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Abstract

GENETIC TASTE VARIATION AND MIXTURE SUPPRESSION: EFFECTS OF 6-*N*-PROPYLTHIOURACIL. Jenny H. Yiee, Valerie B. Duffy (Department of Applied Health Sciences, School of Allied Health, University of Connecticut, Storrs, CT), and Linda M. Bartoshuk (Section of Otolaryngology, Department of Surgery, Yale University School of Medicine, New Haven, CT.)

This study investigated mixture interactions and the nature of mixtures as related to the ability to detect PROP (6-*n*-propylthiouracil). Subjects (N=65) rated the tastes of 0.32 M NaCl, 1 M sucrose, 0.014 M citric acid, 0.00024 M quinine hydrochloride, all six possible mixtures of two, all four possible mixtures of three, and the single mixture of all stimuli. They also rated the taste qualities of foods/beverages (tonic water, lemonade, grapefruit juice, soy sauce, coffee sweetened with sucrose). Bitterness of PROP was rated at the end of the experiment. Subjects used the general Labeled Magnitude Scale (gLMS) with "strongest imaginable sensation of any kind" at the top, which allowed for valid across-group comparisons among nontasters, medium tasters and supertasters of PROP. Intensities of the unmixed stimuli correlated with PROP bitterness, as did the total intensities of the foods/beverages. As the number of components increased, the perceived intensity of the components tended to be suppressed; this suppression varied by PROP status. For some mixtures, supertasters perceived greater intensities than nontasters for unmixed components, but this difference tended to diminish as the number of components increased. For supertasters, adding tastes may ameliorate the bitterness of some foods/beverages. In analytic sensory mixtures, the identity of the components is maintained in the mixture (classic example, low and high notes retain their identity when sounded together). In synthetic sensory mixtures, the identity of the components is lost and new qualitative sensations appear (classic example, red and green lights produce yellow). The analytic nature of taste mixtures has been challenged on the grounds that not all subjects are able to name all components in a mixture. The present study shows that as a group, subjects are able to name all components with the exception of bitterness, which tended to disappear as the number of components increased.

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Introduction

In 1931, Fox discovered segments of the population who could not detect bitterness in the compound PTC (phenylthiocarbamide) when unintentionally aerosolized molecules of PTC were detected as bitter by some in his laboratory, but not others (1). Population and family studies of his observation suggested the ability to detect PTC a recessive trait in the Mendelian fashion (2, 3) as approximately 25% of the population could not detect PTC while 75% could. In the early 1950's Barnicot found PROP (6-*n*-propylthiouracil), a thyroxine analog used at sub-therapeutic levels, to produce the same taste threshold profile as PTC (4). With the advantages of a known toxicity profile without the sulfurous odor of PTC, PROP became the standard in the study of "taste blindness."

With the work of Fernberger, studies of simple detection evolved into looking at perceived intensities. In 1932, Fernberger asked subjects to rate PTC as tasteless, slightly bitter, bitter, very bitter, or extremely bitter (5). However, there could be no way of ensuring that subjects perceived equal ratings with the same intensity, i.e. what does "slightly bitter" mean to different people. Stevens developed a system called "magnitude estimation" in which subjects rated a stimulus, and then rated all subsequent stimuli relative to the first stimulus (6). This ratio property enabled Stevens to assess relationships between perceived intensities and stimuli intensities. Unfortunately, this system, as with Fernberger's system, did not allow for comparisons between individuals.

Dividing intensity ratings by a factor not affected by taste, a technique known as standardization, attempted to solve this problem of across-group comparisons. By dividing by a common factor, one could compare ratings between individuals. An

appropriate common factor was thought to be NaCl (sodium chloride). Early studies suggested that the ability to detect PROP did not correlate to the perceived intensity of NaCl (7). However this is now known to be false, making NaCl an unsuitable standard (8).

In a method referred to as "magnitude matching," Marks and Stevens used audio tones as a standard with the assumption that the perceived intensity of sounds is independent from one's ability to taste PROP (9). Using sounds has proven problematic as one's auditory perception can be skewed by sensory input preceding the stimuli. Thus, if a tone is preceded by an intense taste, one might rate a tone relatively higher. A method of circumventing this phenomenon involves assessing tonal intensities before giving any taste stimuli.

The most current method of scaling is a variation of Green's LMS (Labeled Magnitude Scale). Green's original scale had ratio properties such that a score of "40" was twice as intense as a "20." It was anchored with labeled adjectives: "strongest imaginable" at the top, no sensation at the bottom, and "barely detectable," "weak," "moderate," "strong," and "very strong" filling the remainder (10). This scale was limited by the fact that one person's strongest imaginable taste will vary with the next person's according to their ability to taste PROP and their density of fungiform papillae. The current gLMS (general Labeled Magnitude Scale) in which the "strongest imaginable sensation *of any kind*" anchors the top solves the problem of ceiling effects. A cross-modality (auditory, visual, olfactory, gustatory, tactile) standard appears to be independent of any taste function.

Individuals can be sorted into three groups based on their perception of the bitterness of PROP. Nontasters perceive little bitterness, supertasters perceive the most and medium tasters perceive an intermediate degree of bitterness (11, 12). Early family studies suggested that nontasters carry two recessive alleles for PROP tasting while tasters have one or both dominant alleles (2, 13). A gene largely responsible for the differences between nontasters and tasters was recently discovered on chromosome 7; this gene has been named the PTC gene (14).

PROP status correlates with density of fungiform papillae; supertasters have the most and nontasters the fewest fungiform papillae (15). This work began with Miller and Reedy who found that dyes will not stain fungiform papillae, but do stain taste pores, thus making it possible to visually distinguish between the different anatomical papillae (16). Fungiform papillae contain taste buds with a basket-like cluster of fibers surrounding each taste bud that mediate oral burn (17, 18, 19, 20). Fungiform papillae are also innervated by fibers mediating touch (21,22, 23). Thus it is not surprising that supertasters tend to perceive more intense sensations from tastants (11, 12, 24); oral irritants (25, 26), fats (27, 28), and other thickeners like guar gum (26) used in food products.

The association between PROP status and non-PROP tastants, oral irritants and oral touch indicates that supertasting is unlikely to be explained by a single gene (29). The discovery of the PTC gene permitted the first test of this. Individuals carrying two dominant alleles for the PTC gene are not necessarily supertasters. Other factors contribute to supertasting; these include but are not necessarily restricted to density of fungiform papillae, hormones and pathology (15, 30).

In mixtures of substances with different taste qualities, components usually show suppression (e.g. see 31 and 32 for review) meaning the perceived intensity of a tastant may be less intense when introduced in a mixture versus giving the tastant alone. Prescott, Ripandelli and Wakeling (33) have shown that PROP status is associated with the degree of suppression in four binary mixtures sweet/bitter, sweet/sour, salty/bitter, and salty/sour. Three and four-component mixtures as well as commercial foods have not been as extensively studied. Mixture studies could elucidate the connection between taster status and food preference, as most real-world foods exist as mixtures rather than simple tastes. Some have suggested that taster status affects food preference (34, 35, 36, 37) with possible effects on long-term health.

The nature of mixtures varies across the senses. Audition is said to show analytic mixing (e.g., a low and high note played on a piano are both perceptible). Color vision is said to show synthetic mixing (e.g., mixtures of green and red light produce yellow and the qualities of the components are not perceptible). The nature of taste mixtures has been the subject of controversy. For many years, taste was considered to be an analytic system containing four qualities: salty, sweet, sour and bitter. This issue was revisited in the context of theories concerning the coding of taste quality in the nervous system.

The two competing theories of taste quality coding are the pattern theory and the labeled-line theory. Interestingly, both owe their genesis to Pfaffmann. He first suggested a pattern code for taste quality because he failed to find taste fibers in the cat specific to the four basic tastes: salty, sweet, sour, bitter (38). He concluded that taste quality could not be determined by input from a single fiber, but rather from the pattern of response from a group of fibers (39, 40). Erickson, a Pfaffmann student, developed

this idea (41, 42). As electrophysiological data accumulated, fiber types emerged that fell into the familiar four-quality categories (43). Rather than showing extreme specificity for one quality category, fibers responded "best" to stimuli of one quality but also responded predictably to stimuli with other qualities. For example, the sucrose-best fibers did not respond to NaCl. However the NaCl-best fibers tended to respond to fructose but not to sucrose. This convinced Pfaffmann to propose the labeled-line theory of taste quality because it explained a behavioral conundrum that had puzzled him for some time (44, 45). Squirrel monkeys prefer sucrose to fructose but recordings from their chorda tympani taste nerves showed larger responses to fructose than to sucrose. Pfaffmann concluded that the larger response to fructose came from the sum of responses from the sucrose-best and the NaCl-best fibers; the monkey tasted fructose as sweet plus salty and thus preferred the pure sweet of sucrose.

The pattern theory of taste quality coding is still supported by some investigators doing electrophysiological studies in part for aesthetic reasons: pattern theories have appealing properties (e.g., see 46). However, in an elegant treatment of sensory coding written thirty years ago, Uttal warned us of the folly of assuming that a code we can construct is, in fact, the code used by the nervous system (47).

The nature of taste mixtures is crucial to the pattern theory. Consider what happens when two patterns are combined. The nature of the components is lost in the combination. Adding additional components changes the pattern of the mixture even further. Once a given pattern disappears into the combination, there would be no way to retrieve it as the information is transmitted higher into the nervous system. Thus proponents of a pattern theory must support synthetic taste mixtures. Erickson and his

students did so (48, 49). They asked subjects to describe a series of 2-component mixtures as “singular” or “more than one.” However, subjects were not asked to describe the qualities they perceived. Without this control, the results do not support synthesis since mixture suppression could easily remove one component leaving a “singular” perception of the remaining component (32).

There is overwhelming evidence supporting analytic taste mixtures. For example, when subjects rated the tastes of NaCl, sucrose, HCl and quinine, all two component mixtures, all three component mixtures and the four component mixture, the significant qualities reported for each mixture were those of the components with the exception of components lost through mixture suppression (31). Such a result would be impossible were taste mixtures to be synthetic. Recently Laing has questioned the analytic nature of taste mixtures on the grounds that subjects show imperfect abilities to analyze taste mixtures (50). However, the issue is not whether every subject can analyze every taste mixture perfectly as many factors could degrade performance, but rather whether any subject can do it at all.

Statement of Purpose, Specific Hypotheses, and Specific Aims

One purpose of the present study is to investigate the interactions of mixtures as related to the ability to detect PROP (6-*n*-propylthiouracil) with the hypothesis that mixtures will show suppression dependent upon PROP status. Another purpose is to demonstrate that mixtures have analytic properties with the hypothesis that PROP status will also affect one's ability to distinguish components of a mixture.

Methods

Note: The author performed all production of solutions, procedures, and data collection described in the methods section.

Scaling method

All ratings were obtained with the general Labeled Magnitude Scale (gLMS) (51). This scale is valid for measuring differences across nontasters, medium tasters and supertasters of PROP (52). Since subjects also rated tones and remembered sensations (see below), any of these could be used as standards for the normalization of the gLMS ratings. This normalization converts the scaling with the gLMS to a magnitude matching task (53).

Subjects

Subjects (38 females, 27 males) were recruited from the Yale community though posters and emails. They ranged in age from 17-49 years (mean: 25.1 ± 6.1).

Mixture taste stimuli

A preliminary study (N=13) determined the equi-intense concentrations of the four tastes to be used in the main study; they were 32 M NaCl (N), 1 M sucrose (S), .014 M citric acid (C), and .00024 M quinine hydrochloride (Q). These concentrations were determined in the preliminary study by administering 3 concentrations of each of the four basic tastes (1M N, .32M N, 1M N, .1M S, .32M S, 1M S, .0032M C, .01M C, .032M C, .0001M Q, .00032M Q, .001M Q, and H_2O) in a random order. The reported intensities

were plotted against concentration in order to determine equi-intense concentrations for each taste solution. Solutions for the main experiment then comprised one, two, three, and four component mixtures, a total of 15 solutions. These consisted of N, S, C, Q, NS, NC, NQ, SC, SQ, CQ, NSC, NSQ, NCQ, SCQ, NSCQ, and also pure de-ionized water. The mixtures were made preserving molar concentration. For example, to make the NS solution, the solutes to make 1 liter of .32 M N and 1 liter of 1 M S were dissolved together to make 1 liter of the NS mixture. De-ionized water was also collected and stored at that time for mouth rinsing between mixture solutions. All liquids were stored at 4 degrees Celsius and brought to room temperature in 100mL quantities prior to use.

Subjects first rated tones (50-98 db in 12 db increments; 1000 Hz; random order), then remembered sensations (brightness of a normally lit room, dimly lit restaurant, brightest light seen; loudness of a whisper, normal conversation, loudest sound heard; strongest smell from a flower, strongest pain experienced) and finally the saltiness, sweetness, sourness, and bitterness of the mixture solutions including water. Subjects placed, swished, and spit 5-10 mL of each mixture in their mouth for several seconds in order to assess intensity. Each mixture solution was followed by a swish and spit of room temperature, de-ionized water prior to administration of the next experimental solution.

Following the mixtures, the subjects rated the tastes of the commercial foods lemonade (Countrytime), grapefruit juice (Veryfine), tonic water (Canada Dry), soy sauce (La Choy), and coffee (Bustelo) with no sucrose, with 5%(weight/volume) sucrose, with 10% sucrose, and with 20% sucrose administered in the same manner as the mixture solutions.

Assessment of PROP status

PROP status was determined following the mixture experiment. Subjects rated tones and NaCl solutions presented in blocks in the following order: tones, tones, NaCl, tones, NaCl, tones, PROP, tones, PROP, tones. The blocks consisted of random orders of the same tones presented initially, NaCl solutions (.01 M, .032 M, .1 M, .32 M and 1 M) and PROP solutions (.000032 M, .0001 M, .00032 M, .001 M and .0032 M).

PROP paper

PROP papers were made by soaking 3 cm circles of Whatman grade 1 filter paper in saturated pharmaceutical grade PROP (PROP was saturated in boiling water). Papers were allowed to dry and were then stored in small glassine envelopes. Each paper contained approximately 1.6 mg PROP.

Subjects were instructed to place a PROP paper in the mouth move it around until it was well moistened with saliva and rate the maximum bitterness perceived.

Videomicroscopy

The final step involved painting the subjects' tongues with blue food coloring, flattening the tongue with a plastic microscope slide, and videotaping the tongue at 10x magnification. These videos would later be still-framed in order to count the number of fungiform papillae.

Results

PROP bitterness and the perception of taste mixtures

The scatterplots in Figures 1-4 show the correlations of PROP bitterness with the unmixed stimuli and the mixtures. Note that the perceived intensities of all four single component stimuli correlated significantly with PROP bitterness; the bitterness of quinine showed the highest correlation confirming a previous observation (24).

Saltiness. The saltiness of NaCl correlated with the bitterness of PROP; however, this correlation disappeared when sucrose alone, sucrose and quinine, sucrose and citric acid, or citric acid and quinine were added. The saltiness of all other mixtures remained correlated with bitterness.

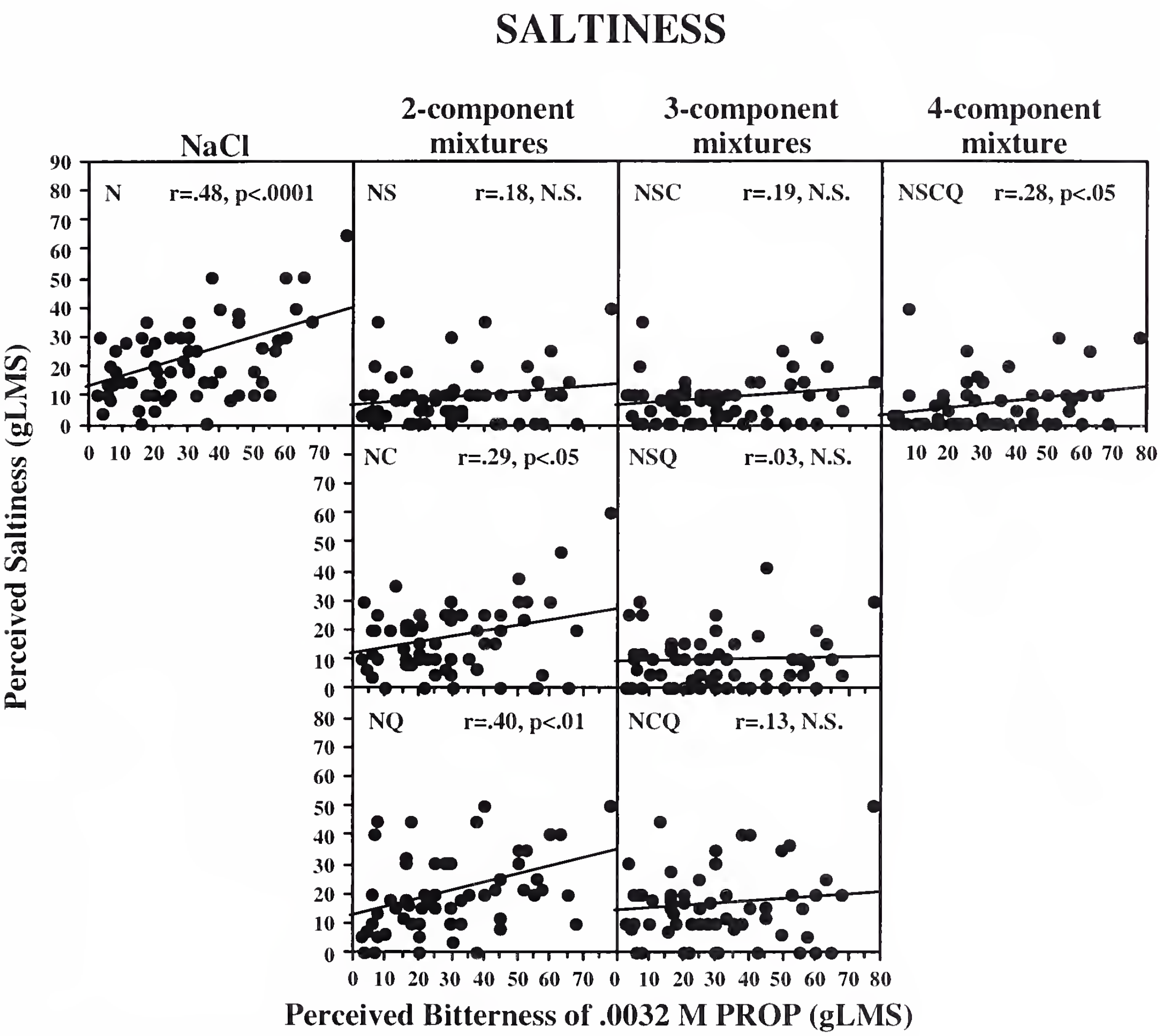

Figure 1. Saltiness of NaCl (N), the 2-component and 3-component mixtures containing NaCl, and the 4-component mixture plotted against the bitterness of .0032 M PROP. Correlation coefficients are shown in each panel. S=sucrose, C=citric acid, Q=quinine hydrochloride.

Sweetness. The sweetness of sucrose correlated with bitterness of PROP. Correlation between subjects' PROP status and sweetness only disappeared in one mixture (sucrose, citric acid and quinine.) The sweetness of all other mixtures remained correlated with bitterness.

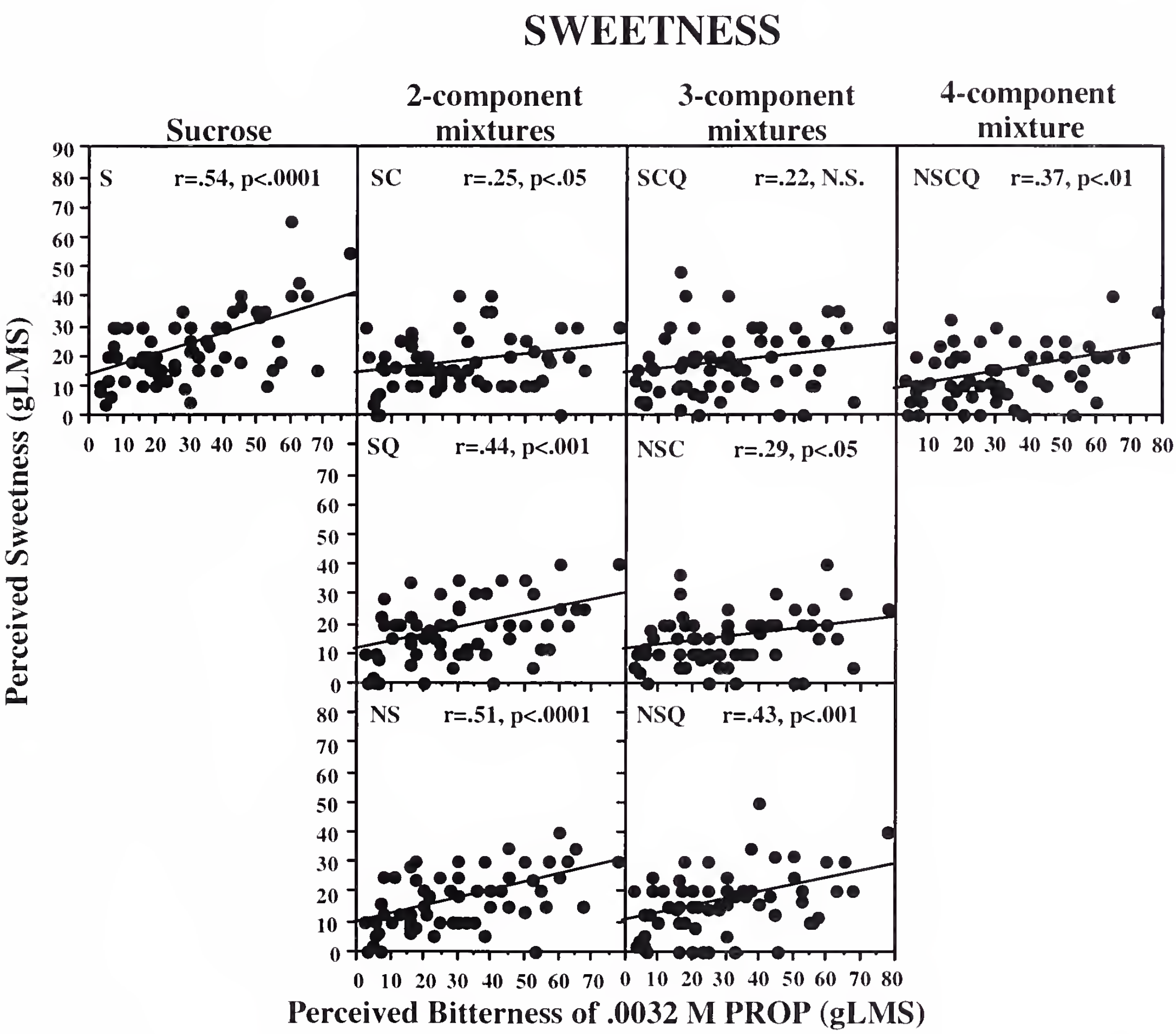

Figure 2. Sweetness of sucrose (S), the 2-component and 3-component mixtures containing sucrose, and the 4-component mixture plotted against the bitterness of .0032 M PROP. Correlation coefficients are shown in each panel. N=NaCl, C=citric acid, Q=quinine hydrochloride.

Sourness. The sourness of citric acid correlated with the bitterness of PROP. Correlation between subjects' PROP status and sourness only disappeared in one mixture (sucrose, citric acid, and quinine.) The sourness of all other mixtures remained correlated with bitterness.

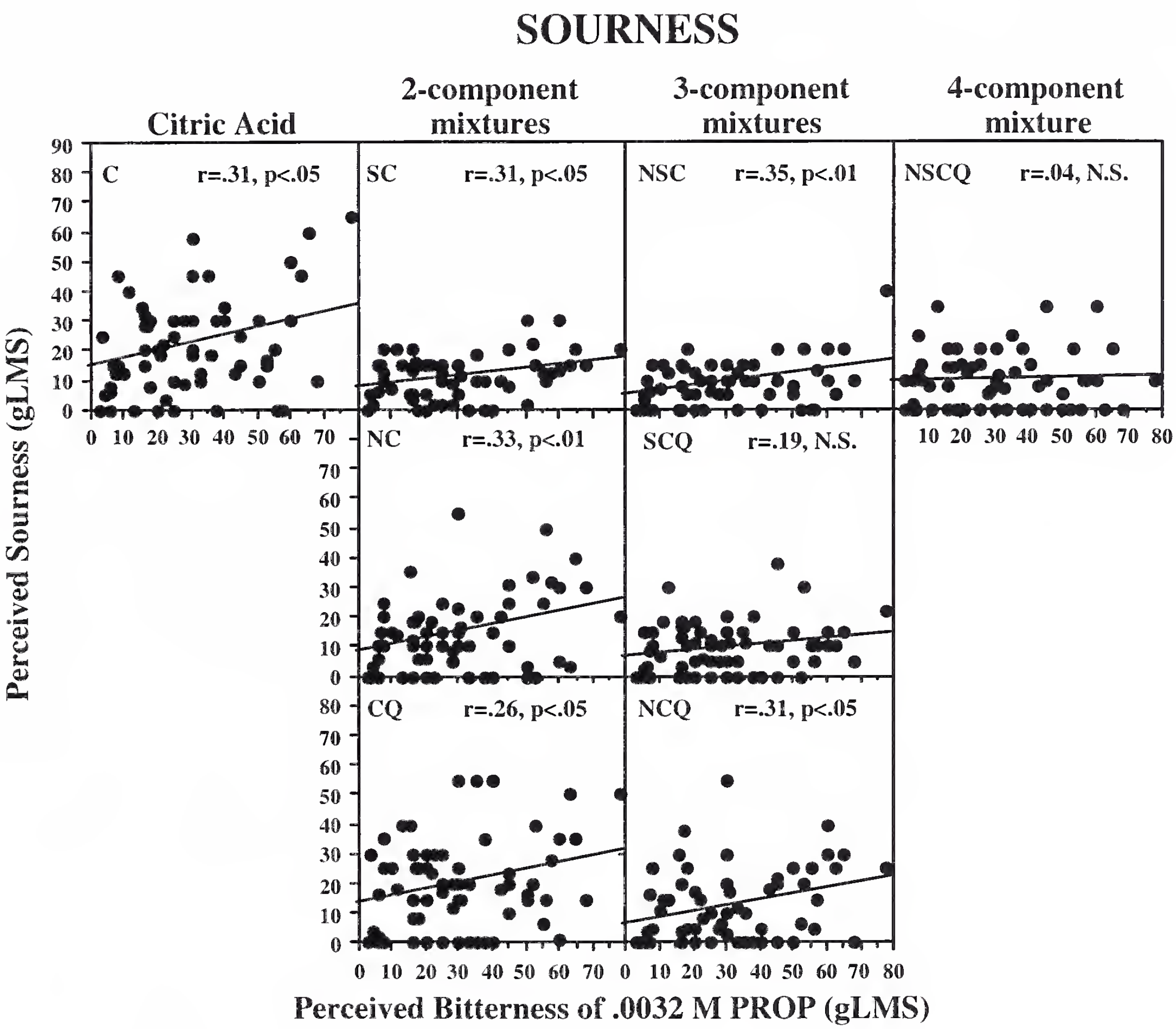

Figure 3. Sourness of citric acid (C), the 2-component and 3-component mixtures containing citric acid, and the 4-component mixture plotted against the bitterness of .0032 M PROP. Correlation coefficients are shown in each panel. N=NaCl, S=sucrose, Q=quinine hydrochloride.

Bitterness. The bitterness of quinine correlated with the bitterness of PROP; however, correlation between subjects' PROP status and bitterness disappeared for all 2, 3, and 4-component mixtures but one. The bitterness of the 2-component mixture of quinine and citric acid remained correlated with PROP bitterness.

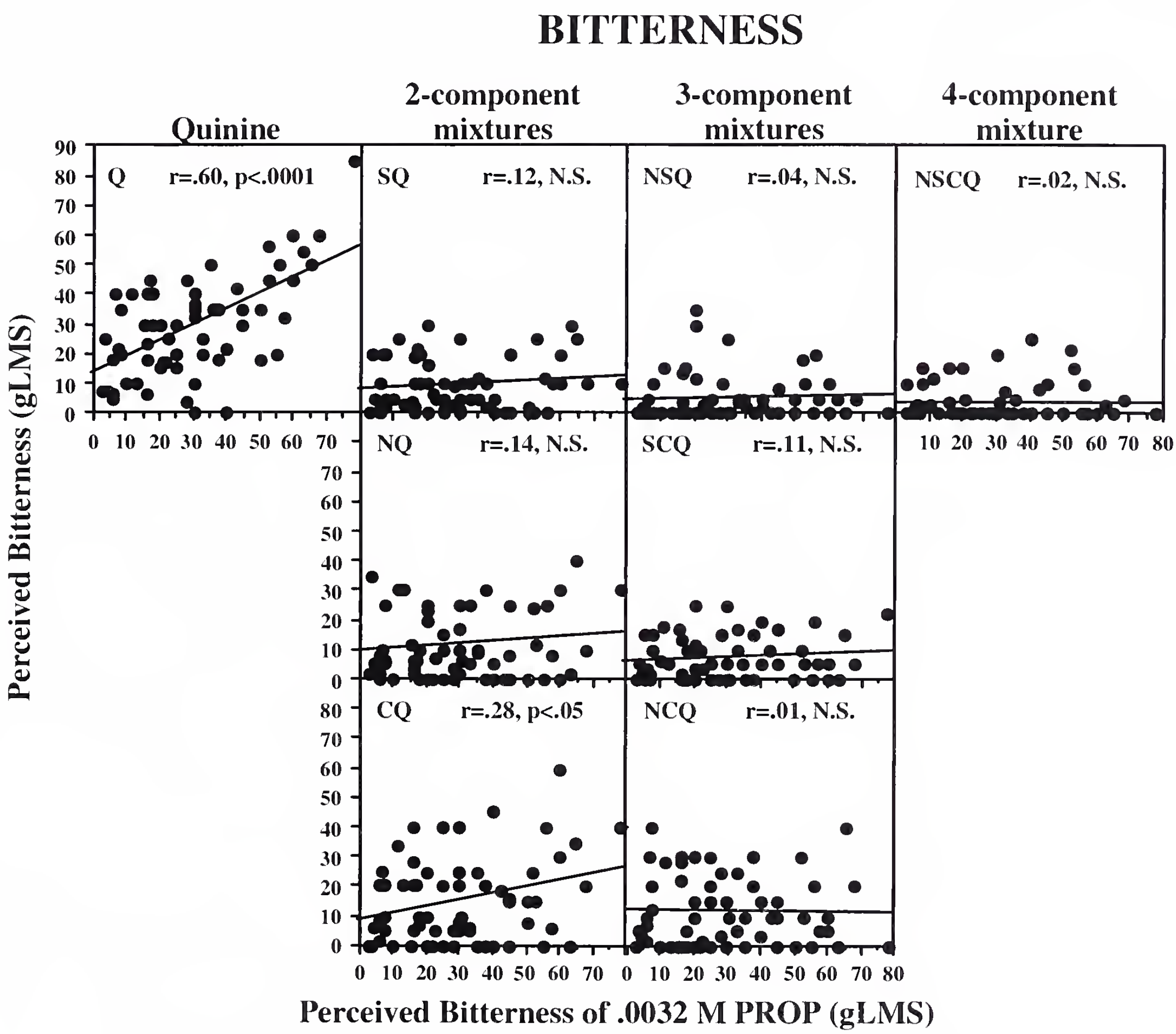

Figure 4. Bitterness of quinine hydrochloride (Q), the 2-component and 3-component mixtures containing quinine hydrochloride, and the 4-component mixture plotted against the bitterness of .0032 M PROP. Correlation coefficients are shown in each panel. N=NaCl, S=sucrose, C=citric acid.

Comparison of gLMS to data normalized to other standards.

Table 1 shows the correlations between the single components and the bitterness of PROP when the data are expressed relative to various standards. Note that analyzed in this manner, the experiment is converted to a magnitude matching experiment. The assumption underlying magnitude matching is that the sensations evoked by the standard are independent of those evoked by the stimuli of interest. Note the similarity of the correlations across the different assumptions.

	Correlation with PROP Bitterness			
Standard	**NaCl**	**Sucrose**	**Citric Acid**	**Quinine**
gLMS	.48 ***	.54 ***	.31 *	.60 ***
Tones (prior to N)	.38 **	.54 ***	.30 *	.63 ***
Brightest light	.31*	.40 **	0.22	.50 ***
Non-taste remembered sensations	.33 **	.47 ***	0.21	.53 ***

* p<.05

** p<.01

*** p<.001

Table 1. Correlation of perceived intensities of single tastants with perceived intensity PROP bitterness using multiple methods of standardization.

Commercial Foods

For all commercial foods tested, total intensities correlated significantly with bitterness of PROP. Of the component tastes in lemonade, only sweet significantly correlated with PROP. For grapefruit juice, only sourness correlated with PROP. For tonic water, only sourness correlated with PROP. For soy sauce, saltiness and sourness correlated. Bitter was not correlated with any of these foods.

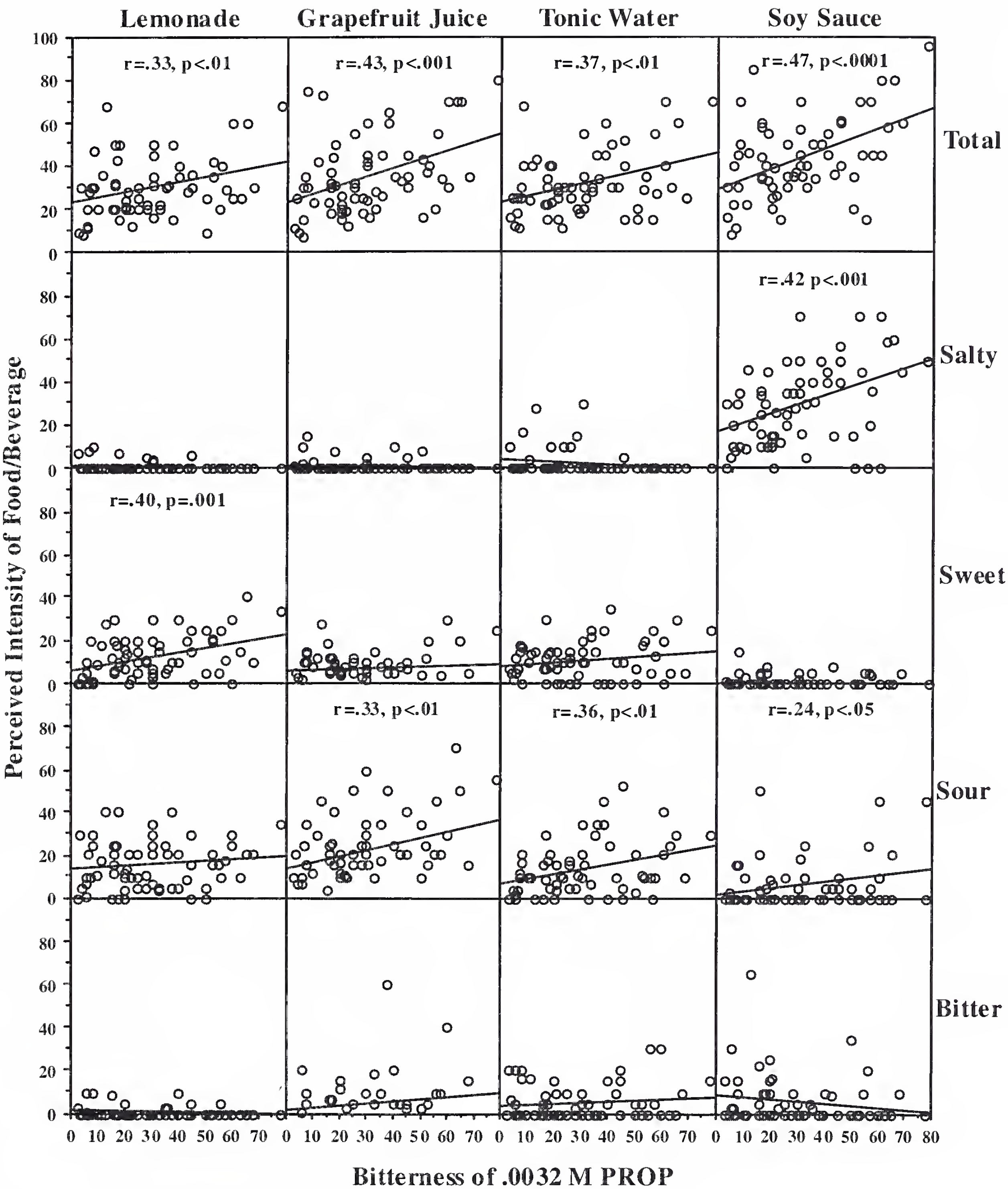

Figure 5. Perceived intensity of salty, sweet, sour and bitter tastes in commercial foods plotted against the bitterness of .0032 M PROP. Correlation coefficients are shown in each panel.

Coffee. Total intensity of coffee remained significantly correlated with PROP at all sugar concentrations. Figure 9 shows that the bitterness of coffee diminished with increasing concentrations of added sucrose. Note the amelioration of the bitterness of coffee by the addition of sucrose.

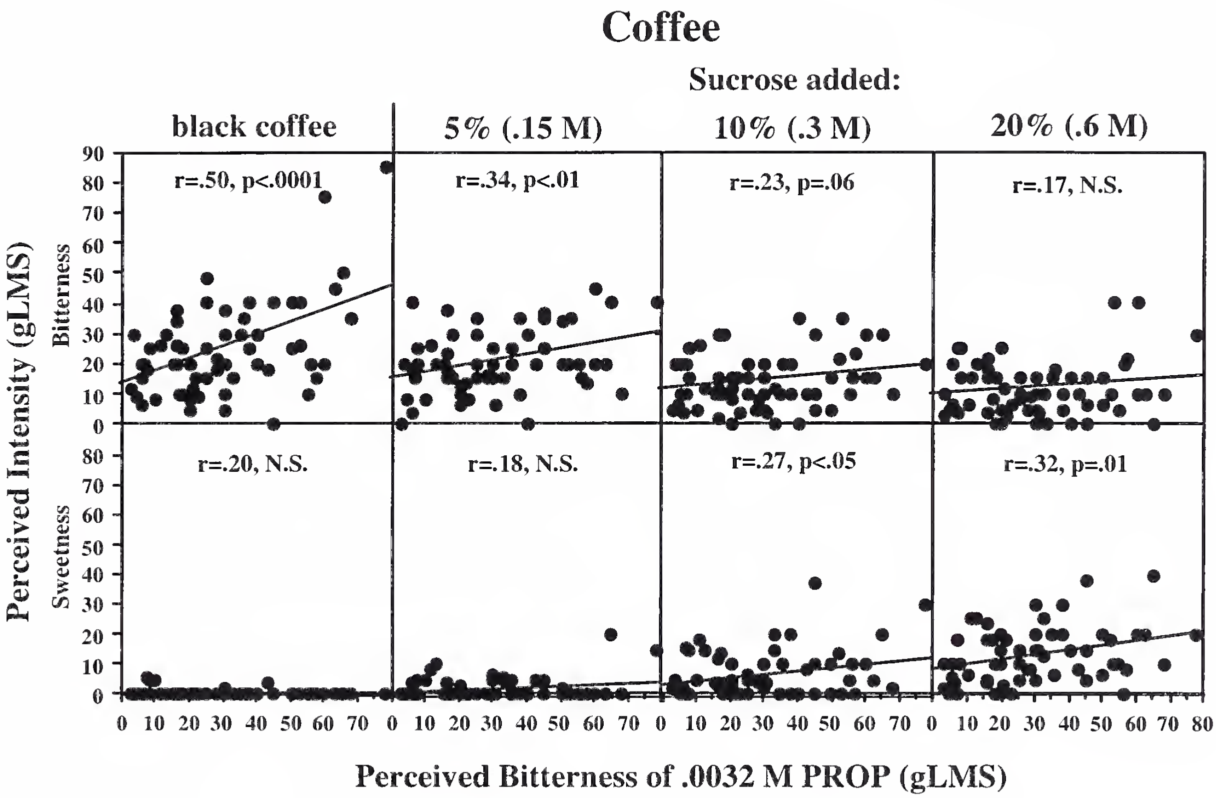

Figure 6. Perceived bitterness (gLMS) of the bitterness and sweetness of coffee plotted against the bitterness of .0032 M PROP.

Taste stimuli: analysis of components of mixtures.

The bar graphs in Figure 7 show the results of ANOVAs on each stimulus. Planned comparisons tested the differences for each quality between the stimulus and water. Note that the group data show analysis of the mixtures: the appropriate components are statistically significant in each mixture. The only exception is the bitter taste of quinine. In two out of the four three-component mixtures and in the four-component mixture, the bitter component is not significant. In these cases the bitter taste has been suppressed by the other components.

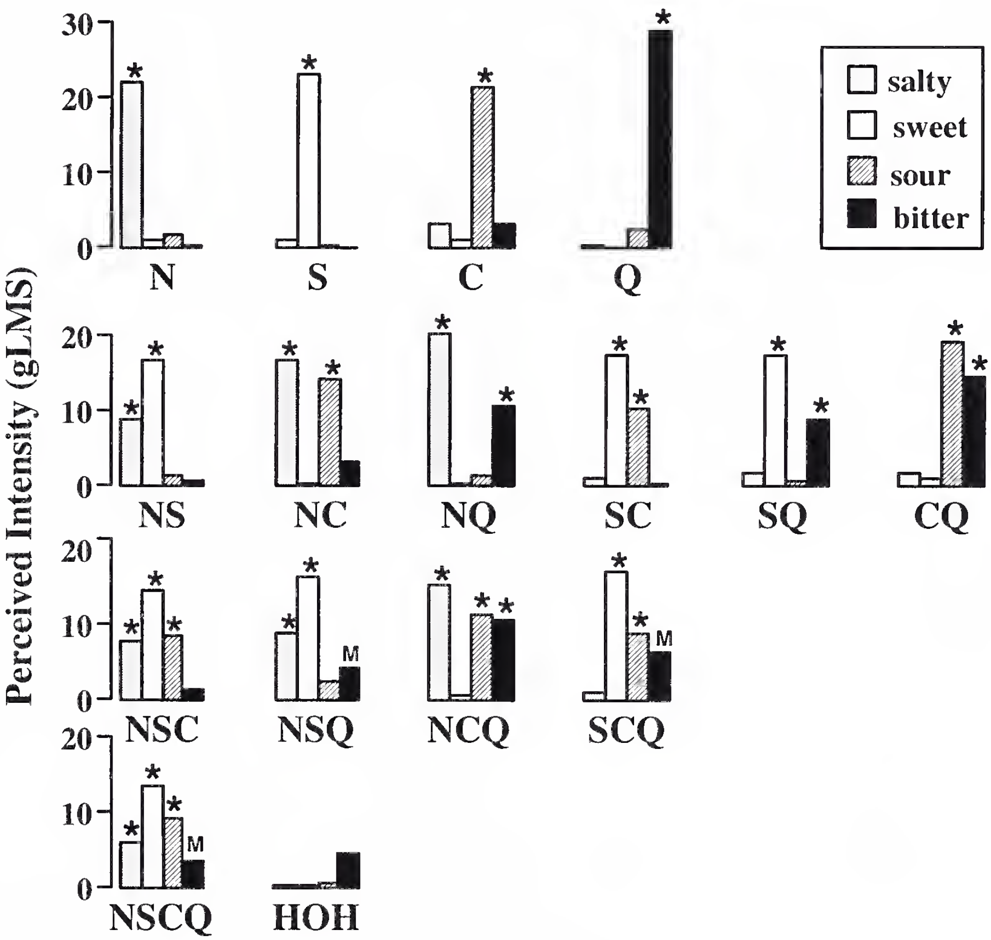

Figure 7. Perceived intensities of the salty, sweet, sour and bitter components of the mixtures as well as water. Labels for the mixture solutions as in Figure 1. Planned comparisons significant (at least $p<.05$) are indicated by stars. "M" indicates a missing component.

Mixture data were evaluated with regard to whether or not each subject analyzed the mixtures correctly. Responses were judged "correct" when they reflected the traditional qualities associated with the stimuli. Note that this was a very conservative standard. Unmixed stimuli can produce atypical qualities (e.g., NaCl can taste sour). These were scored "incorrect" in this analysis. A total of 65 subjects rated 15 different mixture solutions. Figure 8 shows that some subjects analyzed most of the mixtures correctly while others analyzed very few correctly. Figure 9 shows that as the number of components went up, the number of correct analyses went down.

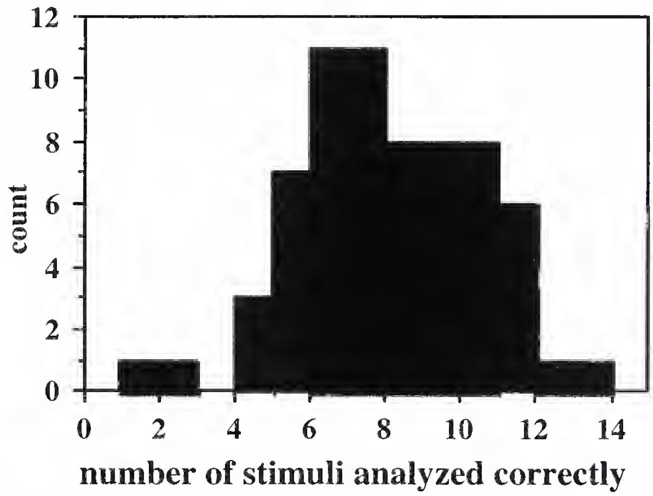

Figure 8. Number subjects with correct analyses plotted against the total number of mixtures subjects correctly analyzed.

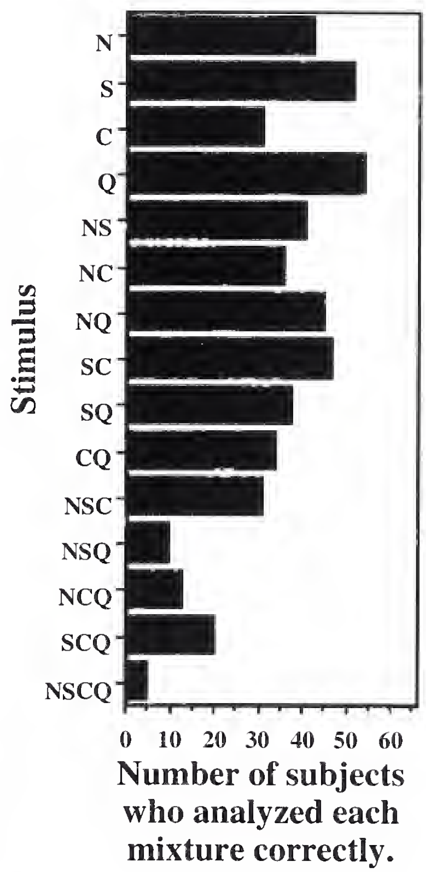

Figure 9. Number of subjects correctly identifying each given mixture.

Figure 10a on the left below shows the number of correctly analyzed stimuli plotted against the number of fungiform papillae; Figure 10b on the right shows the number of correctly analyzed stimuli plotted against the bitterness of .0032 M PROP. Both number of fungiform papillae and ability to detect PROP are significantly correlated with the ability to correctly identify components of mixtures. Supertasters produced the most accurate analyses of the mixtures.

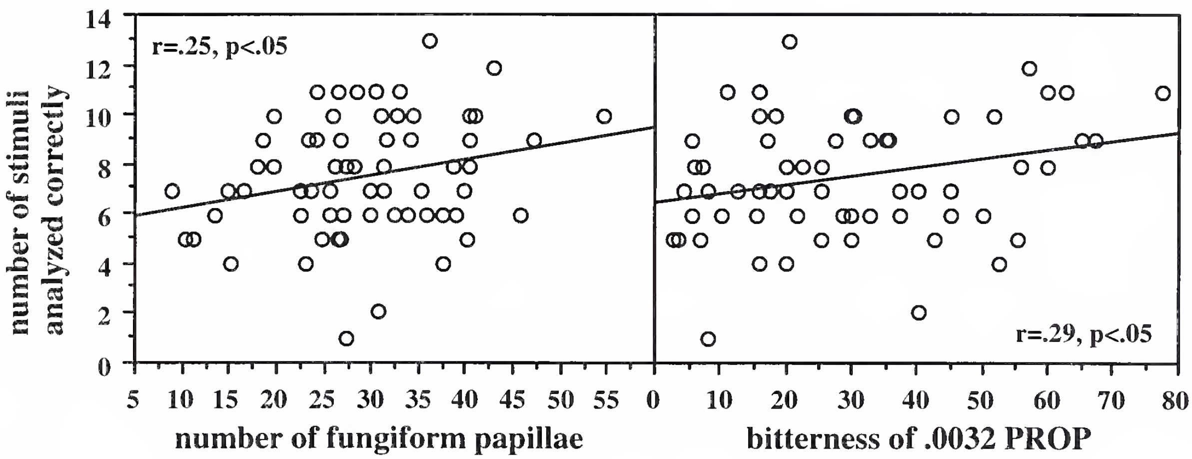

Figure 10a. Number of stimuli correctly analyzed plotted against number of fungiform papillae.

Figure 10b. Number of stimuli correctly analyzed plotted against bitterness of .0032 M PROP (gLMS).

Impact of PROP status.

Mixture suppression interacts with PROP status. Figure 11 shows the average perceived intensity of each component in each of the mixtures plotted against the bitterness of PROP. For example, the 3-component response for each subject was the sum of the total taste intensities for each 3-component mixture divided by 3, the number of 3 component mixtures. Subjects were divided into three groups based on their perceived intensities of the bitterness of .0032 M PROP: lowest 25% (nontasters), middle 50% (medium tasters) and highest 25% (supertasters). ANOVA (PROP group by number of components in the mixture) showed significant main effects for both PROP status ($F(2,186)=6.69$, $p<.01$) and number of mixture components ($F(3,186)=274.76$, $p<.0001$) as well as a significant interaction ($F(6,186)= 7.44$, $p<.0001$).

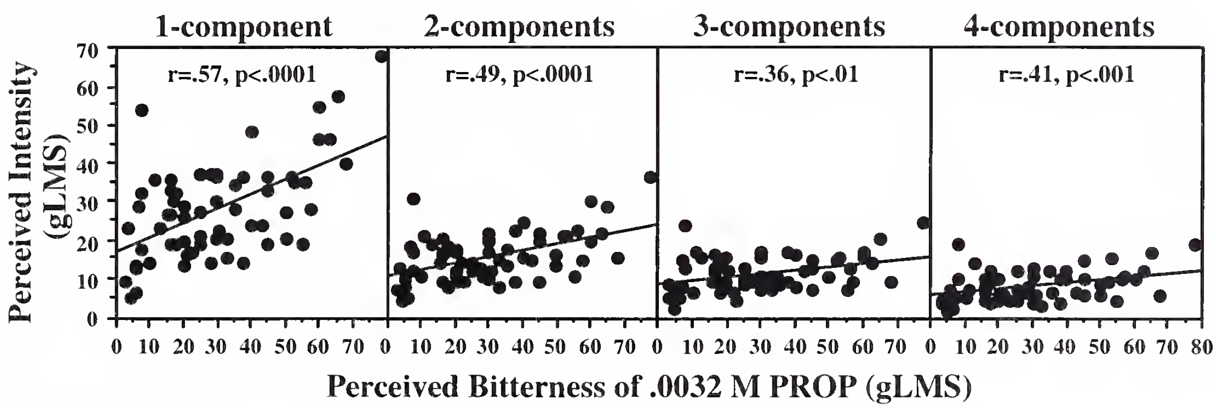

Figure 11. Total perceived intensities of 1, 2 and 3 component mixtures as well as the 4-component mixture plotted against the bitterness of .0032 M PROP. Correlation coefficients are shown in each panel.

Discussion

While some past studies have found no correlation between PROP taster status and the perception of non-PROP tastants (54, 55, 56, 57), others have found correlations (33, 56, 58). This study shows a significant correlation between the perceived intensity of PROP and the perceived intensities of each of the basic tastes. This correlation remained true across many experimental standards including tones, remembered non-taste sensations, and brightest light with the exception of citric acid when controlled by remembered sensations or light. Given the persistence of the correlations throughout multiple normalization methods, we believe taster status affects the perception of the basic tastes.

Our results agree with a previous study by Prescott, who showed that mixture interactions are dependent on PROP taster status (33). Results of the present study extend Prescott's conclusion with more mixture combinations. We have found that taste suppression depends on both the tastants comprising the mixture as well as the PROP status of the taster. Supertasters experienced relatively greater suppression than medium tasters, who in turn experienced more suppression than nontasters. Such PROP status-related suppression negates PROP effects seen in pure solutions, as supertasters no longer experience some tastants as more intense than medium tasters or nontasters. This tends to level the playing field for all. Supertasters, medium tasters, and nontasters will perceive complex tastes as having more similar intensities than the unmixed tastes. This effect was seen most significantly with bitterness where supertasters consistently experienced greater suppression of bitterness than did medium tasters who experienced greater suppression than did nontasters.

In accordance with previous findings of asymmetrical suppression (59, 60, 61), we have found bitterness to be the most easily suppressed of the four basic tastes. The disappearance of statistical significance in perceived intensity ratings between supertasters, medium tasters, and nontasters in six of the seven mixtures containing quinine supports bitterness as the most easily suppressible basic taste. Intensity ratings became statistically equivalent for all tasters when sufficient suppression occurred. With regard to bitterness, CQ was the only 2-component mixture retaining a significant correlation with the perceived intensity of PROP. This suggests citric acid to be a poor suppressor of quinine as supertasters and medium tasters continued to perceive the bitterness of quinine more intensely than nontasters. NaCl is a particularly effective suppressor of quinine as every mixture containing quinine and NaCl showed no PROP effects regardless of other components.

Saltiness is the second most easily suppressed taste given the perceived saltiness ratings of four of the seven NaCl-containing mixtures became statistically equivalent between the taster groups. The only effective suppressor of saltiness in binary combinations was sucrose, suggesting sucrose to be the most potent suppressor of saltiness. NC and NQ remained significantly correlated with PROP, which suggests that citric acid and quinine are poor suppressors of NaCl.

Sourness is more difficult to suppress than both bitterness and saltiness. Only two of seven mixtures containing citric acid showed sour suppression. No binary mixtures were able to suppress sourness. The resistance of sourness to suppression could require more than one other component in a mixture for suppression to be detectable.

Sweetness is the least suppressible of the basic tastes as sweetness was suppressed

in only one of seven mixtures containing sucrose, the mixture SCQ. Sucrose was very adept at retaining its sweetness quality despite the presence of other tastes. Based on the observation that SCQ was the only mixture showing sweetness suppression, one might expect the addition of NaCl to SCQ to continue to show suppression, but interestingly, NSCQ does not. However, as sucrose was the most effective suppressor of NaCl that NaCl would not effectively suppress sucrose is not surprising. Whether the addition of NaCl to SCQ changes the chemical interactions so as the decrease the suppression of sweetness by other components is not known.

Perception of individual tastes in commercial foods showed similarities to data obtained from laboratory mixtures. Paralleling its status as the most easily suppressed quality in laboratory mixtures, bitterness was suppressed in all commercial foods (lemonade, grapefruit juice, tonic water, soy sauce). Sourness retained its correlations to PROP for all foods but lemonade, making it the least suppressible basic taste present in real foods. Conclusions about the interactions of tastes in prepared foods are challenging, as the concentrations of component tastes are not known. Without a baseline, it is difficult to assess changes from that baseline.

While PROP effects decreased when analyzing perceived taste intensities for some individual tastants, the total intensity for all mixtures and commercial foods remained correlated to PROP status. Suppression did not affect total mixture intensity as subjects continued to perceive mixtures as a whole more intensely according to the ability to detect PROP. Mixture suppression cannot merge disparate taste worlds, but can bring them closer together. While the existence of individual taste suppression may be a mechanism to make foods more palatable, the overall intensities still differ according to

taster status.

The effects of sucrose upon the bitterness of coffee illustrate how supertasters can modify foods using mixture suppression. Adding 5% sucrose suppressed bitterness for supertasters to a greater degree than for medium or nontasters. By the 10% mixture, sucrose had rendered coffee essentially equi-intense with regard to bitter for all subjects, regardless of PROP status. Bitterness remained equi-intense to all taster groups at 20% sucrose, though the perceived intensity of sweetness became significantly correlated to PROP status at this concentration. This demonstrates the ability of supertasters to ameliorate the bitterness of coffee with sucrose, perhaps rendering it more palatable.

General observations about mixture suppression were observed. The most potent suppressor in a 2-component mixture tended to remain a potent suppressor in the 3-component mixture. In fact, the first and second most effective suppressors in the 2-component mixtures tended to go on to make up the most effective 3-component mixture suppressors. From mixtures, we observed bitter to be the most easily suppressed of the four tastes. Indeed, in commercial foods, bitter intensity did not produce significant correlation with PROP for any of the foods tested. Given that suppression of bitter is likely to be a commercial goal, the ease with which bitter is suppressed in mixtures advances that goal.

Why bitterness should be the most noxious basic taste to supertasters, but also the most easily suppressed is an interesting question. One might postulate that during the days of primitive man, the ability to detect the bitterness of poisons would lend a Darwinian advantage to survival. However, this acute sense of taste could also deter the supertaster from eating many foods. A regulatory advantage could turn into a nutritional

disadvantage, as finicky eaters are not practical. If supertasters were able to suppress intense tastes by mixing them, as in the case of most prepared foods, they would be able to eat everything medium and nontasters eat, but still retain the ability to distinguish between tastes at a more basic level. Thus, the supertasters, instead of living in an unbearable world of overwhelmingly intense tastes have the best of everything: a discriminating sense of taste, but also the ability to modify this gift through mixtures.

Results of this study differ somewhat from some previously published reports due to two main methodological differences: scaling method and tastant concentration. Much of the literature is based on the use of scales, such as the 9-point scale, which do not produce valid across-group comparisons for PROP studies (51). We believe the gLMS to enable valid comparisons between supertasters, medium tasters, and nontasters, the basis of conclusions regarding genetic variations. Others studies have used correct scales, but created mixtures with components that are not equi-intense as single tastants. One might deduce that when one component of a mixture begins as more intense, it will then dominate a mixture and erroneously appear to produce suppressive effects while itself being resistant to suppression.

The results have relevance for the debate over the nature of taste mixtures. We take the position that taste mixtures are analytic because observers are capable of analyzing them. In correctly analyzing 12 of 15 mixtures, the analysis is not perfect but part of the failure is the ease with which bitterness is suppressed in mixtures. The three mixtures in which bitterness was present but not identified, NSQ, SCQ, NSCQ, were all complex mixtures containing potent suppressors of quinine. Though the group as a

whole was able to identify most components, the ability to identify varies across individuals.

There are some that are remarkably good at analysis of taste mixtures. Supertasters have an advantage because bitterness (at least of quinine) is more affected by PROP status than are the intensities of the other taste qualities. The ability to identify components of mixtures correlated with the ability to detect PROP. It is already known that density of fungiform papillae is one of the criteria comprising taster status (16), however this study shows that those with more fungiform papillae are also more successful at identifying mixture components.

In order for a system to show analytic mixing, subjects need not be perfect at the analysis. Rather, the fact that it can be done at all determines the distinction between analytic and synthetic. In contrast, components in color mixtures cannot be identified correctly no matter how skilled the observer. It is important to note, that while new qualities appear in color mixtures, no new qualities appear in taste mixtures. This is the heart of the distinction between analytic and synthetic mixtures.

In summary, the perceived intensities of basic tastes were found to correlate with the ability to detect PROP. This correlation disappeared for individual tastes in some mixtures as a result of mixture suppression. The degree of this suppression varied according to PROP status and the components making the mixtures. In general, those who detected PROP as more bitter experienced more suppression. Though the perceived intensity of individual tastes showed suppression in some mixtures, overall intensities remained correlated to PROP status for all mixtures and commercial foods. In support of

taste mixtures as an analytic phenomenon, subjects were able to correctly identify components of most mixtures, an ability that varies according to taster status.

References

1. Fox AL. 1931. Six in ten "tasteblind" to bitter chemical. *Sci News Lett.* 9:249.

2. Snyder LH. 1932. Studies in human inheritance. IX. The inheritance of taste deficiency in man. *Ohio J Sci.* 32:436-40.

3. Blakeslee AF, Salmon MR. 1931. Odor and taste blindness. *Eugenical News.* 16:105-10.

4. Barnicot NA, Harris H, Kalmus H. 1951. Taste thresholds of further eighteen compounds and their correlation with PTC thresholds. *Ann Eugen.* 16:119-28.

5. Fernberger SW. 1932. A preliminary study of taste deficiency. *Am J Psychol.* 44:322-6.

6. Stevens SS. 1969. Sensory scales of taste intensity. *Percept Psychophys.* 6:302-8.

7. Blakeslee AF, Salmon TN. 1935. Genetics of sensory thresholds: individual taste reactions for different substances. *Prol Natl Acad Sci.* 21:84-90.

8. Bartoshuk LM, Duffy VB, Lucchina LA, Prutkin J, and Fast K. 1998 PROP (6-n-propylthiouracil) supertasters and the saltiness of NaCl. In *Olfaction and Taste XII.* C. Murphy, editor. New York: New York Academy of Sciences. 855:793-96.

9. Stevens JC, Marks LE. 1965. Cross-modality matching of brightness and loudness. *Proc Natl Acad Sci.* 54:407-11.

10. Green BG, Shaffer GS, Gilmore MM. 1993. A semantically-labeled magnitude scale of oral sensation with apperent ratio properties. *Chem Senses.* 18:683-702.

11. Bartoshuk, LM. 1993. The biological basis of food perception and acceptance. *Food Qual Pref.* 4:21-32.

12. Bartoshuk LM, Conner E, Grubin D, Karrer T, Kochenbach K, *et al.* 1993. PROP supertasters and the perception of ethyl alcohol. *Chem Senses.* 18:526-7.

13. Blakeslee AF, Fox AL. 1932. Our different taste worlds. *J Hered.* 23:97-107.

14. Kim UK, Jorgenson E, Coon H, Leppert M, Risch N, Drayna D. 2003. Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide. *Science.* 299:1221-5.

15. Bartoshuk LM, Duffy VB, Miller IJ. 1994. PTC/PROP tasting: anatomy, psychophysics, and sex effects. *Physiol Behav.* 56:1165-71.

16. Miller IJ, Reedy FE. 1990. Variations in human taste bud density and taste intensity perception. *Physiology and Behavior.* 47:1213-19.

17. Silver WL, Finger TE. 1991. The trigeminal system. In *Smell and Taste in Health and Disease.* T. Getchell, et al. editors. New York: Raven Press. 97-108.

18. Whitehead MC, Beeman CS, Kinsella BA. 1985. Distribution of taste and general sensory nerve endings in fungiform papillae of the hamster. *Am J Anat.* 173:185-201.

19. Finger TE, Nelson GM, Bryant B, Moore PA. 1994. Intragemmal and perigemmal fibers in taste buds: Immunocytochemistry and differential sensitivity to capsaicin. *Neuroscience Abstracts.* 402:12.

20. Nagy JI, Goedert M, Hunt SP, Bond A. 1982. The nature of the substance P-containing nerve fibers in taste papillae of the rat tongue. *Neuroscience.* 7:3137-51.

21. Toyoshima K, Miyamoto K, Itoh A, Shinamura A. 1987. Merkel-neurite complexes in the fungiform papillae of two species of monkeys. *Cell Tissue Res.* 250:237-9.

22. Zahm DS, Munger BL. 1985. The innervation of the primate fungiform papilla-development, distribution and changes following selective ablation. *Brain Res.* 356:147-86.

23. Hilliges M, Astback J, Wang L, Arvidson K, Johansson O. 1996. Protein gene product 9.5-immunoreactive nerves and cells in human oral mucosa. *Anat Rec.* 245:621-32.

24. Ko CW, Hoffman HJ, Lucchina LA, Snyder DJ, Weiffenbach JM, Bartoshuk LM. 2000. Differential perceptions of intensity for the four basic taste qualities in PROP supertasters versus nontasters. *Chem Senses.* 25:639-40.

25. Snyder DJ, Lucchina LA, Duffy VB, Bartoshuk LM. 1996. Magnitude matching adds power to the labeled magnitude scale. *Chem Senses.* 21:673.

26. Prutkin JM, Fast K, Lucchina LA, Snyder DJ, Bartoshuk LM. 1999. Spatial taste testing and genetic taste variation. *Chem Senses.* 2:604.

27. Duffy VB, Bartoshuk LM, Lucchina LA, Snyder DJ, Tym A. 1996. Supertasters of PROP (6-n-propylthiouracil) rate the highest creaminess to high-fat milk products. *Chem Senses.* 21:598.

28. Tepper BJ, Nurse RJ. PROP taster status is related to fat perception and preference. 1998. In *International Symposium on Olfaction and Taste XIX.* C. Murphy, editor. New York: New York Academy of Sciences. 802-4.

29. Bartoshuk LM, Duffy VB, Fast K, Kveton JF, Lucchina LA, *et al.* 2001. What makes a supertaster? *Chem Senses.* 26:1074.

30. Prutkin J, Duffy VB, Etter L, Fast K, Gardner E, *et al.* 2000. Genetic variation and inferences about perceived taste intensity in mice and men. *Physiol Behav.* 69:161-73.

31. Bartoshuk LM. 1975. Taste mixtures: is mixture suppression related to compression? *Physiol Behav.* 14:643-49.

32. Bartoshuk LM, Gent JF. 1985. Taste mixtures: an analysis of synthesis. In *Taste and Olfaction and the Central Nervous System.* D. Pfaff, editor. New York: Rockefeller University Press. 210-32.

33. Prescott J, Ripandelli N, Wakeling I. 2001. Binary taste mixture interactions in PROP non-tasters, medium-tasters, and super-tasters. *Chem Senses.* 26:993-1003.

34. Drewnowski A, Henderson SA, Shore AB. 1997. Genetic sensitivity to 6-*n*-propylthiouracil (PROP) and hedonic resposes to bitter and sweet tastes. *Chem Senses.* 22:27-37.

35. Drewnowski A, Henderson SA, Shore AB, Barratt-Fornell A. 1997. Non-tasters, tasters, and supertasters of 6-n-propylthiouracil (PROP) and hedonic response to sweet. *Physiol Behav.* 62:649-55.

36. Duffy VB, Bartoshuk LM. 1996. Genetic taste perception and food preferences. *Food Qual Pref.* 7:309.

37. Duffy VB, Fast K, Cohen Z, Chodos E, Bartoshuk LM. 1999. Genetic taste status associates with fat food acceptance and body mass index in adults. *Chem Senses.* 24:545-6.

38. Pfaffmann C. 1941. Gustatory afferent impulses. *J Cell Comp Physiol.* 17:243-58.

39. Pfaffmann C. 1955. Gustatory nerve impulses in rat, cat, and rabbit. *J Neurophysiol.* 18:429-40.

40. Pfaffman C. 1959. The afferent code for sensory quality. *Am Psychol.* 14:226-32.

41. Erickson RP. 1963. Sensory neural patterns and gestation. In *Olfaction and Taste*. Y. Zotterman, editor. New York: Macmillan. 205-13.

42. Erickson RP. 1968. Stimulus coding in topographic and nontopographic afferent modalities: on the significance of the activity of individual sensory neurons. *Psychol Rev.* 75:447-65.

43. Frank ME. 1973. An analysis of hamster afferent taste nerve response functions. *J Gen Physiol.* 61:588-618.

44. Pfaffmann C. 1974. Specificity of the sweet receptors of the squirrel monkey. *Chem Senses Flavor.* 1:61-7.

45. Pfaffmann C, Frank ME, Bartoshuk LM, Snell TC. 1976. Coding gustatory information in the squirrel monkey chorda tympani. In *Progress in Psychobiology and Physiological Psychology, vol. 6.* J. Sprague and A. Epstein, editors. New York: Academic Press. 1-27.

46. Smith DV, St. John SJ, Boughter JD. 2000. Neuronal cell types and taste quality coding. *Physiol Behav.* 69:77-85.

47. Uttal, WR. 1973. *The Psychobiology of Sensory Coding.* New York: Harper and Row Publishers.

48. Erickson RP, Covey E. 1980. On the singularity of taste sensations: what is a taste primary? *Physiol Behav.* 25:527-33.

49. Erickson RP. 1942. The across-fiber pattern theory: an organizing principle for molar neural function. In *Contributions to Sensory Physiology, vol. 6.* W. Neff, editor. New York: Academic Press. 79-110.

50. Laing DG, Link C, Jinks AL, Hutchinson I. 2002. The limited capacity of humans to identify the components of taste mixtures and taste-odour mixtures. *Perception.* 31:617-35.

51. Bartoshuk LM, Duffy VB, Fast K, Green BG, Prutkin J, Snyder DJ. 2002. Labeled scales (e.g., category, Likert, VAS) and invalid across-group comparisons: what we have learned from genetic variation in taste. *Food Qual Pref.* 14;125-38.

52. Bartoshuk LM, Fast K, Duffy VB, Prutkin JM, Snyder DJ, Green BG. 2000. Magnitude matching and a modified LMS produce valid sensory comparisons for PROP studies. *Appetite.* 35:277.

53. Bartoshuk LM, Duffy VB, Chapo AK, Fast K, Yiee JH, *et al.* 2004. From psychophysics to the clinic: Missteps and advances. In *The 5th Pangborn Sensory Science Symposium*. Boston: Elsevier.

54. Hall MJ, Bartoshuk LM, Cain WS, Stevens JC. 1975. PTC taste blindness and the taste of caffeine. *Nature.* 253:442-3.

55. Mela DJ. 1989. Bitter taste intensity: the effect of tastant and thiourea taster status. *Chem Senses.* 14:131-5.

56. Leach EJ, Noble AC. 1986. Comparison of bitterness of caffeine and quinine by a time-intensity procedure. *Chem Senses.* 11:339-45.

57. Smagghe K, Louis-Sylvestre J. 1998. Influence of PROP-sensitivity on taste perceptions and hedonics in french women. A study performed without retronasal olfaction. *Appetite.* 30:325-39.

58. Gent JF, Bartoshuk LM. 1983. Sweetness of sucrose, neohesperidin dihydrochalone, and sacarin is related to genetic ability to taste the bitter substance 6-n-propylthiouracil. *Chem Senses.* 7:265-72.

59. Kamen JM, Pilgrim FJ, Gutman NJ, and Kroll BJ. 1961. Interactions of suprathreshold taste stimuli. *J Exp Psychol.* 4:348-56.

60. Moskowitx, HR. 1972. Perceptual changes in taste mixtures. *Percep Psychophys.* 11:257-62.

61. McBurney DH and Bartoshuk LM. 1973. Interactions between stimuli with different taste qualities. *Physiol Behav.* 10:1101-06.