Chem. Senses 27: 31–38, 2002

Bitter Taste of Saccharin and Acesulfame-K

John Horne, Harry T. Lawless, Ward Speirs and Domenic Sposato

Department of Food Science, Cornell University, Ithaca, NY 14853

Correspondence to be sent: Harry Lawless, Department of Food Science, Cornell University, Ithaca, NY 14853, USA.
E-mail: htl1@cornell.edu

Abstract

The relationships among suprathreshold taste responses to acesulfame-K, Na-saccharin and 6-*n*-propylthiouracil (PROP) were examined in two studies. In the first study, the labeled magnitude scale was used with the high anchor labeled as 'strongest imaginable oral sensation' and in the second study, it was labeled as 'strongest imaginable sensation of any kind'. Results from the two procedures were similar. Individual differences among 65 subjects were seen in bitter responses to acesulfame-K and saccharin. Bitter responses to acesulfame-K ands accharin were positively correlated, but showed no significant relationship with responses to PROP bitterness or with PROP taster groups. Saccharin and acesulfame-K may share a common mechanism for bitter taste reception and transduction, one that varies across individuals and is different from mechanisms mediating bitter responses to PROP. Changing the instructions of the labeled magnitude scale induced a context effect. Ratings of sweetness referenced to the 'strongest imaginable sensationof any kind' were lower than ratings referenced to just oral sensations.

Introduction

Salts of saccharin are intensely sweet but also have a bitter taste to some individuals. Helgren *et al.* (Helgren *et al.*, 1955) estimated that ~25% of a European population will detect an off-taste to saccharin described as metallic or bitter. For a time, it was proposed that this unpleasant non-sweet taste was due to impurities in the stimulus, specifically *o*-toluene sulfonamide, a by-product produced during synthesis (McKie, 1921; Cannon, 1954). However, other research showed that the off-tastes were a true property of purified saccharin salts (Rader *et al.*, 1967). Using time-based psychophysical methods, Larson-Powers and Pangborn (Larson-Powers and Pangborn, 1978) showed saccharin to have a lingering bitterness. The bitterness is more pronounced at higher concentrations, producing a flattening of the sweetness function (Moskowitz and Klarman, 1975) and making iso-sweet matches to other compounds difficult to achieve at high levels (Ayya and Lawless, 1992). Acesulfame-K is another intense sweetener with a bitter taste. According to Ott *et al.* (Ott *et al.*, 1991), acesulfame-K has a delayed bitter aftertaste that is more intense and longer in duration than sucrose, aspartame or alitame. Schiffman *et al.* (Schiffman *et al.*, 1985) noted high variability in the intensity and quality of acesulfame-K, due to bitter and metallic sidetastes.

Bartoshuk (Bartoshuk, 1979) found a relationship between 6-*n*-propylthiouracil (PROP) taster status and saccharin bitterness, with PROP tasters being more sensitive to sodium saccharin bitterness at low levels (0.001 and 0.0032 M). At higher concentrations, the group differences attenuated. Since that report, a third group of people with very high PROP sensitivity has been classified as supertasters. These individuals have a pronounced response to suprathreshold concentrations of PROP when assessed relative to NaCl standards. They also are characterized by having a higher density of taste buds and fungiform papillae and lower PROP thresholds than tasters and non-tasters (Reedy *et al.*, 1993; Bartoshuk *et al.*, 1994; Drewnowski *et al.*, 1997). Drewnowski *et al.* (Drewnowski *et al.*, 1997) found a higher level of rated bitterness for 0.0032 M Na-saccharin among tasters and supertasters of PROP than among non-tasters, but no difference among the groups at higher levels. Another study (Gent and Bartoshuk, 1983) collected bitterness responses from PROP tasters and non-tasters but found no differences in ratings when solutions were flowed across the front of the tongue. Nor did they not report any differences for solutions that were sipped in a whole-mouth stimulation method. Ly and Drewnowski (Ly and Drewnowski, 2001) noted that PROP taster differences in the perception of caffeine bitterness were attenuated in taste mixtures.

Informal observations of individual differences in response to acesulfame-K bitterness at higher concentrations raised the following question. Are individuals who are sensitive to the bitter taste of saccharin also sensitive to the bitter taste of acesulfame-K? There are some similarities in the chemical structures, such as the negatively charged nitrogen in the ring structure adjacent to an SO_2 group and acarbonyl (see Figure 1). These structural similarities are consistent with the possibility of common stimulation and

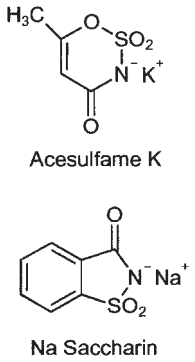

Figure 1 Structures of Na-saccharin and acesulfame-K.

transduction mechanisms. A number of different mechanisms have been proposed for bitter taste transduction (Spielman *et al.*, 1992). Given the observation of wide individual differences in the perception of saccharin and acesulfame-K bitterness, transduction mechanisms for bitter taste other than those responsible for PROP tasting might contribute to these individual differences. Thus we examined the degree of correlation among PROP, saccharin and acesulfame-K tastes across individuals.

After we had conducted the first experiment, Bartoshuk (Bartoshuk, 2000) suggested that the specific instructions to subjects using labeled magnitude scaling (LMS) (Green *et al.*, 1993, 1996) could obscure group differences among PROP tasting groups due to personal context effects. Specifically, supertasters, who live in a world of extreme taste sensations, might show attenuated ratings of the stimuli presented during an experiment. In other words, they might rate the moderately intense experimental stimuli lower than expected due to their implicit comparison to the more intense oral sensations they commonly experience. Contrast effects are common in human judgements (Lawless *et al.*, 2000) and could obscure higher subjective intensities actually experienced by this group within an experimental session. Bartoshuk suggested that instructions should encourage subjects to use the scale with reference to all sensations experienced in life (not just oral sensations) so that a more equivalent contextual basis for scale usage could be achieved. Put more simply, such instructions would provide a common and comparable frame of reference for the taster groups. In accordance with this suggestion, we conducted a second experiment using modified instructions for the LMS without reference to oral sensations but rather instructing subjects to consider the high end as the 'strongest imaginable sensation *of any kind*' (italics added).

Experiment 1: correlations among PROP, saccharin and acesulfame-K

Methods and procedures

Subjects

Thirty-eight volunteers were recruited from the Cornell community (23 females, age range 20–55 years). Twenty-one of these individuals had previously participated in a similar study [experiment 1 of (Sposato, 2000)], and were familiar with the rating scales and techniques employed. Subjects were paid a token incentive for participation and signed an informed consent form explaining the risks and voluntary nature of the procedures.

Stimuli

Standards for the training session consisted of 0.009 mM quinine hydrochloride (form. wt 360.9) as the bitter standard and 4.8 mM citric acid (form. wt 210.1) as the sour standard. Stimuli in the test sessions consisted of the following substances and concentrations: NaCl (form. wt 60.0) at 0.32 and 1.0 M, Na-saccharin (form. wt 202.2) at 0.4 and 2.1 mM, acesulfame-K (form. wt 201.2) at 1.2 and 5.2 mM and PROP (form. wt 170.2) at 1.0 and 3.2 mM. Sweetener concentrations were chosen on the basis of equations from Dubois *et al.* (Dubois *et al.*, 1991) to produce sensations approximately equal to 100 and 225 mM sucrose, representing weak-to-moderate levels of sweet taste intensity. Concentrations of NaCl and PROP were chosen based on the screening tests used by Bartoshuk *et al.* (Bartoshuk *et al.*, 1994). Spring water (Chemung Spring Water, Chemung, NY) served as the diluent and rinse. Sample volumes were 30 ml each and sample temperature was 20 ± 2°C. Samples were labeled with random three-digit codes, using different codes for samples that appeared in multiple sessions.

Procedures

Subjects participated in three experimental sessions. In the first session subjects were screened for their abilities to categorize sour and bitter sensations. Sensations of sourness and bitterness were described to the subjects using examples of lemons for sourness and dark beer, strong coffee, coffee grounds and tonic water for bitterness. Subjects were next presented with a set of three samples, two containing the sour standard and one containing the bitter standard, or vice versa. Samples were coded with random three-digit codes and presented in random order. Subjects tasted the samples and categorized them as sour or as bitter. All subjects correctly categorized their three samples.

In the second and third sessions, subjects rated each of the eight test samples, two concentrations each of PROP, NaCl, saccharin and acesulfame-K. Sweeteners and NaCl were presented first in random order. PROP samples were tasted last in order of increasing concentration. This was done to prevent a strong persistent bitter sensation from affecting the evaluation of other samples in the case of PROP-sensitive individuals. Subjects took the entire sample into their mouths, circulated it for 15 s to cover all oral surfaces and expectorated. Immediately upon expectoration, subjects rated taste intensity for the attributes of sweetness, saltiness, sourness and bitterness using a horizontal version of the LMS with the upper bound of the scale labeled as 'strongest imaginable oral sensation.' Subjects rinsed their

mouths with spring water between each sample. Responses were made by placing a mark on the LMS line displayed on a computer screen, using a mouse. Data were collected using the Compusense 5 System (Compusense, Inc., Guelph, Ontario, Canada).

Analysis

Data were exported from the Compusense system for statistical analyses using Statistica (v.5.1, Statsoft, Tulsa, OK). Analyses included repeated measures ANOVA (subjects random, with PROP taster status as a between-groups factor), simple correlations and principal components analysis (PCA). Varimax normalized rotated solutions were found and factors retained that explained >10% of the total variance. Replicates from the two sessions were averaged after finding that none of the bitter ratings showed a significant replicated difference in ANOVA.

Results

Subjects were classified into PROP non-tasters, tasters or supertasters, based on their PROP ratio (Bartoshuk *et al.*, 1994), defined as follows:

$$\frac{\left[\frac{\text{BR of 1 mM PROP}}{\text{SR of 0.32 M NaCl}} + \frac{\text{BR of 3.2 mM PROP}}{\text{SR of 1.0 M NaCl}}\right]}{2}$$

where BR is the bitter rating and SR is the salty rating.

Subjects with PROP ratios of <0.4 were classified as non-tasters (n = 11), between 0.4 and 1.2 as tasters (n = 14) and >1.2 as supertasters (n = 13).

Figure 2 shows the sweetness and bitterness of each sweet compound. A significant concentration effect was found for both substances for all taste qualities [all $F(1,73) > 7.6$, $P < 0.001$]. As shown in Figure 3, the bitterness responses for the taster groups were distributed throughout the scale range. There were no group differences nor interactions with PROP taster groupings.

Correlations showed the expected positive relationship between bitterness ratings for 1 and 3.2 mM PROP (r = +0.86, $P < 0.001$). A positive correlation was also seen among the pairs of saccharin and acesulfame-K stimuli, as shown in Table 1. The relationship was especially strong at the higher levels of the sweeteners, where bitterness is more apparent to some individuals. The correlation of +0.84 (see Figure 4) was almost as high as the correlation between the two levels of PROP bitterness (probably a ceiling due to measurement error) and shows a strongly related pattern of individual differences.

However, correlations between acesulfame-K bitterness and PROP bitterness were not significantly different from zero, and the same was true for saccharin bitterness and PROP bitterness. No significant correlations were observed between PROP bitterness ratings and sweetness ratings of either sweetener.

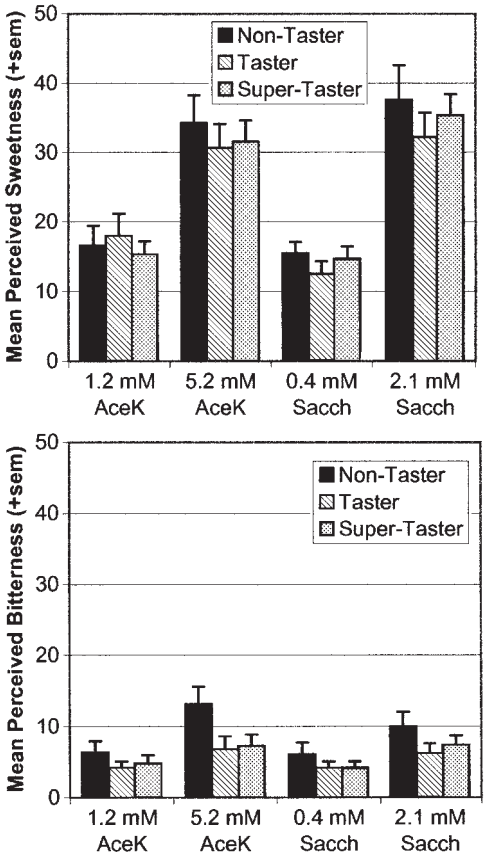

Figure 2 Mean intensity ratings (+ 1 SEM) for the four sweet stimuli, by PROP classification group (experiment 1).

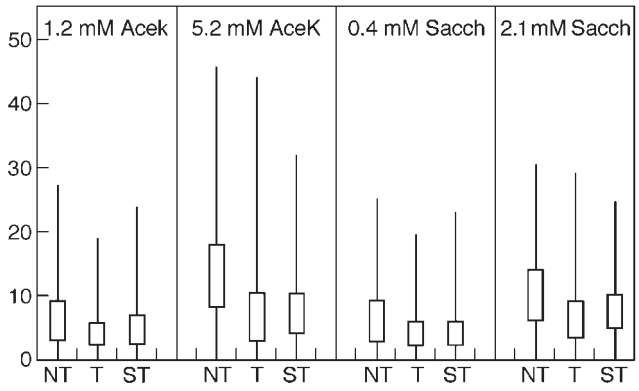

Figure 3 Distribution characteristics of bitterness responses for the four sweet stimuli and three taster groups (experiment 1). The line indicates the range; box limits are 95% confidence intervals around the mean.

PCA also showed this pattern of correlation. The varimax normalized loadings for the first six factors (70% explained variance) are shown in Table 2. The first factor subsumed the largest amount of variance (22%) and may reasonably be interpreted as a general intensity dimension that correlated with many of the side tastes of the stimuli. Saccharin and acesulfame-K sweetness ratings loaded on the second factor and their bitterness loaded on factor 6, separately from the

Table 1 Correlations among bitterness ratings

Stimulus	2.1 mM SAC	1.2 mM ACE-K	5.2 mM ACE-K	1.0 mM PROP	3.2 mM PROP
0.4 mM SAC	0.62*	0.50*	0.49*	0.04	0.11
2.1 mM SAC		0.73*	0.84*	0.06	0.05
1.2 mM ACE-K			0.67*	0.01	0.02
5.2 mM ACE-K				0.20	0.24
1.0 mM PROP					0.86*

SAC = saccharin; ACE-K = acesulfame-K.

*Correlations significant at $P < 0.001$ ($n = 38$), averaged across replicates before analysis.

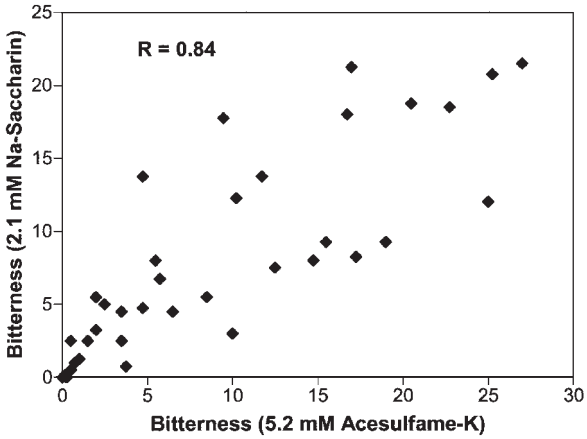

Figure 4 Mean bitterness ratings for 5.2 mM acesulfame-K and 2.1 mM saccharin averaged across replicates for 38 subjects in experiment 1.

PROP bitterness ratings and the PROP ratio index, which loaded on factor 3. Other rotation options (varimax unnormalized, equamax, quartimax) and unrotated solutions were also examined, and in all cases PROP and bitterness of the sweeteners were loaded on separate factors.

Experiment 2: re-examination with modified LMS anchors

Methods and procedures

Subjects

Thirty volunteers from the Cornell community (16 female) completed the study. None of these subjects had participated in experiment 1. Subjects were selected for the study in order to produce equal numbers ofPROP non-tasters, tasters and supertasters (10 per group, classified by the same criteria as in experiment 1), and to have approximately equal gender balance in each group. Seven additional subjects failed to correctly categorize the bitter and sour stimuli in the screening test, so were dismissed from further participation. Subjects were paid a token incentive for participation and signed an informed consent form explaining the risks and voluntary nature of the procedures. Following the third session, one supertaster and one non-taster were dropped from the analysis for rating PROP as sweet, and one taster for rating PROP as sour (sour/bitter confusion), leaving nine subjects per PROP group.

Table 2 Varimax normalized factor loadings—experiment 1

Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
SWHP	0.71					
SWHA		0.88				
SWHS		0.90				
SWLP	0.52					
SWLA		0.79				
SWLA		0.61				
SAHP					0.91	
SAHA	0.78				0.38	
SAHS	0.88					
SALP	0.26				0.84	
SALA	0.73				0.32	
SALS	0.76					
SOHP				0.88		
SOHA	0.54			0.63		
SOHS	0.89					
SOLP				0.92		
SOLA	0.55				0.68	
SOLS	0.84					
BTHP			0.92			
BTHA		0.21				0.79
BTHS		0.25				0.79
BTLP			0.94			
BTLA		0.27				0.74
BTLS	0.59	0.20				0.39
PROP ratio			0.83			
Variance explained (%)	22	12	11	11	11	11

Variable codes: SW = sweetness, SA = saltiness, SO = sourness, BT = bitterness, H = higher concentration, L = lower concentration, S = Na-saccharin, A = acesulfame-K, P = PROP. Factor loadings with magnitude less than 0.4 have been replaced by blanks.

Stimuli

Samples were the same as in experiment 1 except that deionized water served as the diluent and rinse water.

Procedures

The screening task for sour/bitter categorization was modified to include three quinine samples and three citric acid samples. Panelists were required to classify all six correctly into sour and bitter groups. ROP and NaCl stimuli were rated in the second and fourth sessions, and the sweetener samples were rated in duplicate in the third session. Ratings on all scales were modified to change the upper bound label to 'strongest imaginable sensation of any kind'. Statistical analyses were the same as in experiment 1.

Results

Changing the anchoring instructions to the most intense experience rather than most intense oral sensation induced a contextual shift (Figure 5). Ratings of sweetness were 32% lower in this experiment than in experiment 1 [$F(1,124) = 18.63$, $P < 0.001$]. Bitterness ratings were also lower by 24% [$F(1,124) = 3.00$, $P < 0.10$]. The shift in ratings was similar for all three PROP taster groups (no group effect or interaction).

Figure 6 shows the mean ratings of the two sweeteners for the three groups. For bitterness, there were significant interactions of PROP status with sweetener [$F(2,51) = 4.23$, $P < 0.05$] and concentration factors [$F(2,51) = 9.77$, $P < 0.01$], as well as a concentration by substance interaction [$F(1,51) = 5.63$, $P < 0.05$]. As shown in Figures 6 and 7, the PROP interactions were in an unexpected direction, with some PROP non-tasters giving higher bitterness ratings than the other groups to 5.2 mM acesulfame-K and slightly higher ratings to 2.1 mM saccharin. Supertasters gave higher sweetness ratings to the higher level of saccharin than did non-tasters (LSD test, $P = 0.056$). No other group differences were observed on the basis of PROP status.

Examining the correlation pattern, once again bitterness ratings for the two PROP stimuli were correlated as expected ($r = +0.69$, $P < 0.001$). Significant correlations were found for bitterness ratings between the higher levels of acesulfame-K and saccharin ($r = +0.64$, $P < 0.001$), between the lower levels of the two sweeteners ($r = +0.38$, $P = 0.051$) and between the bitterness ratings of 2.1 mM saccharin and 1.2 mM acesulfame-K ($r = +0.51$, $P < 0.01$). One significant but negative correlation was observed between the PROP ratio and 5.2 mM acesulfame-K bitterness ($r = -0.40$, $P < 0.05$). In the correlation pattern there was evidence of a weak but positive relationship of PROP responses to sweetness intensity. The bitterness of 3.2 mM PROP was

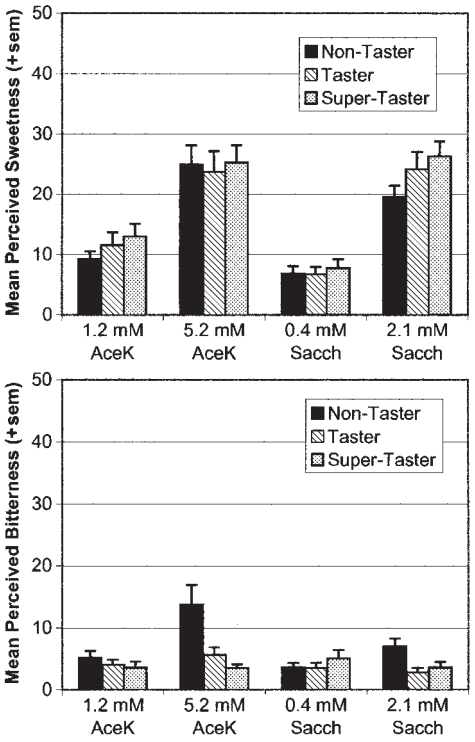

Figure 6 Mean intensity ratings (+ 1 SEM) for the four sweet stimuli, by PROP classification group (experiment 2).

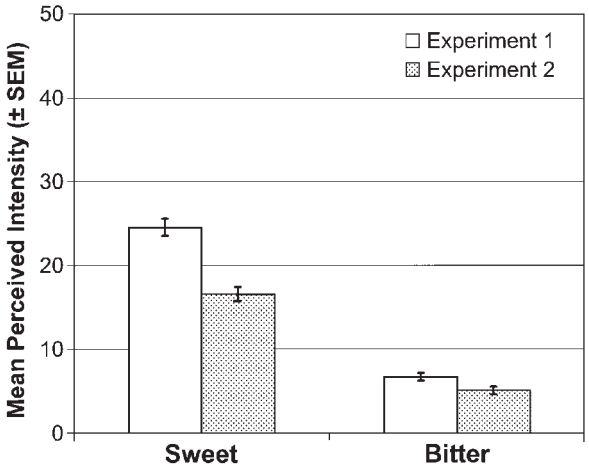

Figure 5 Means (± 1 SEM) for sweetness and bitterness in the two experiments, collapsed across all sweeteners, showing the contextual shift.

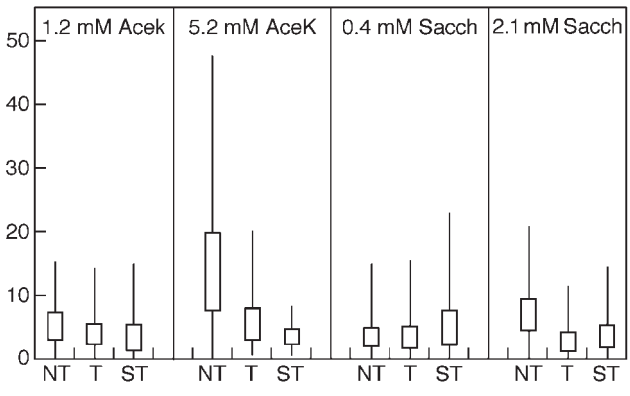

Figure 7 Distribution characteristics of bitterness responses for the four sweet stimuli and three taster groups (experiment 2). The line indicates the range; box limits are 95% confidence intervals around the mean.

correlated with the sweetness of 5.2 mM acesulfame-K ($r = +0.41$, $P < 0.05$), with 1.2 mM acesulfame-K ($r = +0.38$, $P < 0.05$) and with 2.1 mM saccharin ($r = +0.34$, $P < 0.10$).

Factor loadings following the PCA are shown in Table 3. A general intensity factor was seen in the first factor, and PROP bitterness was included in factor 2. Factor 3 captured the variance associated with bitterness of the four saccharin and acesulfame-K stimuli, suggesting a pattern of inter-correlation orthogonal to the other ratings and separate from PROP. Bitterness indices were constructed in an analogy to the PROP ratio, taking the sum of bitterness ratings for each sweetener and dividing by the saltiness of NaCl. The saccharin index and acsulfame-K index were positively correlated ($r = +0.47$, $P < 0.05$), but neither was significantly correlated with the PROP ratio.

Table 3 Varimax normalized factor loadings—experiment 2

Variable	Factor 1	Factor 2	Factor 3	Factor4	Factor 5
SWHP	0.72				
SWHA					0.80
SWHS					0.88
SWLP	0.72	–0.45			
SWLA					0.75
SWLA					0.59
SAHP					
SAHA	0.77				
SAHS	0.84				
SALP	0.55				
SALA					
SALS	0.64				
SOHP	0.60				
SOHA				0.84	
SOHS	0.42		0.51	0.56	
SOLP				0.60	
SOLA	0.46			0.71	
SOLS				0.77	
BTHP		0.75			
BTHA		–0.49	0.58		
BTHS			0.81		
BTLP		0.87			
BTLA			0.65		
BTLS			0.66		
PROP ratio			0.81		
Variance explained (%)	17	13	12	12	12

Variable codes: SW = sweetness, SA = saltiness, SO = sourness, BT = bitterness, H = higher concentration, L = lower concentration, S = Na-saccharin, A = acesulfame-K, P = PROP. Factor loadings with magnitude less than 0.4 have been replaced by blanks.

Discussion

There are three different approaches to examination of the overlap or relationships among taste compounds. One is cross-adaptation, in which the adaptation to one compound is tested against various subsequent test stimuli (McBurney *et al.*, 1972). Reduction in the taste intensity of the second compound is interpreted as evidence for common receptor or transduction mechanisms. This provides the most direct psychophysical evidence for common pathways, but has been so far limited to areas of the dorsal anterior tongue that can easily be stimulated with flowing solutions. The second common approach is preclassification of taster/non-taster groups (e.g. for PROP tasting), with subsequent tests of group differences for sensitivity to a test compound or comparison of suprathreshold responses (Bartoshuk, 1979). This approach requires a control for other differences among the classified groups, such as a difference in general taste sensitivity or scale usage tendencies (Delwiche *et al.*, 2000). A third approach is to examine correlations among thresholds or among suprathreshold responses for pairs of test compounds (Yokomukai *et al.*, 1993; Delwiche *et al.*, 2000). Unlike the 'group differences' approach, this allows an estimation of common variance that may reflect the degree of overlap in taste receptor and transduction mechanisms for the two compounds. This approach also provides a graded estimate of the overlap, rather than a binary decision about a null hypothesis. The present experiments used both the group comparison and correlational approaches to assess the commonalities among bitter responses to PROP, saccharin and acesulfame-K.

These studies confirm the notion that there are individual differences in responsiveness to suprathreshold bitterness of Na-saccharin and acesulfame-K, and that these patterns of sensitivity are correlated across individuals. If a person finds a strong bitter taste to a solution of Na-saccharin, he or she is likely to find that an equi-intense solution of acesulfame-K is also strongly bitter. Such responses, however, are not well predicted by PROP status. This is consistent with the findings of Bartoshuk and Drewnowski *et al.* (Bartoshuk, 1979; Drewnowski *et al.*, 1997), who found a PROP taster difference for very low levels of saccharin but no difference at moderate-to-high intensity levels. Ly and Drewnowski (Ly and Drewnowski, 2001) also noted attenuated differences between PROP taster groups for the bitterness of caffeine when a sweetener was added, and hedonic differences between the groups were eliminated. Differences between PROP taster groups and the patterns of correlation may be easier to uncover with simple bitter stimuli than with more complex tastes, such as these sweet–bitter stimuli, or with real foods.

Examining the bitter ratings of the sweet compounds, considerable residual variability persists beyond the shared variance of saccharin and acesulfame-K and beyond PROP status. In addition to some shared mechanisms of bitterness reception and transduction, there may be non-overlapping modes of stimulation, other chemical or peri-receptor access factors coming into play, or even general taste sensitivity differences between individuals that are unrelated to a saccharin bitterness dimorphism.

In spite of modification of the LMS verbal anchor, the patterns of results from both studies were similar in terms of the bitterness correlations. As noted in the introduction, one could predict paradoxically low responses from PROP supertasters as a kind of context effect if their frame of reference is a generally more intense set of oral experiences (Bartoshuk, 2000). This is reasonable given that the LMS, like other scaling methods, is prone to context effects that influence the frame of reference in the subject's scaling behavior (Lawless *et al.*, 2000).The search for a scaling method that would provide a common metric across individuals is still desired for comparison purposes, and methods such as cross-modality matching and magnitude matching have been applied for that purpose [for an overview, see Bartoshuk (Bartoshuk, 2000)]. Borg's assertion for the category-ratio scale was that having a comparison to the strongest imaginable sensation might provide a common frame of reference (Borg,1982). Although this seems reasonable, there is no direct evidence to support this assertion.

A general contextual shift in the form of contrast occurred, wherein the more intense imagined experience led to lower intensity ratings for all taster groups. The most intense experience of any kind for most people would presumably be more intense in memory than the most intense oral experience. Judgements in the context of overall experience were lower than judgements in the context of oral experience. This effect is consistent with the findings of Green *et al.* (Green *et al.*, 1996), who noted a lowered response range when LMS ratings were cross-referenced to oral sensations rather than specific taste qualities. One would expect oral sensations that include sensations like chili pepper to be more intense than sensations of sweetness. Relative to this more intense frame of reference, ratings are lowered, a form of contrast.

Given the diversity in bitter molecules and the genetic diversity in both humans and other mammals in their sensitivities to different bitter compounds, bitter taste transduction is likely to involve multiple mechanisms (Speilman *et al.*, 1996). One important mechanism appears to be blockage of outward potassium flow by substances such as the potent bitter compound denatonium (Brand, 1997). Denatonium also appears to result in a release of intracellular calcium stores, possibly mediated through a second messenger system. IP3 and diacyl glycerol (DAG) have both been implicated as second messengers in bitter taste transduction. DAG controls a protein kinase and IP3 could affect the release of calcium from intracellular stores. Another possibility is that the activation of gustducin in a G-protein-coupled receptor system stimulates a phosphodiesterase enzyme. This would somewhat paradoxically cause a decrease in cyclic nucleotides, such as cAMP. If cAMP is gating an inhibitory channel, lower levels could stimulate membrane depolarizing events (Brand, 1997). Recently, a novel family of 40–80 G-protein-coupled receptors have been identified in humans and mice that respond to bitter tastants (Adler *et al.*, 2000; Chandrashekar *et al.*, 2000). More than one receptor is apparently expressed within the same taste cell, which would help explain why chemically diverse bitter tastants give rise to similar sensations. At this time, it is not known what mechanisms of bitter taste transduction are activated by saccharin and acesulfame-K. However, the present results support the notion of some overlap of those mechanisms, mechanisms which differ among individuals.

Acknowledgements

Supported by NIH grant RO1 DC-00902. Some of these data are from the MS thesis of Domenic Sposato, and were presented at the 2000 and 2001 meetings of the Association for Chemoreception Sciences. The order of authorship is alphabetical, reflecting equal contributions.

References

Adler, E., Hoon, M.A., Mueller, K.L., Chandrashekar, J., Ryba, N.J.P. and **Zuker, C.S.** (2000) *A novel family of mammalian taste receptors*. Cell, 100, 693–702.

Ayya, N. and **Lawless, H.T.** (1992) *Quantitative and qualitative evaluation of high-intensity sweeteners and sweetener mixtures.* Chem. Senses, 17, 245–259.

Bartoshuk, L.M. (1979) *Bitter taste of saccharin related to the genetic ability to taste the bitter substance 6*-n-*propylthiouracil*. Science, 205, 934–935.

Bartoshuk, L.M. (2000) *Comparing sensory experiences across individuals: recent psychophysical advances illuminate genetic variation in taste perception*. Chem. Senses, 25, 447–460.

Bartoshuk, L.M., Duffy, V.B. and **Miller, I.J.** (1994). *PTC/PROP tasting: anatomy, psychophysics and sex effects*. Physiol. Behav., 56, 1165–1171.

Borg, G. (1982) *A category scale with ratio properties for intermodal and inter individual comparisons*. In Geissler, H.G. and Petzold (eds), Psychophysical Judgment and the Process of Perception. VEB Deutscher Verlag der Wissenschaften, Berlin, pp. 25–34.

Brand, J.G. (1997) *Biophysics of taste*. In Beauchamp, G.K. and Bartoshuk, L.M. (eds), Smelling and Tasting. Academic Press, San Diego, CA, pp. 1–24.

Cannon, D.R. (1954) *Stepping-stones to saccharin*. Chem. Engng, 61, 150, 152, 154.

Chandrashekar, J., Mueller, K.L., Hoon, M.A., Adler,E., Feng, L., Guo, W., Zuker, C.S. and **Ryba, N.J.P.** (2000) *T2Rs function as bitter taste receptors*. Cell, 100, 703–711.

Delwiche, J.F., Butelic, Z. and **Breslin, P.A.** (2000) *Covariation in human bitterness perception to eleven compounds*. Chem. Senses, 25, 598.

Drewnowski, A., Henderson, S.A. and **Shore, A.B.** (1997) *Genetic sensitivity to 6*-n-*proprylthiouracil (PROP) and hedonic responses to bitter and sweet tastes*. Chem. Senses, 22, 27–37.

Dubois, G.E., Walters, D.E., Schiffman, S.S., Warwick, Z.S., Booth, B.J., Pecore, S.D., Gibes, K., Carr, B.T. and **Brans, L.M.** (1991) *Concentration–response relationships of sweeteners: a systematic study*. In Walters, D.E., Orthoefer, F.T. and Dubois, G.E. (eds), ACS Symposium Series 450. Sweeteners: Discovery, Molecular Design and Chemoreception. Boston, MA, American Chemical Society, pp. 261–276.

Gent, J.F. and **Bartoshuk, L.M.** (1983) *Sweetness of sucrose, neohesperidin dihydrochalcone and saccharin is related to genetic ability*

to taste the bitter substance 6-n-*propylthiouracil*. Chem. Senses, 7, 265–272.

Green, B.G., Shaffer, G.S. and **Gilmore, M.M.** (1993) *Derivation and evaluation of a semantic scale of oral sensation magnitude with apparent ratio properties*. Chem. Senses, 18, 683–702.

Green, B.G., Dalton, P., Cowart, B., Shaffer,G., Rankin, K. and **Higgins, J.** (1996) *Evaluating the labeled magnitude scale for measuring sensations of taste and smell*. Chem. Senses, 21, 323 –334.

Helgren, F.J., Lynch, M.J. and **Kirchmeyer, F.J.** (1955) *A taste panel study of saccharin 'off-taste'*. J. Am. Pharmaceut. Assoc., 44, 353–355.

Larson-Powers, N. and **Pangborn, R.M.** (1978) *Paired comparison and time–intensity measurements of the sensory properties of beverages and gelatins containing sucrose or synthetic sweeteners*. J. Food Sci., 43, 47–51.

Lawless, H.T., Horne. J. and **Speirs, W.** (2000) *Contrast and range effects for category, magnitude and labeled magnitude scales*. Chem. Senses, 25, 85–92.

Ly, A. and **Drewnowski, A.** (2001) *PROP (6*-n-*propylthiouracil) tasting and sensory responses to caffeine, sucrose, neohesperidin dihydrochalcone and chocolate*. Chem. Senses, 26, 41–47.

McBurney, D.H., Smith, D.V. and **Shick, T.R.** (1972) *Gustatory cross adaptation: sourness and bitterness*. Percept. Psychophys., 11, 228–232.

McKie, P.V. (1921) *Examination of some method of ascertaining the purity of saccharin*. J. Soc. Chem. Ind., 40, 150–152.

Moskowitz, H.R. and **Klarman, L.** (1975) *The tastes of artificial sweeteners and their mixtures*. Chem. Senses Flav., 1,411–421.

Ott, D.B., Edwards, C.L. and **Palmer, S.J.** (1991) *Perceived taste intensity and duration of nutritive and non-nutritive sweeteners using time–intensity evaluations*. J. Food Sci., 56, 535–542.

Rader, C.P., Tihanyi, S.G. and **Zienty, F.B.** (1967) *A study of the true taste of saccharin*. J. Food Sci., 32, 357–360.

Reedy, F.E. Jr, Bartoshuk, L.M., Millerm, I.J., Duffy, V.B., Lucchina, L. and **Yanigasawa, K.** (1993) *Relationships among papillae, taste pores and 6*-n-*propylthiouracil (PROP) supra threshold taste sensitivity*. Chem. Senses, 18, 618–619.

Schiffman, S.S., Crofton, V.A. and **Becker, T.G.** (1985) *Sensory evaluations of soft drinks with various sweeteners.* Physiol. Behav., 34, 369–377.

Spielman, A.I., Huque, T., Whitney, G. and **Brand, J.G.** (1992). *The diversity of bitter taste signal transduction mechanisms*.In Corey, D.P. and Roper, S.D. (eds), Sensory Transduction, 47. Rockefeller University Press, New York, pp. 307–324.

Spielman, A.I., Nagai, H., Sunvala, G., Dasso, M., Breer, H., Boekhoff, I., Huque, T., Whitney, G. and **Brand, J.G.** (1996) *Rapid kinetics of second messenger production in bitter taste*. Am. J. Physiol., 270, C926–931.

Sposato, D. (2000) *Individual differences in bitter taste perception of saccharin and acesulfame-K*. MS thesis, Department of Food Science, Cornell University.

Yokomukai, Y., Cowart, B.J. and **Beauchamp, G.K.** (1993) *Individual differences in sensitivity to bitter-tasting substances*. Chem. Senses, 18, 669–681.

Accepted September 10, 2001