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Taste masking analysis in pharmaceutical formulation development using an electronic tongue

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Abstract

The purpose of this study is to assess the feasibility for taste masking and comparison of taste intensity during formulation development using a multichannel taste sensor system (e-Tongue). Seven taste sensors used in the e-Tongue were cross-selective for five basic tastes while having different sensitivity or responsibility for different tastes. Each of the individual sensors concurrently contributes to the detection of most substances in a complicated sample through the different electronic output. Taste-masking efficiency was evaluated using quinine as a bitter model compound and a sweetener, acesulfame K, as a bitterness inhibitor. In a 0.2 mM quinine solution, the group distance obtained from e-Tongue analysis was reduced with increasing concentration of acesulfame K. This result suggests that the sensors could detect the inhibition of bitterness by a sweetener and could be used for optimization of the sweetener level in a liquid formulation. In addition, the bitterness inhibition of quinine by using other known taste-masking excipients including sodium acetate, NaCl, Prosweet® flavor, and Debittering® powder or soft drinks could be detected by the e-Tongue. These results further suggest that the e-Tongue should be useful in a taste-masking evaluation study on selecting appropriate taste-masking excipients for a solution formulation or a reconstitution vehicle for a drug-in-bottle formulation. In another study, the intensity of the taste for several drug substances known to be bitter was compared using the e-Tongue. It was found that the group distance was 695 for prednisolone and 686 for quinine, which is much higher than that of caffeine (102). These results indicate that the taste of prednisolone and quinine is stronger or more bitter than that of caffeine as expected. Based on the group distance, the relative intensity of bitterness for these compounds could be ranked in the following order: ranitidine HCl > prednisolone Na > quinine HCl∼phenylthiourea > paracetamol ≫ sucrose octaacetate > caffeine. In conclusion, the multichannel taste sensor or e-Tongue may be a useful tool to evaluate taste-masking efficiency for solution formulations and to compare bitterness intensity of formulations and drug substances during pharmaceutical product development.

Keywords: Taste sensor; e-Tongue; Bitterness; Quinine; Caffeine; Formulation; Solution; Excipients; Principal component analysis; Bitterness inhibition; Preformulation

1. Introduction

Excessive bitterness of the active pharmaceutical ingredients in oral liquid or suspension formulation, sublingual or buccal formulation is a major taste problem facing pharmaceutical scientists. In the early development stage, bitterness of formulations can have an impact on clinical study design when a double-blinded trial is needed. Later, the bitterness of formulations can influence pharmaceutical selection by physicians and patients and thus affect acceptance and compliance. To inhibit or block the bitterness, both physical and chemical methods have been employed. Use of capsules, polymer coatings, microencapsulation, complexation, taste-masking excipients, and chemical modifications have been reported (FuLu et al., 1991; Ueda et al., 1993; Fukumori et al., 1988; Bechtol et al., 1981; Katsuragi et al., 1997; Mullarney et al., 2003). Generally speaking, taste is comprised of five basic qualities: sourness produced by hydrogen ions such as HCl, acetic acid, and citric acid; saltiness produced mainly by NaCl; sweetness produced by sugars; and bitterness produced by quinine, caffeine and $MgCl_2$. The last one is umami, which is the Japanese term for “deliciousness”, and is produced by monosodium glutamate contained in seaweeds, disodium inosinate in meat and fish and disodium guanylate in mushrooms (Pfaffmann, 1959; Kawamura and Kare, 1987). Biologically, the sensations of taste in humans occur when molecules trigger signals in the mouth

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that are sent to the brain, where a specific taste sensation is registered. The taste transduction is mediated by specialized neuroepithelial cells, referred to as taste receptor cells, organized into groups of 40–100 cells, which form taste buds. Taste buds are ovoid structures, the vast majority of which are embedded within the epithelium of the tongue. Different taste modalities appear to function by different mechanisms. For example, a salty taste appears to be mediated by sodium ion flux through apical sodium channels (Keast et al., 2001), while a sour taste seems to be mediated via a hydrogen ion blockade of potassium or sodium channels (Kinnamon and Roper, 1988). Sweet and bitter tastes are transduced by G protein-coupled receptors (Kinnamon and Cummings, 1992). To date, more than 80 putative bitter receptors have been identified (Matsunami et al., 2000). Nevertheless, the taste transduction mechanisms are complex and not fully elucidated.

The main method for the taste measurement of a drug substance or a formulation is by human sensory evaluation, in which tasting a sample is relayed to inspectors. However, this method is impractical for early stage drug development because the test in humans is expensive and the taste of a drug candidate may not be important to the final product. Therefore, taste-sensing analytical devices, which can detect tastes (especially bitterness) have been desired for a long time. It has been reported that a multichannel taste sensor (i.e., an electronic tongue or e-Tongue), whose transducer is composed of several kinds of lipid/polymer membranes with different characteristics can be used to detect taste (Toko, 1996). Taste information is transformed into a pattern composed of the electronic signals of the lipid membrane potentials. The sensor measures taste quality since different electric potential patterns are obtained for substances producing different taste quality. Also, similar patterns are obtained for substances producing the same taste quality (Takagi et al., 1998; Miyanaga et al., 2002). However, those reported studies were conducted by pilot e-Tongues with short life sensors, which significantly limited its application. Recently, a taste analyzing system manufactured by Alpha MOS has become commercially available. The taste sensors consist of silicon transistors with an organic coating that governs sensitivity and selectivity of each individual sensor. The life of the sensors could last as long as 1 year.

In this work, the e-Tongue with seven taste sensors was evaluated for its application in taste masking analysis during pharmaceutical formulation development. Objectives of this study were: (1) to assess the response and selectivity of seven sensors to compounds with different tastes; (2) to evaluate the feasibility to utilize e-Tongue in liquid formulation design; (3) to investigate the potential use of e-Tongue in ranking relative bitterness of compounds.

2. Experimental

2.1. Materials

Quinine HCl, quinine sulfate dehydrate, caffeine anhydrous, ranitidine HCl, phenylthiourea, sucrose octaacetate, and tartaric acid were purchased from Sigma Chemical Co. (St. Louis, MO). Sodium chloride, sodium acetate, and sodium saccharin were purchased from Fisher Scientific, (Pittsburgh, PA). 0.1 M Sodium L-glutamate (MSG), 0.1N HCl, 0.1 M NaCl, prednisolone Na, and paracetamol were from Alpha MOS Inc. (Hillsborough, NJ). Acesulfame K, pharma grade, was supplied from Nutrinova (Summerset, NJ). Soft drinks—Coca-Cola®, Sprite®, Diet Sprite®, and Dr. Pepper® were purchased from various supermarkets. Debittering flavor® and Prosweet flavor®, commercial bitterness-suppressing agents, were supplied by Flavors of North America (Carol Stream, IL) and Virginia Dare (Brooklyn, NY), respectively. All chemicals were of the highest grade available and used without further purification.

2.2. Equipment

An αAstree liquid and taste analyzer (e-Tongue) connected with LS16 autosampler unit, taste sensors and reference electrode was purchased from Alpha MOS Inc., and the system was equipped with a data acquisition and analysis software package. A taste sensor set—KIT #2 for pharmaceutical application (ZZ2806, AB2806, BA 2806, BB2806, CA2910, DA2806, and JE2806) was also from Alpha MOS Inc. The reference electrode (Ag/AgCl) was from Metrohm AG.

2.3. Methods

2.3.1. General sample preparation and analysis

The compounds tested were weighed out and dissolved in purified water. All testing beakers contained 80–100 mL of solution. When the reference electrode and sensors were dipped into a beaker containing a test solution, a potentiometric difference between each individually coated sensor with the Ag/AgCl reference electrode was measured and recorded by the e-Tongue software. Each sample was analyzed for 120 s. The liquid sensors and the reference electrode were then rinsed with purified water for 10 s after each sample analysis. Using well-conditioned sensors, each sample was usually tested eight times by the rotation procedure (i.e., the first round of measurements of all samples was completed before the next round of measurements was started).

2.3.2. Cross-selectivity test

Five compounds were used for the cross-selectivity test including tartaric acid (sourness), sodium saccharin (sweetness), quinine (bitterness), NaCl (saltiness), and MSG (umami). Tartaric acid, sodium saccharin, NaCl and MSG were made at the same concentration (10 mM) while quinine was made at 1 mM. Solutions were analyzed using the e-Tongue as described above.

2.3.3. Bitterness-masking of quinine

Solution samples (250 mL) were prepared using purified water for evaluation of suppression of bitterness of quinine by a sweetener, acesulfame K and other known bitterness taste-masking excipients. Quinine was kept at a constant level of 0.2 mM with varying concentrations of acesulfame K (0.1, 1.0,

and 5.0 mM) or with a predetermined level of taste-masking excipients (100 mM sodium acetate and NaCl, 0.5% Prosweet flavor®, and 0.2% Debittering flavor®). For each sample containing quinine, a corresponding placebo was prepared. Samples were then analyzed as described previously and the difference between the sample containing quinine and its placebo was determined by the e-Tongue.

2.3.4. Vehicle selection for reconstitution of drug-in-bottle formulation

Quinine sulfate dehydrate was used as a model compound and commercially available soft drinks were utilized as reconstitution vehicles, including Coca-Cola®, Sprite®, Diet Sprite®, and Dr. Pepper®. All drinks were de-carbonated using sonication prior to the experiment. Quinine sulfate dehydrate at a concentration of 0.5 mg/mL was prepared in water or an individual soft drink and the solutions were analyzed using the e-Tongue as described above.

2.3.5. Qualitative evaluation of bitterness of active pharmaceutical ingredients

The taste of several known bitter active pharmaceutical ingredients (API) or chemicals was evaluated including ranitidine, prednisolone, quinine, paracetamol, caffeine, phenylthiourea, and sucrose octaacetate. All samples were prepared in purified water at a concentration of 10 mM. Samples were then analyzed by the e-Tongue as described previously and the distance between the water placebo and the sample containing API was determined.

2.3.6. Data analysis

Data collected by the e-Tongue were reviewed, and the last five replicates out of eight assays were treated by multivariate statistical methods. The last five repeats usually have less variation due to the nature of sensors. A multivariate analysis, i.e., principal component analysis (PCA), was used by the αAstree e-Tongue in order to reduce the dimensional space without losing information. Data points were expressed in the seven-dimensional spaces, because there were seven-channel outputs. For each sample, a cluster could be obtained in a PCA map. Distance between a pair of data clusters (i.e., the placebo sample and the sample with test compound) was then determined. The distance is used to assess the similarity between a pair of samples and bitterness intensity of a chemical.

In addition, using the PCA the most abundant information contained in the original data could be transformed into the first principal component (PC1), and the second and third most abundant information is transformed into the second and third principal components (PC2 and PC3), respectively. In this way, the important information from the raw data can be extracted in the order of importance. A PCA map can be obtained by plotting PC1 against PC2 or PC3. This map shows the discrimination and similarities between the different samples and groups. A discrimination index (DI) with a range of 0–100 is reported from the PCA map. The higher index number indicates less similarity between samples or groups.

3. Results and discussion

3.1. Cross-selectivity of taste sensors to different taste substances

Seven sensors are made from silicon transistors with an organic coating that governs sensitivity and selectivity of each individual sensor. The coatings have been developed to ensure good repeatability, sensitivity and selectivity. Details on sensor materials have not been disclosed by the manufacturer due to a current patent application. From literature, taste sensors are usually composed of lipids and polymers (Toko, 1996). Typical lipids are decyl alcohol, oleic acid, dioctyl phosphate, trioctylmethylammonium chloride, while typical polymers are polyvinyl chloride and dioctyl phenylphosphate (Takagi et al., 1998).

Cross-selectivity of each sensor to chemicals with different tastes is important for e-Tongue technology. With a set of cross-selective taste sensors, each sensor could concurrently contribute to the detection of most substances in a sample although the sensitivity to various chemicals is different. This is especially true in a liquid matrix where several compounds can contribute to the same taste attribute. Thus, a set of cross-selective sensors is needed to provide a global liquid and taste perception. The cross-selectivity of the seven sensors (ZZ, AB, BA, BB, CA, DA, and JE) was evaluated on the five basic tastes: sourness (tartaric acid), sweetness (sodium saccharin), bitterness (quinine), saltiness (NaCl), and umami (MSG). Tartaric acid, sodium saccharin, NaCl and MSG were made at the same concentration (10 mM) while quinine was made at 1 mM. As shown in Fig. 1, all seven sensors responded to the five basic tastes, which indicate a good cross-selectivity. However, the sensitivity of each sensor to different chemicals varies. For example, sensor ZZ showed a high sensitivity to umami taste and a low sensitivity to acid taste (Fig. 1). But, sensor BA showed equal sensitivity to all five basic tastes. These results suggest that the αAstree sensors used in e-Tongue analysis are cross-selective.

3.2. Response of taste sensors to different concentrations of quinine

Quinine is the most commonly used model compound in bitterness studies. Electrical response of sensors to quinine at different levels was evaluated using the αAstree e-Tongue. Fig. 2

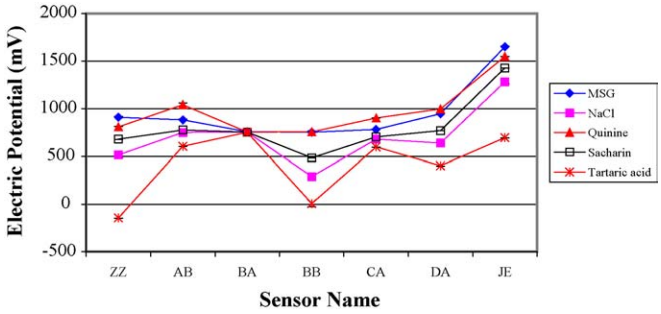

Fig. 1. Response patterns of sensors for five representative tastes.

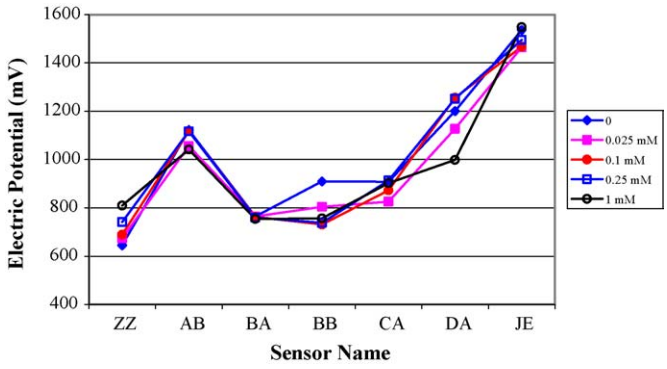

Fig. 2. Response patterns of sensors to different concentrations of quinine.

shows the response patterns of quinine at different concentrations. Overall, the sensors DA and JE showed higher electric potentials while the sensors ZZ, BA and BB had lower electric potentials. All the sensors were positively charged. As the quinine concentration increased, the outputs of electric signals from seven sensors were changed. For the sensors ZZ and CA, the electric potentials increased with an increase in concentration of quinine. For other sensors, characteristic changes in response patterns were not observed. Nevertheless, the results indicated that the taste sensors could detect the concentration change of a chemical in solution. Because the taste sensor analyzer is very sensitive, even a 10 mV change in response can be differentiated in the seven dimensional spaces by e-Tongue.

3.3. Application of e-tongue in liquid formulation design

3.3.1. Optimization of sweetener level

Sweeteners are commonly used for masking bitterness taste in food and pharmaceutical industries. The effect of a sweetener, acesulfame K (Ace K), on masking quinine bitterness was evaluated by e-Tongue and a PCA map was configured to determine the system discrimination power between the samples using the data generated. As shown in Fig. 3, the cluster of each sample was small, indicating good reproducibility of the analysis; and a clear discrimination between different sample pairs (active versus placebo) was observed. Table 1 lists the R.S.D. values from

Table 1
Assay variation on masking bitterness of quinine by Acesulfame K

Sensor ID	R.S.D.[a] (%)							
	APIQ1	APIQ2	APIQ3	APIQ4	PQ1	PQ2	PQ3	PQ4
ZZ	1.3	1.2	1.3	1.3	0.8	1.5	1.1	1.1
AB	0.3	0.3	0.3	0.6	0.6	0.3	0.4	0.4
BA	4.2	4.6	5.2	5.9	3.9	4.5	4.7	5.6
BB	0.9	0.7	0.5	0.6	0.8	0.8	0.6	0.6
CA	1.2	1.4	1.1	1.0	1.2	1.5	0.9	0.8
DA	1.2	1.1	0.8	0.6	0.9	1.1	1.0	0.9
JE	0.5	0.7	0.4	0.3	0.6	1.0	0.4	0.3

PQ1: water, APIQ1: 0.2 mM quinine; PQ2: 0.1 mM Ace K, APIQ2: 0.1 mM Ace K + 0.2 mM quinine; PQ3: 1.0 mM Ace K, APIQ3: 1.0 mM Ace K + 0.2 mM quinine; PQ4: 5.0 mM Ace K, APIQ4: 5.0 mM Ace K + 0.2 mM quinine.

[a] R.S.D.: relative standard deviation (R.S.D. was calculated from last five determinations of a single sample).

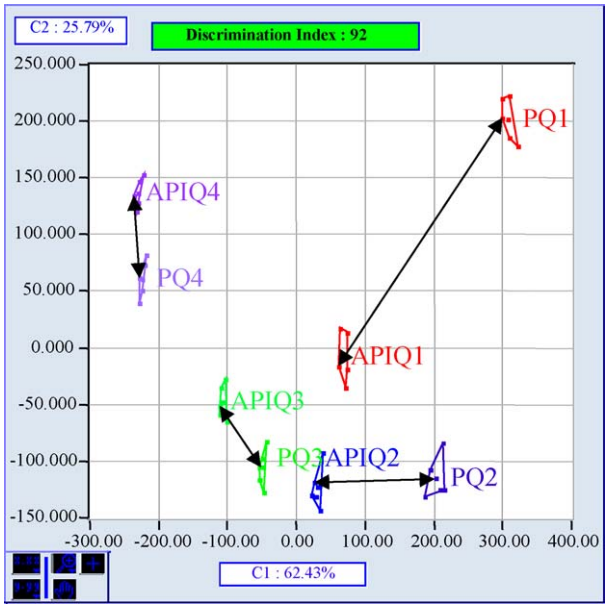

Fig. 3. A PCA map for quinine in the presence of different level of Acesulfame K. Keys: PQ1—water, APIQ1—0.2 mM quinine; PQ2—0.1 mM Ace K, APIQ2—0.1 mM Ace K + 0.2 mM quinine; PQ3–1.0 mM Ace K, APIQ3—1.0 mM Ace K + 0.2 mM quinine; PQ4—5.0 mM Ace K, APIQ4—5.0 mM Ace K + 0.2 mM quinine.

the analysis. As can be seen, the R.S.D. values for all the samples were less than 6%. These data suggest that the assay variation of the sensors is minimal and that reproducible results can be generated.

The distances between the data clusters for each quinine-containing sample and its matching placebo were calculated. The distance between water (PQ1) and 0.2 mM quinine (APIQ1) was 338, indicating great difference in the taste of these two solutions. When Ace K, a sweetener, was added into the quinine solution, the distance was reduced to 245 with 0.1 mM Ace K, 125 with 1.0 mM Ace K, and 98 with 5.0 mM Ace K, respectively (Fig. 4). Reduction of the distance in the presence of Ace K suggests that the bitterness of quinine was inhibited. At the level of 5.0 mM, the bitterness of quinine can be reduced by

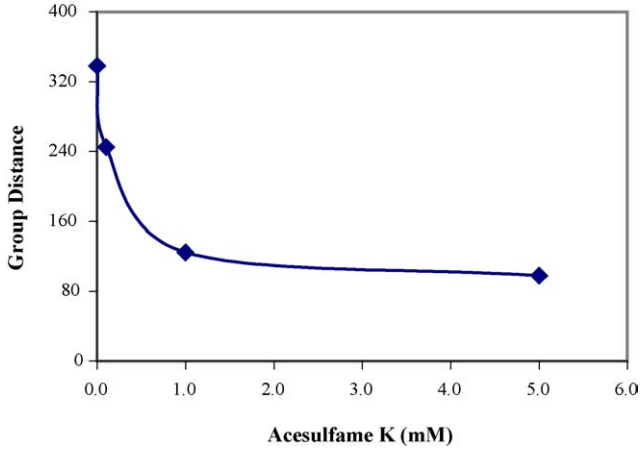

Fig. 4. Changes in group distances for quinine in the presence of different level of Acesulfame K.

71.0%, and thus taste of quinine solution containing 5 mM Ace K (APIQ4) should be closer to the taste of 5 mM Ace K solution (PQ4). Also, at the level of 5.0 mM Ace K, reduction of the group distance has reached plateau (Fig. 4), suggesting that the masking efficiency of Ace K reached maximum. Thus, the optimal concentration of Ace K to mask the bitterness of quinine should be between 1 and 5 mM. These results indicate that suppression of bitterness of quinine by a sweetener could be assessed using the αAstree e-Tongue and an appropriate placebo formulation for quinine solution could be designed using an appropriate concentration of a sweetener.

3.3.2. Selection of appropriate taste-masking agents

Other bitterness-masking excipients were also evaluated on inhibition of bitterness of quinine including sodium acetate and Debittering flavor®. Sodium acetate has been shown to provide good inhibition of bitterness for several pharmaceuticals (Keast and Breslin, 2002) and Debittering flavor® was recommended by a flavor scientist from the Flavor of North America Company. Again, the distance for quinine in the presence of a taste-masking excipient was decreased compared to those solutions without any bitterness-masking agent as determined by e-Tongue (Table 2). The ranking order of the bitterness-masking efficiency is 100 mM sodium acetate > 100 mM NaCl > 5.0 mM Ace K > 0.2% Debittering flavor® > 0.5% Presweet® flavor. The data suggest that inhibition of bitterness of quinine by the known bitterness-masking agents can be observed using e-Tongue. The e-Tongue could be used not only for screening a suitable taste-masking excipient but also for evaluating the level of a taste-masking excipient in a solution formulation.

3.3.3. Selection of vehicle for reconstitution of drug-in-bottle formulation

In the early stages of pharmaceutical development, the goal is to get the drug candidate into humans as quickly as possible so that a go- or no-go-decision can be made according to the human safety profile. Thus, a simple formulation, such as drug-in-bottle (DIB) for reconstitution, offers the fastest way to enable the Phase I clinical trials. Using the DIB approach, an appropriate reconstitution vehicle must be selected according to the chemical stability of the drug in the vehicle and the taste of the solution. Many soft drinks are a good choice for the reconstitution vehicle because they are commercially available such as Coca-Cola®, Sprite®, Diet Sprite®, and Dr. Pepper®, and capable to mask unpleasant taste by the sweeteners and inorganic salts in the drinks. However, the chemical composition is different in various soft drinks, thus tastes of these drinks are slightly different from each other, which may provide different taste masking efficiency to a drug substance. As seen in Table 3, the distance between water and quinine solution at a concentration of 0.5 mg/mL was 525, indicating a significant taste difference between the two samples. When quinine was dissolved in soft drinks, the distance between the soft drink and drug solution decreased when compared with water as a vehicle. Among Sprite®, Diet Sprite®, Dr. Pepper®, and Coca-Cola®, the shortest distance was obtained from Diet Sprite® and the estimate value was 200, e.g. 61.9% inhibition of the distance (Table 3). A shorter distance indicates better similarity between a vehicle and its drug solution. Thus, the results provided information not only on the best vehicle for taste masking purpose but also on the matching placebo needed for clinical trials. If a drug-in-bottle formulation for a new drug candidate is used in the first-human-dose study, e-Tongue could be used for selecting a vehicle for powder reconstitution and its matching placebo.

Table 2
Inhibition of bitterness of quinine by bitterness-masking agents determined by e-Tongue

Bitterness-masking agent	e-Tongue results	
	Distance	Inhibition (%)
Quinine (0.2 mM)	198	0
Quinine + acesulfame K (5.0 mM)	118	40.0
Quinine + sodium acetate (100 mM)	100	49.5
Quinine + sodium chloride (100 mM)	110	44.4
Quinine + Presweet® flavor (0.5%)	165	16.7
Quinine + Debittering® flavor (0.2%)	145	26.8

Table 3
Inhibition of bitterness of quinine using different soft drinks determined by e-Tongue

Sample ID	Drug concentration (mg/mL)	Distance	Inhibition (%)
Quinine sulfate in water	0.5	525	0
Quinine sulfate in Sprite®	0.5	310	41.0
Quinine sulfate in Diet Sprite®	0.5	200	61.9
Quinine sulfate in Dr. Pepper®	0.5	251	52.2
Quinine sulfate in Coca-Cola®	0.5	399	24.0

Although e-Tongue technology is useful in optimizing a sweetener concentration in a formulation and evaluating taste enhancers and taste-masking flavors as discussed above, it has been found to be less useful in a comparative study between complex liquid formulations. Usually, a liquid formulation includes big portion of sugars and other sweeteners with small portion of taste enhancer, flavor, and viscosity modifier. However, optimization of a liquid formulation is mainly focused on taste enhancers and flavors. When assessed by e-Tongue, electronic signals are dominated by a large amount of sugars and sweeteners and thus small changes in the taste enhancer and flavor may not be detected in different formulations by the equipment. Improvement can be made in the future by optimization of taste sensors for higher sensitivity and selectivity.

3.4. Qualitative evaluation of bitterness of APIs

Although the sensors of e-Tongue used in this study are mainly used for the determination of similarity between two solution formulations, it may still be possible to utilize the equipment for a qualitative evaluation of compound bitterness. For a group of compounds, the group distance between a compound and water may indicate the degree of bitterness or taste.

Table 4
Comparative evaluation of known bitter drug substances using e-Tongue

Drug substance	Distance
Caffeine	102
Quinine HCl	686
Sucrose octaacetate	285
Phenylthiourea	680
Ranitidine HCl	804
Paracetamol	453
Prednisolone Na	695

A larger distance between water and a compound may imply stronger taste or bitterness for the compound. Thus, a relative rank order of bitterness could be obtained based on the distance data.

To test the hypothesis, several drug substances known to be bitter have been selected and evaluated by e-Tongue. All compounds were tested at the same concentration. Using multivariate statistical analysis, the group distance between a compound and water was calculated. Prednisolone and quinine are known to have a very bitter taste at the tested concentration while caffeine and sucrose octaacetate used as common food additives are less bitter. From our study, the group distance was 695 for prednisolone and 686 for quinine, which is much higher than that of caffeine at 102 (Table 4). This result from the e-Tongue indicates that the taste of prednisolone and quinine is much stronger than that of caffeine as expected. For other known bitter compounds tested, the group distance was 804 for ranitidine and 680 for phenylthiourea, 453 for paracetamol, and 285 for sucrose octaacetate, which are all higher than that of caffeine. Based on the group distance, the relative ranking of bitterness for these compounds would be in the following order:

$$\text{ranitidine HCl} > \text{prednisolone Na} > \text{quinine HCl} \sim \text{phenylthiourea} > \text{paracetamol} \gg \text{sucrose octaacetate} > \text{caffeine}$$

It is realized that this ranking method works only when a relationship between the bitterness of a compound and the distance from the e-Tongue is linear. However, it is not clear if such relationship is linear. Although our data indicated a correct ranking order for bitterness of prednisolone, quinine, sucrose octaacetate, and caffeine, additional study such as a human sensory panel or use of bitterness prediction module should be conducted to verify the feasibility for such application.

4. Conclusions

A multichannel taste sensor system, i.e. e-Tongue was evaluated for the feasibility of analyzing bitterness suppression of a formulation and comparison of taste intensity of chemicals in formulation development. The sensors appeared to be cross-selective for five basic tastes: sourness, sweetness, bitterness, saltiness, and umami. This cross-selectivity is exhibited by a different response profile for five basic taste components. To different concentrations of quinine, the response patterns of the seven sensors were similar while the electric outputs from each individual sensor differed slightly. The e-Tongue showed that the bitter taste of quinine could be masked to a certain degree by known bitterness-masking excipients including acesulfame K, NaCl, sodium acetate, NaCl, Prosweet® powder, and Debittering® powder. An e-Tongue can be used as a tool to optimize the level of a sweetener for masking bitter taste and to select an appropriate vehicle for reconstitution of drug-in-bottle formulation. In addition, several drug substances were evaluated for relative bitterness rank order, which was ranitidine HCl > prednisolone Na > quinine HCl ∼ phenylthiourea > paracetamol ≫ sucrose octaacetate > caffeine.

In conclusion, the multichannel taste sensor system may be a useful tool to evaluate taste-masking efficiency for a solution formulation, to develop a matching placebo, and to rank the taste or bitterness of new chemical substances.

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