June 2001: 163–169

# The Science and Complexity of Bitter Taste

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*Food choices and eating habits are largely influenced by how foods taste. Without being the dominant taste sensation, bitter taste contributes to the complexity and enjoyment of beverages and foods. Compounds that are perceived as bitter do not share a similar chemical structure. In addition to peptides and salts, bitter compounds in foods may include plant-derived phenols and polyphenols, flavonoids, catechins, and caffeine. Recent studies have shown that humans possess a multitude of bitter taste receptors and that the transduction of bitter taste may differ between one compound and another. Studies of mixture interactions suggest further that bitter compounds suppress or enhance sweet and sour tastes and interact with volatile flavor molecules. Caffeine, a natural ingredient of tea, coffee, and chocolate, has a unique flavor profile. Used as a flavoring agent, it enhances the sensory appeal of beverages. Research developments on the genetics and perception of bitter taste add to our understanding of the role of bitterness in relation to food preference.*

## Introduction

Taste is the main influence on food choices.[1] Generally, people like sweet and dislike bitter tastes, yet not all bitter tastes are unpleasant to the consumer. In certain foods, a limited degree of bitterness is expected and enjoyed.[2,3] Without being the dominant sensation, bitterness helps to balance the flavor profile of beverages and foods. Mixture interactions among sweet, bitter, and sour tastes, and between taste and volatile flavor elements, add to the complexity and to the enjoyment of tea, coffee, chocolate, fruit juices, and other beverages.

Of the four basic tastes—sweet, sour, salty, and bitter—bitter is the most complex and perhaps the least understood. Among bitter compounds in foods are amino acids and peptides, esters and lactones, phenols and polyphenols, flavonoids and terpenes, methylxanthines (caffeine), sulfimides (saccharin), and organic and inorganic salts.[3] The fact that such structurally diverse compounds can elicit a single bitter taste suggests that multiple mechanisms are responsible for the perception and transduction of bitterness.[4,5] Some of these mechanisms may be common to the perception of both bitter and sweet. Small changes in chemical structure can convert bitter compounds to intensely sweet or vice versa. Bitter and sweet tastes in solution can enhance or suppress each other, with the interplay between bitter and sweet occurring at the neuronal level.[6]

The ability to perceive some bitter tastes varies greatly across individuals. In some cases, it can be an inherited trait.[7] The only recorded instance of taste polymorphism in humans is the genetic "blindness" to the bitter taste of phenylthiocarbamide (PTC) and 6-*n*-propylthiouracil (PROP). Sensory studies have linked the ability to taste PTC/PROP, a dominant trait, with heightened sensitivity to such bitter compounds as caffeine[8,9] and naringin.[10,11] Whereas the phenotypic taste responses to PTC/PROP are well studied, the gene responsible for this trait has not been described and its exact location is unknown.[12,13]

The focus of human taste research now includes bitter as well as sweet tastes. So far, studies of taste genetics in humans have only explored bitter taste.[12,13] The most recent studies on candidate taste receptors in humans and mice also involve the perception of bitter.[14,15] Studies on mixture psychophysics have likewise focused on interactions of bitter with sour and salty tastes.[16,17] Interactions of bitter with food flavor components have long been an interest of the food industry.[3] The contribution of these research developments to a better understanding of the role of bitterness in beverages and foods is the main topic of this review.

## Mechanisms of Bitter Taste Perception

Taste transduction begins when a stimulus comes into contact with a taste receptor cell. Whereas each taste bud may contain 75–150 epithelial cells, only a few are exposed at the taste pore at any one time.[4] Most taste buds are clustered in fungiform, foliate, and circumvallate papillae on the tongue surface, though some can also be found on the soft palate, epiglottis, or even pharynx. As a result, taste sensation can differ with the proportion of taste buds

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that are stimulated, depending on whether the stimulus is swallowed or not.[16]

Taste stimuli influence receptor cells in a variety of ways. Direct interaction of taste stimuli with ion channels on the cell membrane is most important for the perception of salty and sour. By contrast, the perception of sweet and bitter involves specialized taste receptors coupled with proteins.[4,18] Such proteins exert their effects through second messengers, cyclic AMP (cAMP) or inositol triphosphate (IP3), that act on targets within the cell.[19] According to current thinking, there are at least two—if not more—transduction mechanisms for bitter taste. One pathway may involve a G-protein that stimulates enzyme-activated IP3, leading to a release of calcium from cell stores. Another mechanism for the perception of bitter and sweet tastes may involve G-protein, α-gustducin, that activates enzyme phosphodiesterase to decrease intracellular cAMP.[20] Direct blocking of $K^+$ channels by bitter tastants may also occur.[4]

Bitter taste perception may involve not only multiple transduction mechanisms, but also a large number of receptors. The number of different bitter taste receptors in humans that are linked to gustducin is estimated at 40–80, far more than previously thought.[14] 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.[14] The T2Rs are expressed in all taste buds of circumvallate and foliate papillae, and in palate taste buds.[14] Whereas T2Rs are rarely expressed in fungiform papillae, those fungiform taste buds that do express T2Rs have a full repertoire of different receptors, suggesting that each cell may recognize multiple bitter tastants. A follow-up study showed these receptors to be highly specialized. A human bitter taste receptor (hT2R-4) responded only to denatonium and PROP, whereas a mouse receptor (MT2R-5) responded only to cycloheximide.[15] The perception and transduction of bitter tastes is a complex and specialized system.

The perception of bitter and sweet tastes may share some common pathways.[5,21] Small structural changes convert some compounds from bitter to sweet. Neohesperidin, a bitter flavonoid, converts to neohesperidin dihydrochalcone (DC), an intense sweetener. By contrast, sucrose esters such as sucrose octaacetate are intensely bitter. Saccharin and many other intense sweeteners have a bitter aftertaste, especially at high doses.[21] This array of taste receptors and transduction mechanisms suggests that the responses to sweet and bitter tastes may have a major role in food selection.

## Genetics of Bitter Taste Perception

Behavioral genetic studies of taste perception in humans have focused on two bitter compounds, PTC and PROP. Genetic linkage studies have linked the ability to taste PROP with a chromosome locus at 5p15, with a modifier locus on human chromosome 7.[12,13] Thought to be a dominant trait, PROP tasting is shown by 70% of Caucasians.[7] The proportion of tasters among Asians and African Americans is estimated to be 90% or higher. Recent studies also identified a separate subgroup of extremely sensitive PROP "supertasters."[7] Supertasters, most of whom are women, tend to have more fungiform papillae and a higher density of taste buds per papilla. Opinions differ as to whether PROP supertasters are also more sensitive to sweetness, salt, and to the oral sensation of fat.[1,7]

Strains of mice are differentially sensitive to bitter tastes, suggesting that multiple genes may be involved.[12,13] Studies in humans have linked PTC/PROP tasting with heightened sensitivity to such bitter compounds as caffeine, saccharin, and quinine hydrochloride, but not urea.[7,11,12] Taste detection thresholds for PTC and caffeine were correlated in some early studies.[8] PROP tasters were also more sensitive to the aftertaste of caffeine measured for up to 4 minutes in a time-intensity study.[22] More recent work on the relationship between taste responsiveness to PROP and the perceived bitterness of caffeine[9] showed that most PROP tasters also gave high bitterness ratings to caffeine solutions. By contrast, caffeine-insensitive respondents were more likely to be PROP nontasters. These data, summarized in Figure 1, are consistent with past reports that the PROP gene may confer both a specific ability to taste PROP and a more general sensitivity to other bitter tastes, including caffeine.

Whether PROP tasting is associated with altered sensitivity to sweet is debatable. In some studies, PTC/PROP tasters gave higher intensity ratings to dilute solutions of sucrose, saccharin, and neohesperidin dihydrochalcone.[7]

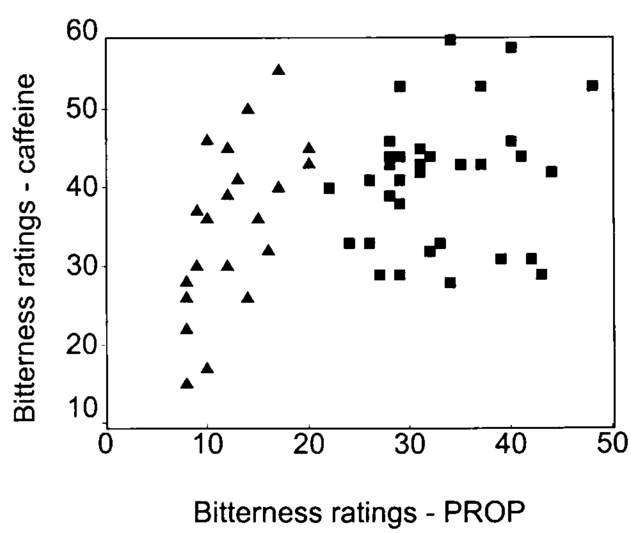


**Figure 1.** Summed bitterness ratings for seven PROP solutions of increasing concentrations plotted against summed bitterness ratings for seven caffeine solutions, by PROP taster status (■ tasters; ▲ nontasters). From reference 9, with permission.

However, other studies failed to replicate those findings.[9,11] There was no evidence for the notion that PROP supertasters were highly sensitive to the oral sensation of dairy fat.[23] Contrary to suggestions that PROP tasting might entail aversions to sweet beverages, no differences in soft drink preferences by PROP taster status were observed. Furthermore, sweetening caffeine solutions with neohesperidin DC obliterated any differences in preferences for caffeine solutions between PROP tasters and nontasters.[9]

## Bitter Taste and Aging

The ability to detect very low concentrations of bitter and salty tastes declines with age. By contrast, the perception of sweet and sour remains relatively stable. Not all bitter compounds are equally affected. Whereas the sensitivity to PTC/PROP, quinine, and caffeine declined with age, sensitivity to urea did not. In judging more concentrated taste solutions, elderly subjects found bitter, but not the other three tastes, to be less intense than did young subjects.

Age-related deficits in taste were most pronounced when testing was localized to specific areas of the tongue. Instead of whole-mouth tasting, the taste solution was applied to localized areas of the tongue using a cotton swab. Scientists believe that whole-mouth perception may compensate for some of the regional deficits, such that older respondents may not even be aware that they have experienced a taste loss.

The decline in the perception of bitter and salty tastes may influence food choices and eating habits. Generally, intensely bitter and salty tastes are perceived as unpleasant. There were no major deficits in the scaling of saltiness in mashed potatoes or tomato juice, and no evidence for an age-related rise in salt consumption. By contrast, the perceived bitterness of PROP solutions declined with age. Older women expressed an increased liking for bitter cruciferous vegetables and salad greens. The perception of bitter intensity declines with age and may influence the liking for bitter in beverages and foods.

## Mixture Interaction Studies

Beverages are complex mixtures of tastes, flavors, and textures. Some compounds are present at above-threshold levels, whereas others such as caffeine may be present at below-threshold levels. These different tastants can enhance or suppress each other depending on their concentration, the nature of the food or beverage, and the experimental methods involved.[16,17]

At near-threshold concentrations, mixtures can be tasted even when each of their components is too weak to be tasted separately.[6] Individual detection thresholds decline as the number of mixture components increases. The taste synergy of mixtures is such that multiple ingredients can enhance weak intrinsic flavors or modify an existing flavor profile.[24,25] For example, certain intense sweeteners enhance each other at weak but above-threshold concentrations.[26] The degree of such enhancement can depend on the particular sweetener and its concentration. Above-threshold levels of caffeine enhanced sourness but masked the perception of sweetness in water solutions.[27]

Moderate to strong concentrations are more likely to show mixture-suppression effects.[16,17] Each component is perceived as less intense than when it is tasted separately. For example, the bitterness of caffeine can be suppressed by sugar, acid, or salt. Natural sweeteners (sucrose) suppressed the bitterness of caffeine more effectively than aspartame or saccharin.[28,29] Caffeine and acids could enhance or suppress each other depending on concentration. At subthreshold levels, weak sourness of citric acid was suppressed by caffeine.[30] Above threshold, the sourness of citric acid was enhanced by caffeine bitterness.[31] At high concentrations, mixture interactions could go either way. In one study, strong citric acid enhanced the bitterness of a wide range of caffeine concentrations.[31] In related studies on sweet and sour, McBride[32,33] found that sweetness suppressed acidity, whereas acidity suppressed sweetness. Fructose was more susceptible to suppression than sucrose, an important point in the flavor formulation of soft drinks.

Caffeine bitterness was also suppressed by sodium salts. Bitter compounds and sodium salts showed asymmetrical suppression, such that bitterness was suppressed to a variable degree, whereas saltiness was generally unaffected.[16] Though mixture suppression effects can be substantial, there are no instances of two tastes canceling each other, as can be the case with colors and tones. Because the effects of some taste mixtures may involve multiple transduction mechanisms, it can be difficult to predict how a given mixture will behave. Optimizing mixture interactions for consumer acceptance has been the province of flavor chemists.

Studies in taste psychophysics suggest that mixture suppression effects are neurally mediated and do not involve tastant competition for the same receptors in the oral cavity.[6] The suppression of PTC bitterness by sucrose was much greater among PTC tasters than nontasters, suggesting that the effect depended on perceived bitterness as opposed to PTC concentration.[6,34] Analogous results were recently obtained by Ly and Drewnowski[9] for PROP solutions sweetened with neohesperidin DC. These data, summarized in Figure 2, suggest that mixture interactions may further depend on genetic taste factors and individual sensitivity to bitter taste.

The perceived intensity of a taste stimulus may also increase when an odorant is added.[35] Whereas laboratory studies have focused on mixtures of pure tastants in water, the taste of beverages involves multiple interactions

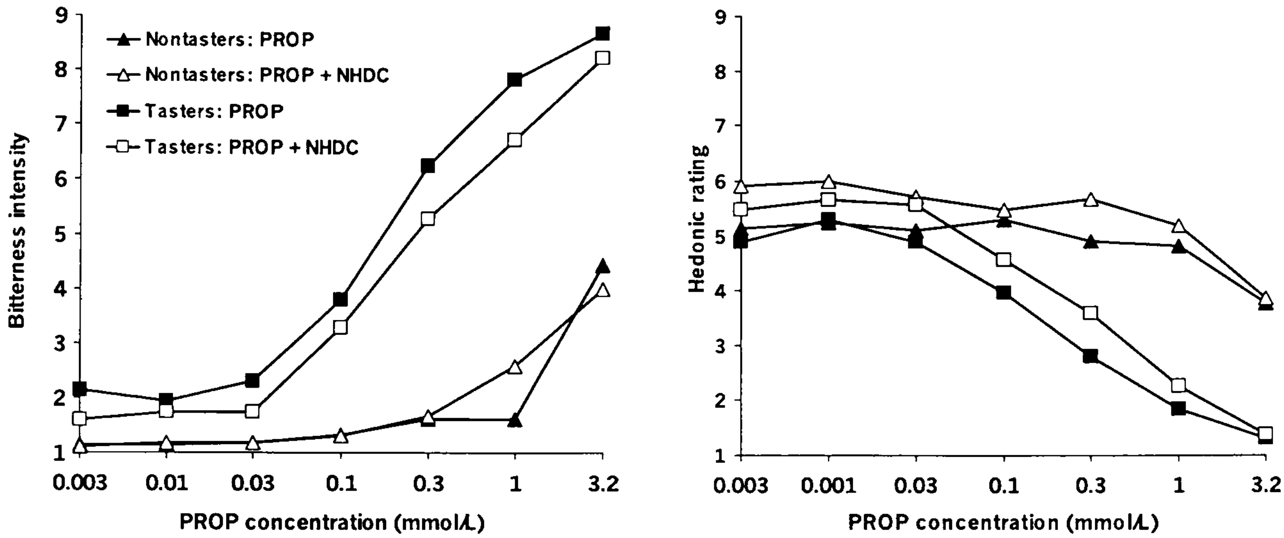


**Figure 2.** Bitterness intensity (left panel) and hedonic ratings (right panel) for 7 PROP solutions, before and after the addition of neohesperidin dihydrochalcone (NHDC), by PROP taster status. From reference 9, with permission.

among different tastes and between taste, aroma, viscosity, and temperature. Studies of coffee-sucrose as opposed to caffeine-sucrose mixtures showed that mixture suppression was affected by flavor.[36,37] At similar perceived intensities, caffeine bitterness or coffee flavor were suppressed by sucrose but the perception of sweetness was not affected by coffee or caffeine. Follow-up studies using ternary mixtures of caffeine, sucrose, and a vehicle (water, carboxymethylcellulose, or gelatin) showed that both sweetness and bitterness were suppressed even more.[38]

## The Flavor of Foods and Beverages

Taste, aroma, and mouthfeel all contribute to the flavor of foods. Whereas the four basic tastes are sweet, sour, salty, and bitter, the range of taste experiences is far more extensive.[5] Humans describe caffeine and quinine as purely bitter, calcium chloride as bitter-salty, and urea as bitter-sour. The quality and the temporal profile of the taste experience may also vary. Saccharin has been described as sweet with a bitter aftertaste, whereas catechins are bitter compounds with a sweet aftertaste. Caffeine has a unique temporal profile that builds up faster than quinine, has a slower rate of decay, and shows a much more prolonged aftertaste.[39] The time to maximum bitterness can be as long as 13 seconds. This breadth and duration of taste quality that makes caffeine unique for beverage applications results from the parallel activation of a broad array of ion channels, specialized taste receptors, and second messengers associated with taste cell membranes.[5]

Much of food's flavor is perceived through the olfactory impression. Humans can distinguish between several thousand odors that are sometimes detected at remarkably low concentrations. The current thinking is that the olfactory system recognizes patterns and searches for similarities among groups and classes of odors. The important odor attributes are intensity, quality, and the hedonic tone. Caffeine forms complexes with volatile flavor molecules, altering their solubility, and modifying their perceived flavor impact. Studies reported that caffeine altered the solubility of such compounds as ethyl benzoate and anisole, as well as terpenes and furans.[40]

Odor molecules may stimulate trigeminal nerve endings as well as olfactory receptors. Carbonated beverages, alcohol, or the sensation of menthol are perceived through the trigeminal nerve. Capsaicin, the active ingredient of chili peppers, stimulates pain fibers as opposed to taste receptors. Recent studies showing that PROP tasters may be more responsive to hot peppers and alcohol suggest that genetic taste markers and trigeminal perception may well be linked.[7]

Mouthfeel refers to texture, as it is perceived in the mouth in the course of drinking and swallowing. Among terms used to describe the mouthfeel of beverages are smooth, viscous, and creamy, as well as foamy, clean, cool, or lingering.[41] Pure caffeine has been described as having a "cottony" mouthfeel and it produces a drying effect. Beverages containing caffeine are sometimes said to have a "clean" bitter taste and tea containing caffeine has been described as "brisk."[42]

## The Bitter Taste of Caffeine

Caffeine, a methyl xanthine, is present in coffee, tea, and chocolate. It is generally present at low (mmol/L) concentrations and need not be the major bitter ingredient. The taste of coffee—bitter and astringent—is largely due to phenolic acids as opposed to caffeine. It is roasting that determines coffee flavor: the rich dark roast is actually somewhat lower in caffeine content than the more acid light roast. Coffee aroma, a major factor in coffee enjoyment, is due to several hundred volatile chemicals including alcohols, ketones, aldehydes, and esters.[3]

The taste, pungency, and color of fermented teas also derive from phenolic compounds, including catechin and epicatechin, and their oxidation products. Depending on molecular weight, catechins can be bitter or astringent.[2,3] Epicatechin is generally more bitter than catechin.[2,3] The bitterness and astringency of teas have been ascribed to the combination of catechins, saponin, amino acids, and caffeine.[2] Caffeine provides the needed "briskness" and greatly contributes to the sensory appeal of teas. Complex interactions between caffeine and tea catechins account for the complexity of tea flavor.[42]

Fermented cocoa contains polyphenols, catechins, anthocyanins, and caffeine.[43] Bitterness of chocolate is partly due to catechins in fermented cocoa that are variously described as bitter with sweet aftertaste or as bitter and astringent.[2] Additional bitter elements are provided by caffeine, theobromine, and the interaction of theobromine and diketopiperazines during roasting.[3]

Tea, coffee, and chocolate are complex taste and flavor mixtures that contain multiple bitter phytochemicals, including caffeine. Their sensory appeal often depends on the subtle balance of sweet, acid, and bitter tastes, combined with multiple flavor elements and sometimes the texture of fat. Chocolate, in particular is a complex mixture of flavor elements, bitter, sugar, and fat. Some of the same flavor combinations are used in the formulation of soft drinks.

## Caffeine As Flavoring Agent

Flavor is the complex of sensations allowing us to identify the presence and identity of beverages and foods. These flavor sensations include not only taste and aroma, but also mouthfeel and even visual and auditory aspects of foods. Caffeine is a widely used flavoring agent[44] that contributes to the popularity and enjoyment of beverages and foods. It is generally used in soft drinks at levels of 100 mg/L (0.5 mmol/L) with rare products containing up to 200 mg/L (1.0 mmol/L).

A concentration of 0.5 mmol/L caffeine represents a near- or below-threshold level. Studies have placed caffeine threshold in water at 0.5 mmol/L (or 94 mg/L). The observed threshold in fruit juice or custard was approximately double that. Caffeine thresholds can be reduced with sensory training: Pangborn[30] obtained caffeine thresholds of 1.5 mmol/L with naïve panelists and reduced them to 0.4 mmol/L following training.[45] Generally, the perception of the bitter taste of caffeine declines with age.[46]

In addition to the mixture effects and taste-flavor interactions described above, caffeine may potentiate the impact of some intense sweeteners. Schiffman et al.[47,48] found that adaptation of the tongue to methylxanthines potentiated the taste of Ace-K, saccharin, and neohesperidin DC. The enhancement was reversed by adenosine suggesting its potential involvement as a second messenger in both sweet and bitter perception. However, caffeine did not affect the perceived sweetness of aspartame, sucrose, fructose, or cyclamate.[28] Not all studies have replicated those effects. Mela[49] reported that caffeine did not affect the taste of sweeteners, and other studies found no effects of caffeine or adenosine on the perception of sweet taste.[50]

The complexity of interactions among different tastes and flavors makes the perception of individual mixture ingredients especially difficult. The perception of mixtures can involve analysis, synthesis, or fusion.[33] In an analytic model, all individual components can be separately perceived; in a synthetic model, no individual components are separately perceived; and a fusion model allows the perception of more than one ingredient without the ability to identify it. The perceived pleasantness of beverages and foods is independent of the ability to recognize and identify any one ingredient.

One recent study[51] of 25 adults examined the taste of caffeine-free cola and cola to which different concentrations of caffeine (range 0.2–8.2 mmol/L) had been added. Using a simple overall difference test with 20 exposures and an arbitrary cutoff point of 75% correct, respondents correctly identified all caffeine-containing beverages except two with subthreshold concentrations of caffeine (0.2 and 0.5 mmol/L). Above-threshold concentrations of caffeine were described as bitter and unpleasant.[51]

The data were widely misinterpreted as showing that caffeine could not have been a flavoring agent. As documented above, however, caffeine can exert its effects at below-threshold or near-threshold levels. Furthermore, the study was seriously flawed from the sensory evaluation standpoint. First, tests for an overall difference in taste are not the same as attribute tests. In the latter, respondents concentrate on a single attribute, such as bitterness or a lingering aftertaste, and ignore all others. Studies show that thresholds for attended stimuli are often lower than for unattended stimuli.[52,53] An attribute difference test would have been a more appropriate procedure. Second, simple difference tests always use a placebo control, such that same-same pairs are presented along with same-different pairs. That serves to compare the placebo effect with the treatment effect following the same number of exposures.[54] Because the study failed to include a placebo control condition, no appropriate statistical tests could be conducted. That design flaw makes the study difficult to interpret. Finally, hedonic preferences as opposed to intensity ratings are the major influence on food preferences and food choices. In the published study,[51] all but one subject reported preferring the flavor of caffeinated cola to caffeine-free cola.

A recent "taste test" conducted by Consumer Reports[55] likewise reported that only 24% of middle school students were able to identify the soda they had preferred earlier—caffeinated or noncaffeinated. That test required the students to come up with correct answers five times in a row. That study took no account of probability statistics. Assuming that the students identified a given soda with 75% certainty, the probability of five correct answers in a row would be 0.75 to the fifth power, or only 0.24. As in the previous study, the flavor of the caffeinated beverage was more preferred.

## Flavor Perception and Hedonic Response

The taste system identifies foods and beverages for human consumption. Whereas most laboratory studies have focused on intensity, food choices are influenced by the quality and perceived pleasantness of beverages and foods.[56,57] Consumers can rate overall palatability without being consciously aware of all food ingredients, especially those present at near-threshold levels. Breslin[16] makes a point that though bread is not perceived as salty, bread without salt is unpalatable. Similarly, respondents who rated high-fat and low-fat dairy spreads as equivalent in both fatness and creaminess, tended to prefer the high-fat version.[41] Though judged as equal in fat content, the stimuli were hedonically different. In the same way, colas and caffeinated soft drinks provoke a wide range of taste and flavor experiences that directly contribute to preferences.

Caffeine, in particular, exerts its effects at near-threshold levels, whether in tea or in selected soft drinks (Table 1). The amount of caffeine that can be added to beverages and foods is self-limited by its bitterness threshold because at above-threshold concentrations caffeine is perceived as bitter and unpleasant. Its flavor properties, including a unique temporal profile, and documented interactions with sweeteners, acids, and volatile flavor molecules contribute to the flavor profile of beverages and foods. Caffeine is an integral part of many beverages, including soft drinks, and contributes to their sensory appeal.

**Table 1.** Caffeine Content of Foods and Beverages

| | Caffeine Content (mg) | |
|---|---|---|
| **Item (serving size)** | **Typical** | **Range** |
| Coffee (250 mL) | | |
| Brewed, drip | 100 | 60–180 |
| Instant | 65 | 30–120 |
| Decaffeinated | 3 | 1–5 |
| Espresso (30 mL) | 40 | 30–50 |
| Tea (250 mL) | | |
| Brewed tea—green, black, oolong | 60 | 25–110 |
| Instant | 28 | 24–31 |
| Iced | 25 | 9–50 |
| Soft drinks (250 mL) | | |
| Cola and citrus beverages | 24 | 20–40 |
| Cocoa beverage (250 mL) | 6 | 3–32 |
| Dark chocolate (30 g) | 20 | 5–35 |
| Milk chocolate (30 g) | 6 | 1–15 |

Adapted from reference 58.


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