was linked to its genistein and dadzein contents (35).

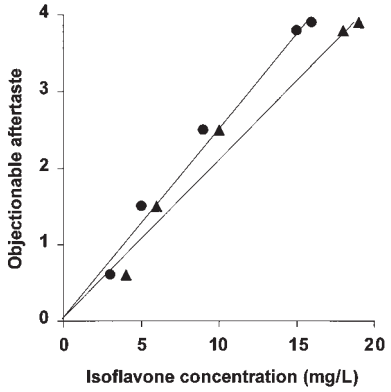

FIGURE 2. Relation between the objectionable aftertaste (on a scale of 0–4) and the amount of dadzein (●) and genistein (▲) present in soy milk. Data from reference 35.

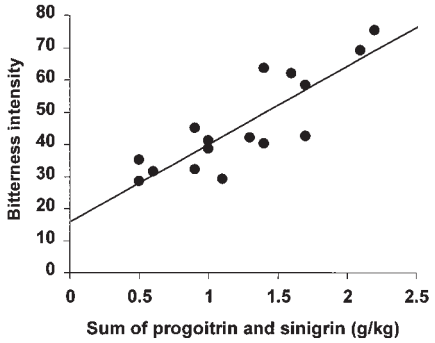

FIGURE 3. Mean bitterness intensity ratings (on a scale of 0–100) for 16 cultivars of Brussels sprouts as a function of combined progoitrin and sinigrin content (g/kg). Data from reference 36.

BITTER GLUCOSINOLATES IN CRUCIFEROUS VEGETABLES

Organosulfur compounds are another plant defense against predation. Cruciferous vegetables (broccoli, cauliflower, kale, turnips, collards, Brussels sprouts, cabbage, kohlrabi, rutabaga, Chinese cabbage, and bok choy) contain stable glucosinolates in the amounts of 0.5–1 g/g (18, 19, 27, 72). Glucosinolates are natural pesticides, being toxic to insects (27, 76). The major glucosinolates in cabbage and Brussels sprouts—sinigrin, progoitrin, and glucobrassicin—are toxic to rats (27). Their goitrogenic activity and instances of kale poisoning in cattle are well described in the literature (27). Excessive glucosinolate concentrations in animal feed have been associated with signs of disease in dairy cattle (98) and with thyroid, liver, and kidney toxicity in animal models (99). Crambe meal in broiler chick diets has toxic effects and is not recommended for long-term feeding (100). As with citrus flavonoids, concentrations of bioactive compounds are generally higher in young sprouts than in mature plants (75). Three-day-old broccoli sprouts contained higher concentrations of sulforaphane than did the mature plant (33).

Brassica glucosinolates, otherwise known as mustard oil glycosides, tend to be bitter. Studies showed that these compounds are responsible for the unpleasant taste of cruciferous vegetables, raw or cooked. Because the enzyme myrosinase is inactivated by cooking, food scientists took the position that sinigrin, as opposed to its metabolites, was responsible for the bitter taste of Brussels sprouts (27). Most taste panelists (71% and 79%) rated sinigrin and gluconapin, respectively, as bitter. In contrast, glucobrassicin and progoitrin were rated as bitter by fewer panelists (21% and 9%, respectively) (27). There was a 0.90 multiple correlation between the content of the 4 glucosinolates in Brussels sprouts and the overall perceived bitter taste (18, 19).

The correlation between the sinigrin content of fresh Brussels sprouts and the resulting bitterness of the cooked product was 0.74 (18, 19). Again, taste panelists were extremely sensitive to very low concentrations of *Brassica* glucosinolates. Concentrations of sinigrin that were detected by the consumers were ≈106 mg/L. Concentrations of vinyloxazolidine that were detected by 50% of the respondents were as low as 12 mg/L (27).

Recent studies showed that the sum of sinigrin and progoitrin concentrations (g/kg) in 16 Brussels sprouts cultivars was linked directly to perceived bitterness of the cooked product (36, 101). These data are shown in **Figure 3**. Higher bitterness ratings were associated, in turn, with a higher proportion of consumers who rated the product as "too bitter" and as having "poor taste" (**Figure 4**). Higher concentrations of sinigrin and progoitrin were associated with a sharply reduced number of consumers who remarked that the product had "good taste" (**Figure 5**). These data strengthen earlier reports that glucosinolate concentrations in cruciferous vegetables are the principal barrier against consumer acceptance (27).

ACRID AND PUNGENT ISOTHIOCYANATES

Enzyme myrosinase (β-thioglucoside glucohydrolase), liberated when plant cells are damaged, promotes hydrolysis of glucosinolates to pungent and highly reactive isothiocyanates, hydrogen sulfate, and glucose (33). Isothiocyanates, otherwise known as mustard oils, are the key phase 2 enzyme inducers. Although inducer potency can vary by cultivar, maturation, handling, and storage, it is directly linked to the glucosinolate content of the original plant.

Volatile isothiocyanates, or mustard oils, have been described as pungent, acrid, corrosive, and lachrymatory or tear-inducing. Some are described as garlic-like or watercress-like and are said to provoke a tingling sensation (102). The aversive pungent odor of phenylethyl isothiocyanate can be detected at 6 ppb, whereas the cabbage-like smell of 2-propenyl isothiocyanate is used in repellant aerosols (27). Bitter goitrin, 5-vinyloxazolidine-2-thione, is the chief breakdown product of progoitrin (27). Taste responsiveness to 5-vinyloxazolidine-2-thione, a breakdown product of progoitrin, may be genetically mediated because it shows the same bimodal characteristics as do PTC and PROP (18, 19). Whatever their putative health effects, these compounds contribute little to eating pleasure.

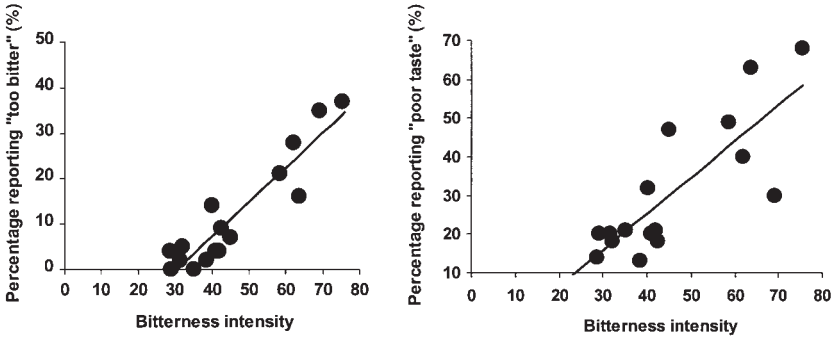

FIGURE 4. Relation between bitterness intensity (on a scale of 0–100) and the proportion of consumers who remarked that the product was "too bitter" or had "poor taste." Data from reference 36.

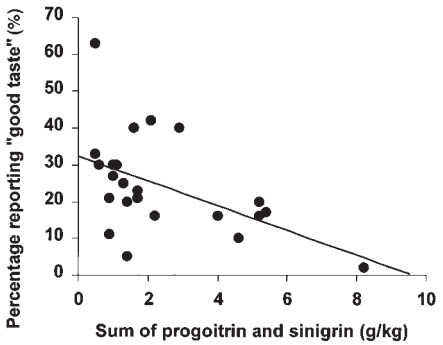

FIGURE 5. Relation between progoitrin and sinigrin content of Brussels sprouts and the proportion of consumers who remarked that the product had "good taste." Data from reference 36.

BITTER AND TOXIC PHYTOCHEMICALS

Some dietary phytochemicals are bitter, toxic, and lethal. Plants in the cucurbitaceae family can be so bitter as to be inedible. Cultivated species, selected for low bitterness and low toxicity, include cucumbers, gherkins, zucchini, squash, pumpkins, and melons. Cucurbitacins, or oxygenated tetracyclic triterpenes, are toxic and their consumption has been linked to illness and death. Bitter zucchini, containing 50–600 ppm cucurbitacins, has toxic effects in humans in doses of 3 g (27). Cucumbers are often rejected by the consumer because of excessive bitterness.

Kidney, haricot and navy beans, black-eyed peas, and lima beans contain cyanogenetic glycosides. Black lima bean is most bitter and most toxic—its importation is restricted to varieties yielding <200 ppm hydrogen cyanide. (27). Bitter cyanogentic glycosides are contained in kernels of almonds, lemons, limes, apples, pears, cherries, apricots, prunes, and plums. Some of these compounds are purported to have a use in chemoprevention.

THE DEBITTERING OF PLANT FOODS

Bitterness in plant foods has been described as a sensory defect with a major economic effect (20, 36). The degree of bitterness depends on the cultivar, strain, ripening, and storage conditions. Industry efforts have focused on the formation of bitter compounds, their role during the transition from raw to ripened product, and their breakdown in food or juice. Responding to taste-driven consumer demand, the food industry generally removes phenolic compounds, flavonoids, isoflavones, terpenes, and tannins from foods destined for human consumption. Because of such efforts, the current food supply is less bitter than it might otherwise be (20).

Potential approaches to removing bitter phytochemicals include selective breeding of new and less bitter cultivars (18, 19, 73, 103, 104). For example, high concentrations of sinigrin and progoitrin in Brussels sprouts are generally regarded not as a health benefit but as a major sensory defect (27). Apart from unpleasant taste, high concentrations of progoitrin can cause contact dermatitis. Food scientists have argued that progoitrin should be bred out of *Brassica* crops that are intended for human consumption (104).

The undesirable characteristics of glucosinolates in *Brassica* vegetables have long been known to the food industry. Removal of progoitrin and reduction in sinigrin was thought to reduce bitterness and increase consumer acceptance (104). In vitro assays of bitter compounds were used to detect, screen, and remove the most bitter varieties. Bitter taste had been identified as the main reason for avoidance of vegetables and was reported as being the least well tolerated for *Brassica* vegetables, spinach, squash, and onions (30, 73, 103). The current health-oriented push toward selective breeding of phytonutrient-rich and therefore more bitter varieties runs counter to the published studies on vegetables and consumer acceptance (30, 73, 103).

Creation of new and less bitter cultivars has also occurred with other crops. A wholesale reduction of glucosinolates in such oilseed crops as rapeseed and Crambe abyssinica was carried out successfully worldwide (105). The development of a transgenic citrus fruit, free of limonin, was also described in the literature (106).

Some scientists have argued that these modifications may have had unintended consequences. Many bitter phytochemicals are associated with resistance of the developing and mature plant to microbial, insect, or pest attack. It has been suggested (79) that plant varieties that have been selected for palatability by humans are usually more susceptible to disease, leading to increased reliance on synthetic pesticides.

Bitter compounds are also removed from processed foods. Some of the common debittering processes are summarized in **Table 2**. In many cases, these methods are patented and their details are guarded commercial secrets of a particular food company (56).

Beany flavor, bitter taste, and flatus factors pose a major barrier to the inclusion of more soy products in the Western diet (122). Solvents, precipitation, filters, and microorganisms have all been used to produce nonbitter and bland soy. Most debittering processes were designed to remove oxidized soy lipids and bitter peptides (121). However, isoflavones are probably removed as well. Early attempts to supplement foods with soy protein met with limited success, again because of taste factors (97). Although hydrolyzed soy proteins are added to soups to enhance flavor, their bitterness is often minimized by the addition of gelatin or maltodextrins (37).

Bitter phenolic compounds are routinely adsorbed to resins, trapped on polymers, precipitated, extracted with solvents, or converted to nonbitter compounds. Phenolic compounds and tannins are removed from wine by a variety of procedures (88). Protein "fining" of wine uses egg white, casein, gelatin, or isinglass to remove phenols and thereby lower astringency and bitterness of the wine. Wine tannins are also adsorbed with the use of polyvinyl polypyrrolidone matrixes (54). Aging of wine reduces both bitterness and astringency because phenols continue to polymerize and eventually precipitate. Young red wines sold without being aged sometimes have high residual sugar concentrations (1–3%) to reduce bitterness and astringency. Sugar has also been added to wines to reduce bitter taste (54).

Bitterness can be masked. Cyclodextrin, a common commercial product, dissolves flavonoids and masks the bitter taste of citrus juice. Because flavonoids are still present in the juice, their bioactive potential is unchanged. Other effective ways of reducing bitterness of plant foods involve cooking or the addition of fat, sugar, or salt. The time-honored techniques of sautéing, caramelizing, braising, or pickling of vegetables improve palatability by masking bitter taste of raw plant foods.

PHYTONUTRIENTS IN DISEASE PREVENTION

Diets high in vegetables and fruit have been associated with reduced cancer risk (5); many studies focused on the

TABLE 2
Summary of industrial debittering processes to remove bitter phytonutrients from foods

Phytonutrient class	Typical compound	Food	Debittering process	Reference
Flavanones	Naringin	Grapefruit juice	Adsorption to polymers	74, 107, 108
	Naringenin	Orange juice	Passage through resins	56, 109, 110
Flavones	Tangeretin		Passage through enzyme matrix	111, 112
	Nobiletin		Passage through microbial mass	113–116
	Sinensetin		Accelerated ripening with ethylene	116
Triterpenes	Limonin		Use of cyclodextrin polymers	117, 118
			Genetic engineering: transgenic citrus trees	106
Flavans	Catechin, epicatechin	Tea	Fermentation	65, 82
		Chocolate	Removal of chocolate liquor	84
	Catechin polymers	Wine	Precipitation with proteins: egg white, casein, gelatin, isinglass	53, 54
	Epicatechin polymers: procyanins		Adsorption to polyvinyl polypyrrolidone	53, 54
	Polyphenols (tannins)		Aging to precipitate tannins	87
			Residual sugar	53, 54
Isoflavones	Genistein and daidzein	Soy products	Selective breeding	27
	Genistin and daidzin		Use of solvents (hexane)	119, 120
			Use of microorganisms	121
			Adsorption to resins	121
			Membrane ultrafiltration	
			Precipitation (cyclodextrin)	
Glucosinolates	Sinigrin	*Brassica* vegetables	Selective breeding	27
	Progoitrin		Nonbitter cultivars	36, 105
	Glucobrassicin		Altered growth conditions	73, 103
Isothiocyanates			Cooking	

chemoprotective role of phytochemicals. Chemoprotective agents generally belong in 1 of 3 categories: those that block metabolic activation of carcinogens, those that prevent the formation of carcinogens from precursors, and those that suppress neoplasia in cells previously exposed to carcinogens (123, 124). Phytonutrients and their metabolites elicit a variety of biological activities, acting as antioxidants, phytoestrogens, or enzyme inducers (125). Among the most promising compounds under study are bitter phenols and polyphenols, flavonoids, isoflavones, and glucosinolates.

Phenolic acids, catechins, flavonols, and polymeric anthocyanins in wine were reported to have antioxidant activity (126, 127). Although the bioavailability of phenols and polyphenols is a matter for further research, only small amounts of food polyphenols estimated at ≤30 mg/d are absorbed (17). However, even such low amounts may have a potent antioxidant effect in vivo (17). Even at very dilute concentrations (10 μmol/L) in vitro, phenolic compounds had antioxidant effects (128).

Plant flavonoids may protect against LDL oxidation through a reduction of free radicals, chelation of metal ions, or protection or regeneration of α-tocopherol (9, 17, 123). Studies of their anticarcinogenic action focused on the activation of enzymes involved in the metabolism of xenobiotics (phase 2 enzymes). Naringin, the bitter flavonoid component of grapefruit juice, or its metabolites, are reported to inhibit the activity of cytochrome P-450 (49).

Glucosinolates and isothiocyanates are also regarded as dietary protectors against cancer (7). Isothiocyanates inhibit the activation of carcinogens by cytochrome P-450 (phase 1) enzymes and promote detoxification of activator carcinogens by inducing phase 2 enzymes. Phase 2 enzymes inactivate carcinogens by neutralizing their toxic properties and speeding their elimination from the body (33). Some phase 2 enzymes function as inhibitors of cytochrome P-450 (7). The results of early studies (18, 19) and more recent data suggest that one of the most potent inducers is sulforaphane, or 4-methylsulfinylbutyl isothiocyanate (33), which is derived from glucoraphanin. Inducer potency has been linked to concentrations of bitter sinigrin, progoitrin, glucobrassicin, gluconapin, and glucoraphanin. As a result, several clinical studies attempted to feed patients large amounts of *Brassica* vegetables daily. In some cases, respondents were fed 300 g Brussels sprouts/d for 3 wk or 500 g broccoli/d for 12 d (11). Other studies used a mix of Brussels sprouts, cabbage, broccoli, and cauliflower in the amount of 400 g/d (11).

Epidemiologic outcomes of diets high in vegetables and fruit were summarized in a recent report (4). Research has focused on vegetables rather than fruit, with special emphasis on green leafy and *Brassica* vegetables, citrus fruit, soybeans, and red wine. Population-based studies (9, 129) showed that the risk of coronary heart disease was reduced at higher estimated intakes of flavonoids (apigenin, kaempferol, luteolin, myricetin, and quercetin). Data on diet and colon cancer (64) also show a significant decline in risk with higher consumption of vegetables, green leafy vegetables, and cabbage. There is a general consensus that a diet higher in plant foods than is the current norm is associated with improved health and reduced disease risk. However, the most potent plant products are also likely to be the most bitter and therefore the most aversive to the consumer.

THE DILEMMA OF THE FOOD INDUSTRY

The competing demands of taste and health pose a dilemma for the food industry. The major determinant of food selection is taste. Foods that are bitter, acrid, or astringent tend to be rejected by the consumer—and generally for the right reasons. The instinctive rejection of bitter taste may not be modifiable because it is a key mechanism for survival.

Bitter taste is the main reason for the rejection of diverse food products (23, 30). Bitterness of cruciferous vegetables has been linked repeatedly to their low acceptance (30, 48). Focus groups

conducted by the National Cancer Institute before the 5-A-Day project found that dislike of certain vegetables was a major barrier to vegetable consumption (130). In other studies, bitter *Brassica* vegetables were thought to taste good only if sauces were added, that is, after the addition of fat, sugar, or salt (131). Excessive bitterness lowers the acceptablity of citrus juices (81). The taste of soy proteins and some soy products is generally described as objectionable (35). Bitterness of wine is reduced by aging and the removal of phenols and polyphenols (53, 54). The food industry has engaged in these practices for years in response to consumer demand.

Not all bitterness is rejected automatically (132). In selected foods and beverages, a certain degree of bitterness is expected. In coffee, beer, and wine, bitterness is paired with a desirable attribute: caffeine or alcohol (132–134). Although liking for some degree of bitterness can be acquired in adult life, excessive bitter taste in citrus juices, coffee, or beer is usually objectionable. The threshold for what is or is not acceptable may vary from one person to another because individual taste response to bitter varies enormously. Inherited taste factors, compounded by sex and age, add an extra layer of complexity to the acceptance of bitter plant foods by the consumer. Food scientists acknowledge that it is difficult to blend concentrations so that bitterness levels are optimal for everyone (20).

Consumer food choices are driven primarily by the demands of taste, cost, and convenience (31). Recent suggestions (33) that people ought to select broccoli by inducer potency and then eat it raw run counter to consumer research. Suggestions that "cooking should be performed, if at all, by steaming, microwaving, stir frying or rapid boiling" (33) run counter to the basic principles of gastronomy. Standard methods of cooking vegetables, developed over hundreds of years (135), that make liberal use of fat, sugar, and salt (135) are unlikely to be abandoned. However, the recent identification of human bitter-taste receptors (42, 43) is bound to have an industry-wide effect given that the debittering of foods remains a very common problem.

PHYTONUTRIENTS AND FUNCTIONAL FOODS

Genetic modification of foods to optimize health represents one of the newest frontiers in nutrition science. So-called functional foods can be tailored to contain increased concentrations of phytonutrients with chemopreventive characteristics. Although the definition of functional foods is still evolving, functional ingredients are commonly defined as safe dietary substances that beneficially affect specific targets in the body beyond providing adequate nutrition (136). A related definition of foods for specific health use, adopted by the Japanese Ministry of Health and Welfare, refers to "processed foods containing ingredients that aid specific bodily function in addition of nutrition" (137). Much research and media interest has focused on phytonutrients found in soy products, *Brassica* vegetables, citrus fruit, cranberries, green tea, grapes, and wine. Processed foods that incorporate new functional ingredients or enhance the concentrations of existing ones are being developed.

Food and nutrition scientists regard phytonutrients as the third functional component of food, after nutrients and taste components (137). Although the primary function of food is to provide nutrients, its secondary function concerns sensory attributes such as taste and flavor. The tertiary function, said to be independent of the previous 2, is to prevent disease at the molecular level (137). However, it now appears that the secondary and tertiary functions are linked, if not at odds with each other. For the most part, plant-based phytochemicals are bitter and therefore aversive to the consumer. The discovery of a family of ≥50 different bitter-taste receptors only confirms how important sensitivity to bitter taste was to evolution and survival. Research on plant-based functional foods presents several challenging opportunities for cancer biology and nutrition science. However, issues of taste and behavioral nutrition ought to be considered as well.

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