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Taste sensor: *The pharmaceutical taste analyser*

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Abstract

Taste sensor is an intelligent electronic cum biophysical device that could be explored to artificially reproduce the sense of taste, which is otherwise a complex, comprehensive sense of man. Several kinds of foodstuffs, mineral waters and pharmaceutical formulations could be discriminated/differentiated easily using the taste sensor. Different electric potentials generated by chemical substances after interaction with the lipid/polymer membrane of the taste sensor is the basis of taste discrimination by the sensor. Hence, the taste sensors can be considered as a valuable tool in the evolution of bitterness intensity in function of time, which is essential in the selection of an optimal formulation. In the present study we have tried to explain the theory, composition and functioning of a taste sensor along with the potential applications of the same.

Key Words: Taste • Tastant • Taste masking • Bitterness • Lipid/Polymer membrane

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Introduction

Taste is a survival mechanism, alerting us to potentially harmful or potentially nutritious substances. The receptors for taste sensation are located in the taste buds. There are nearly 10,000 taste buds located on the tongue of young adults and a few are found on soft palate, inner surface of cheeks, pharynx and epiglottis. Each taste bud is an oval body consisting of three kinds of epithelial cells: supporting cells, gustatory cells and basal cells [1]. The gustatory system generally has two basic functions. The first is the clear distinction between the nutritive and beneficial compounds and the second is the detection of potentially harmful or toxic substances. Taste receptor cells must be able to detect wide range of tastes from simple ions to complex molecules [2].

Taste receptors can be categorized (on the basis of taste perception) into five primary categories: Sweet, Sour, Salt, Umami and Bitter

Sweet receptors respond to substances such as sugar, saccharin and some amino acids.
Sour receptors respond to hydrogen ions (H^+) or acidity of the solution.
Salty and Bitter receptors respond to metal ions in solution and alkaloids respectively.
Umami ("Delicious"), a taste discovered by the Japanese, is elicited by the amino acids.

Glutamate which appears to be responsible for the "beef taste" of steak and the flavor of monosodium glutamate, a food additive.

Taste Compounds
1) Sweet Sugar,Saccharin,Alcohols,Some Amino Acids
2) Sour Acids (HCl, Acetic acid, Citric acid)
3) Salt Metal ions, NaCl
4) Umami Mono sodium glutamate (Sea Weeds) Disodium inosinate (Meat, Fish)Disodium guanylate (Mushrooms)
5) Bitter Alkaloids (quinine,nicotine,caffeine,morphine) Aspirin, $MgCl_2$

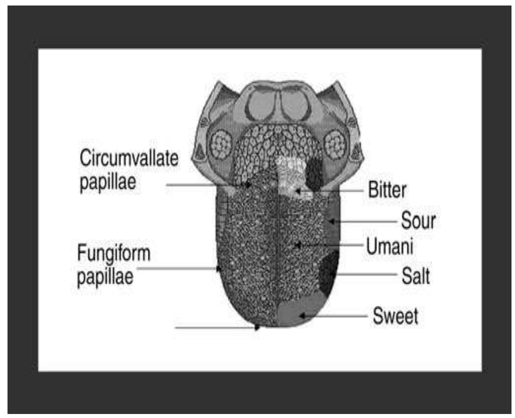

Table 1: Different compounds with there respective tastes.

Fig. 1: Location of various taste receptors on human tongue.

Biological Mechanism of Taste Perception

Human tongue that perceives taste is made up of cells. Taste papillae can be seen on the tongue as little red dots or raised bumps, particularly at the front of the tongue. Taste buds are a collection of cells on these papillae; the buds are generally invisible by the naked eye [3]. The cell's skin, biological membrane, consists of a double layer of lipid molecules and proteins. Lipids are oil-like substances contained in our bodies. Lipids are made up of the water loving (hydrophilic) part and the water hating (hydrophobic) part. There is a lot of water in both the inside and outside of the cell and hence lipid molecules make up a double layer on the biological membrane, with the hydrophilic part facing the inside and outside of the cell. In water, the membrane is electrically charged because the hydrophilic parts of lipid molecules are ionizing. Also, the inside and outside of the cell are full of different concentrations of salt-like substances.

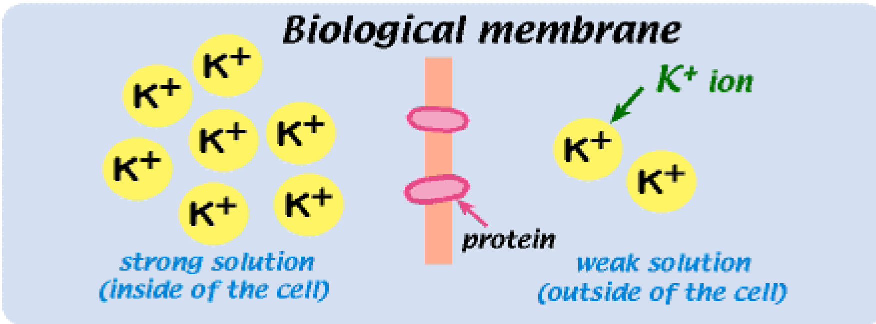

Fig. 2: **Flow of K^+ ions in biological membrane**

As shown in Fig. 2, K^+ ions flow from the inside to the outside of cell, because the membrane permeates to K^+ ions and the concentration is higher in the inside. This electric current due to K^+ ions flow causes the electric potential difference between the cell interior and exterior. It is called a membrane potential, which is affected by some kinds of chemical substances contained in the cell exterior [4].

Chemicals that stimulate gustatory receptor cells are known as tastants. When a tastant is dissolved in saliva, it makes contact with the plasma membrane of the gustatory hairs, which are the sites of taste transduction. The result is a receptor potential that stimulates exocytosis of synaptic vesicles which in turn liberates neurotransmitter molecules that triggers nerve impulses.

Taste Evaluation

Human sensory evaluation is the main method for the taste measurement of a drug substance or a formulation. This method requires a large, trained taste panel, elaborate analysis and sophisticated interpretation apart from being time consuming and expensive. Data derived by such a method is highly subjective, limited and potentially biased.

The electronic tongue apparatus: **Taste sensors / Biomimetic sensors / E tongue** offer a good solution to all these challenges. Some potential advantages of taste sensors include:

- As a quality control tool for flavored products and recipients.
- Measuring the efficiency of method of taste masking of bitter drugs. Development of optimized taste masked formulations.
- Quantifying bitterness of drug substances especially if the drug supply is limited.
- Benchmark analysis for carrying comparative studies on taste masking and other studies or analysis in which taste is involved.

Taste Sensor

The artificial taste sensors can be designed to mimic the mammalian taste sensors. The transducer is replaced by lipid polymer membranes that act as taste buds or taste recepting organs. The human brain is replaced by the computer which back propagates the signals or tastes received. The algorithm used for data processing is based on artificial neural network, which functions according to the learning and recognition pattern utilized by the human brain. It has been reported that a multi channel taste sensor whose transducer is composed of several kinds of lipid/polymer membranes with different characteristics can be used to detect taste. Taste information is transformed into a pattern composed of electronic signals of the lipid membrane potentials. The sensor measures taste quality since different substances produce different electric potential pattern. The lipid/polymer membrane is a soft, transparent film of 200 μm thickness.

Lipids used for preparing the membrane includes oleic acid, oleyl amine, decyl alcohol. Composition of lipids in the membrane depends upon the substance to be analyzed e.g. for amino acids measurements, hybrid membranes composed of dioctyl hydrogen phosphate and methyl trioctyl ammonium chloride are used. Commonly used polymers for preparing the membrane includes polyvinyl chloride and dioctyl phenyl phosphate [5,6]. Each lipid/polymer membrane is fitted on the part of a plastic tube, which has a hole, such that the inner part of the cylinder is isolated from the outside. The end of the cylinder is sealed with a stopper that holds an Ag/AgCI electrode. The tube is filled with 3 M KC1 solution. Eight detecting electrodes thus prepared were separated to two groups, and connected to two electrode holders, which could be controlled mechanically by a robotic arm, as illustrated in Fig. 2 [7,8].

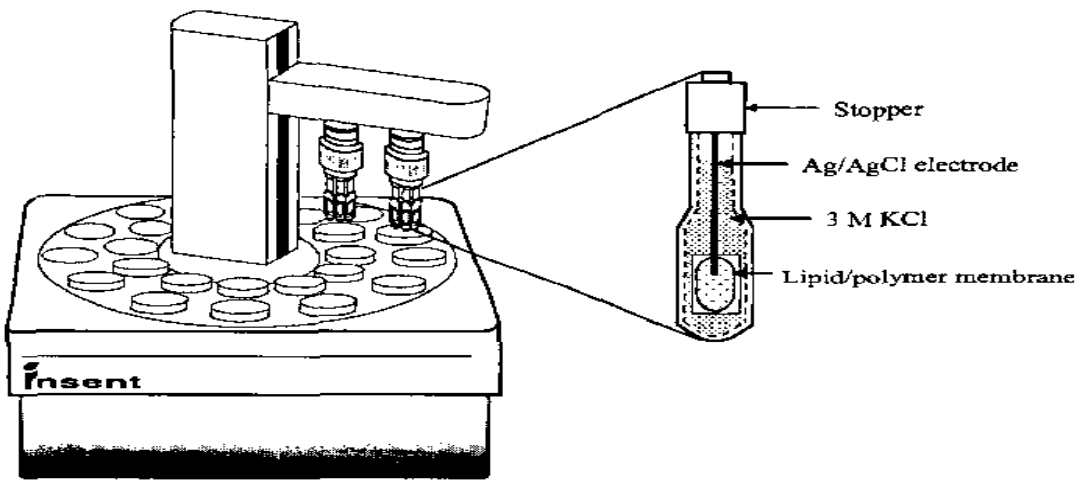

Fig. 3: Commercially sold taste-sensing system (SA402BJ Intelligent Sensor Technology, Inc.).

The artificial taste sensor, other wise known as 'Electronic Tongue' has been used for the estimation of food tastes by mimicking human gustatory system [6]. It consists of an array of sensing elements, and a data processing unit as an alternative for the human tongue and the brain respectively. The sensing element consists of an array of transducers that are nonselective and non-specific like that of human taste buds. The sensor array generates a pattern, which is in close proximity with the characteristics of the samples analyzed [6,8,9-14].

Fig. 4 illustrates the interaction between chemical substances to produce taste and a lipid/polymer membrane used in the taste sensor. Sodium ions producing saltiness make electrostatic interaction with the membrane, while hydrogen ions producing sourness bind to the hydrophilic part of the membrane. Umami taste substances such as MSG (Monosodium Glutamate) and IMP (Inosine Mono Phosphate) interact with the membrane accompanied with weak binding. Sweet substances accept protons from the membrane to result in the decrease in membrane potential. Bitter-tasting substances such as quinine and L-tryptophan penetrate into the hydrophobic part of lipid membrane to increase the membrane potential. In this way, the chemical nanostructures of taste substances are recognized by the lipid membrane by different mechanisms. The response electric potential is different for chemical substances showing different taste qualities in each membrane and, furthermore, is different in other membranes. The difference of reception mechanism is nothing but the difference of taste quality.

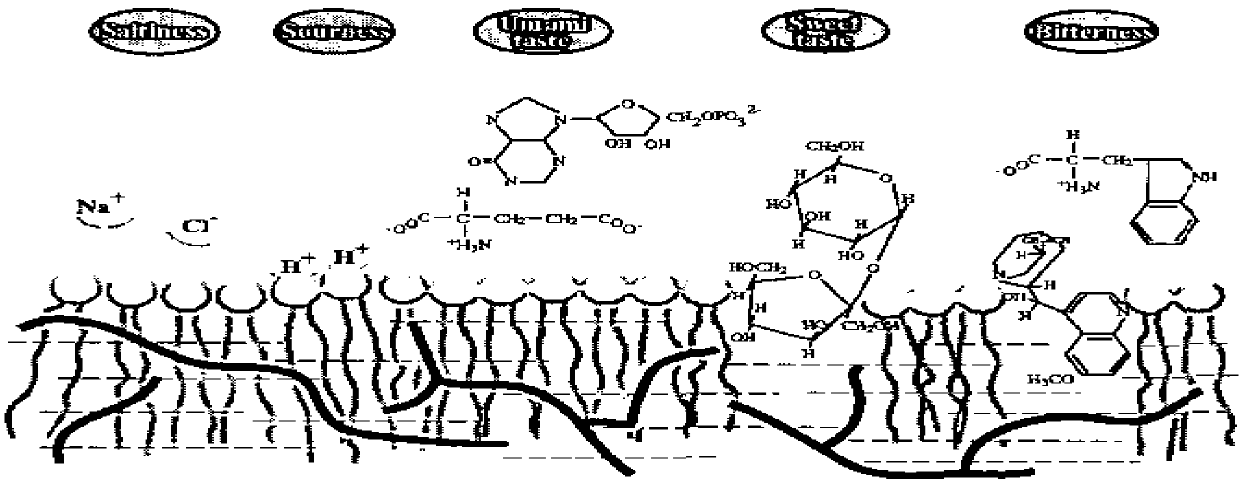

Fig. 4: Interaction between chemical substances to produce taste and lipid/polymer membrane. MSG and IMP are shown in umami taste, quinine and L tryptophan being shown in bitter taste.

General Applications

I) As a qualitative tool for checking hardness of water

Environmental pollution has diminished drinking water quality. Hence drinking water quality evaluation has become critical these days. Taste of mineral water is quite subtle and hence it is difficult for humans to discriminate between different brands of water. Hence taste sensors responds well to different kinds of mineral water. Even very low concentrations of taste substances can be easily discriminated between different brands of mineral water because of high sensitivity of taste sensors to ions [4]. Koseki et al. researched the pH dependence of the taste of alkaline electrolyzed water (AEW) made by electrolyzing bottled mineral waters by sensory evaluation using biomimetic sensors and concluded that electrolysis probably improved the taste of water with a higher calcium concentration by reducing the calcium concentration; however, the effect of electrolysis on water with a calcium concentration of 10 mg/L is likely to be the result of the pH increase alone [15]. The taste sensors are capable to distinguish between different types of mineral waters based on their high sensitivity to ions [16].

II) Effluent water analysis

Toxic substances in factory drains could be easily analyzed with taste sensors. Many pollutants such as CN^{-}, Fe^{3+}, Cu^{2+} could be measured in a few minutes with the detection limits lower than regulations of drain [4]. Nistor et al. evaluated the potential use of biosensors, not as quantitative tools for phenol analysis, but rather as screening tools indicating a certain trend, i.e. compounds present or not present, and potential correlation with sample toxicity and also studied the effect of several potentially interfering compounds on the sensor response [17].

III) Measurement of smell

Taste substances differ from odor substances in that they have low molecular weight and low volatility. Odorous ingredients can be extracted and concentrated from food samples by distillation using evaporator. Therefore "flavored water" can be prepared using these odorous extracts. Smell of food samples can be evaluated by subjecting flavored water to testing with the help of taste sensors [18].

Kataoka et al. experimented on bottled nutritive drinks and found a positive linear correlation between the intensities of sourness and bitterness determined by the human volunteers and those predicted by the taste sensor. The pungency intensity, as evidenced in gustatory sensation tests, was also predicted by sensor output and taste sensor seems therefore to be a potentially useful tool in evaluating the palatability of bottled nutritive drinks [19].

IV) Qualification of the beverages and food items

Taste sensors can be used as comprehensive tool for maintaining the quality of liquid beverages like beer thereby avoiding batch-to-batch variation in the taste of the beverages. While the sensors could be applied to beverages, it can also be used for analysis of the taste of gelatiniform or solid foods. When eating food, humans first masticate the food with their teeth and then taste it. Therefore, a mixer can be used in place of teeth for crushing the food item (whose taste is to be evaluated) before measuring their quality using taste sensors. Thus taste of food items could be easily qualified with sensitivity and selectivity with the help of taste sensors [4]. Moreover, these sensors can be used effectively as a quality control tool for discriminating between fresh and spoiled milk and to follow the deterioration of milk quality when it is stored at different temperatures or storage conditions [20]. Umami taste intensity of green tea has been graded meticulously by taste sensors. Sensory analyzed results showed high degree of correlation to the human gustatory sense [21].

Pharmaceutical Applications

I) Selection and optimization of appropriate taste masking agents / methods

Various taste masking agents could be screened for the effectiveness using taste sensors. Once appropriate taste masking agent has been identified, next step would be quantification of the masking agent. High sensitivity and selectivity of taste sensors is helpful for optimization of the concentration of the masking agent. However it has been found less useful in comparative studies between complex liquid formulations. Usually, a liquid formulation includes large portion of sugars and other sweeteners with small portion of taste enhancers, flavors and viscosity modulators. However optimization of a liquid formulation is mainly focused on taste enhancers and flavors while assessment of liquid formulations by taste sensors, electronic signals are dominated by a large amount of sugars and sweetness and flavors may not be detected [22]. These techniques may also be employed for the development of novel pharmaceutical taste masking technologies that can be conclusively optimized by taste sensors. Furthermore, these sensors could be used to evaluate the taste-masking and sustained-release characteristics of pharmaceutical formulations [23].

Hashimoto et al. worked on quantitative prediction of the bitterness-suppressing effect of sweeteners (sucrose or sugar alcohols) on the bitterness of famotidine (or quinine sulfate as control) solutions using an artificial taste sensor and concluded that the sugar alcohols in the tablet seem to be effective in the bitterness-suppression of famotidine from these tablets, especially in the initial phase (within 30 s) of the disintegration process [24].

Kayumba et al. evaluated quinine sulphate pellets for flexible pediatric drug dosing using electronic tongue. Eudragit E PO was used for coating quinine sulphate pellets. Selection of the optimal formulation among pellets having different coating thickness was made by electronic tongue that evaluated bitterness intensity in function of time [25].

II) Qualitative evaluation of bitterness of APIs

Taste sensors could also be utilized for the qualitative analysis of bitter compounds. Moreover artificial taste sensors could be used for quantitative bitterness prediction and comparative bitterness examination of bitter APIs [26]. Zheng and Keeney found that for a group of compounds, the group distance between a compound and water may indicate the degree of bitterness or taste. A larger distance between water and a compound may imply stronger taste or bitterness of the compound. Thus a relative rank order of bitterness could be obtained based on the distance data, which may further be a result of the taste sensing and technology. Prednisolone and quinine are found to be very bitter while caffeine and sucrose octaacetate (food additive) are less bitter. Based on group distance, the relative ranking of bitterness of these compounds would be in the following order: Ranitidine HCl > Prednisolone Na > Quinine HCl ~ Phenyl thiourea > Paracetamol > Sucrose octaacetate > Caffeine [22].

Kataoka et al. investigated the use of the artificial taste sensor in the evaluation of some medicinal plants and chinese medicines with bitter and/or astringent tastes, and assessed the possible application of the sensor in the evaluation of taste and quality control of medicinal products. Else more, the berberine content in extracts of medicinal plants was evaluated by the taste sensor, and it was shown to be possible to use the taste sensor for the quality control of medicinal plants [27].

Conclusion

Taste sensors can provide a technically suitable and cost effective method for screening and analyzing taste in the early stages of the development of API/formulations, thereby eliminating both safety concerns and subject bias effects. In conclusion, taste sensors may be useful in evaluating taste masking efficiency for a formulation, development of a matching placebo and for ranking the taste/bitterness of new chemical substances. Miniature sensor chips could be possible futuristic approaches for the development of widely applicable taste sensor technology in this new generation of the IT world.

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