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The latest trends in the taste assessment of pharmaceuticals

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To date, the most widely used method for measuring the taste characteristics of pharmaceutical preparations is psychophysical evaluation by a taste panel. However, conventional chemical analyses, on the basis of release studies, have been shown to be useful subsidiary methods. More recently, novel *in vitro* taste assessment apparatus and methodologies have been developed for high-throughput taste screening and quality control. Biomimetic taste sensing systems (BMTSSs), such as multichannel taste sensors or electronic tongues with global selectivity, have been welcomed by both pharmaceutical scientists and the industry as a whole. As we discuss here, the emerging *in vitro* approaches for assessing taste characteristics of taste masked drug and drug products will result in a decreased reliance on human panel tests.

Introduction

Taste has an important role in the development of oral pharmaceuticals, with respect to patient acceptability and compliance, and is one of the prime factors determining the market penetration and commercial success of oral formulations, especially in pediatric medicine. Hence, pharmaceutical industries invest time, money and resources into developing palatable and pleasant-tasting products and industries adopt various taste-masking techniques to develop an appropriate formulation.

Taste assessment is one important quality-control parameter for evaluating taste-masked formulations. Any new molecular entity, drug or formulation can be assessed using *in vitro* or *in vivo* methods for taste (Table 1). *In vivo* approaches include human taste panel studies, electrophysiological methods and animal preference studies. Several innovative *in vitro* drug release studies utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods have been reported in the literature for assessing the taste of drugs or drug products. The multichannel taste sensor, also known as the electronic tongue or e-tongue, is claimed to determine taste in a similar manner to biological taste perception in humans. Furthermore, such taste sensors have a global selectivity that has the potential to classify an enormous range of chemicals into several groups on the basis of properties such as taste intensities and qualities.

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In vivo approaches for taste assessment

In *in vivo* studies, stimuli are applied on to the tongues of either humans or animals. The stimulus interacts with receptors embedded in the membrane of the taste buds and the information is ultimately transduced as an electrical signal, which is further transmitted along the nerve fiber to the brain, where taste is perceived. Such studies include human taste panel studies, electrophysiological methods and animal preference tests.

Human taste panel studies

Human taste panel studies evaluate tastants (food, chemicals, drugs and so on) by estimating the gustatory sensation responses in healthy human volunteers within well-controlled procedures. Such studies are therefore also known as physiological evaluation, psychophysical evaluation, gustatory sensation tests, sensory tests or taste trials. They are sensitive measures of taste and are statistically designed to minimize bias and variable responses within

1359-6446/06/$ - see front matter doi:10.1016/j.drudis.2007.01.010

TABLE 1

The current status of *in vitro* and *in vivo* taste assessment approaches

Method	Description	Applications	Limitations
Taste panel studies	Sensory analysis of tastants in trained healthy human volunteers	Well established and standard method for the taste assessment of drugs and drug products	Extensive training, subjectivity, toxicity, low throughput, time consuming, human ethical issues
Electrophysiological methods	Response of tastants from glossopharngeal or chorda tympani nerve	Screening of new drug molecules, assessment of taste difference	Involvement of surgery, capital investment on equipments, low throughput, difficulties in data analysis and interpretation, animal ethical issues
Animal taste preference tests	Animal behavioural methodology to obtain data that parallels physiological investigations	Screening of new molecules by assessment of animal preference	Qualitative test, low throughput, animal ethical issues
In vitro drug release studies	Study of release of tastant from pharmaceutical formulations	Formulation development tool, quality control	Not applicable in case of liquid medicines, namely solutions
In vitro assay method	Biochemical assay involving measurement of activation of gustducin and/or transducin	Rapid-throughput screening of bitterness and bitterness inhibitors, determination of molecular mode of action	Not applicable in gustducin/transducin-independent taste modifiers
Biomimetic taste sensing systems	Electrochemical sensors coupled with chemometric methodologies for qualitiative and quantitative analysis	Rapid-throughput screening of tastants and taste-masking agents, formulation development and optimization, benchmark analysis, buccal dissolution simulation and quality control	Require completely dissolving or suspending the oral medicine in water

and between human volunteers. Well-established methodologies for performing sensory analysis can be broadly divided into five types, namely discrimination tests, scaling tests, expert tasters, affective tests and descriptive methods, and they have been excellently discussed elsewhere [1]. Volunteers assess the taste quality and intensity of standard and test stimuli on different adjective scales. Such scales include various properties of the sample, such as overall intensity, sweet, sour, salty, bitter, metallic, cooling, hot, spicy, burning, anesthetic, astringent, medicinal, minty/menthol, warming, sharp, alcohol, painful, irritating, stinging, dry, peppery and paper [2]. Each adjective can be rated on an intensity scale ranging from zero (none at all) to four or perhaps even up to nine points (with the highest point on the scale referring to the maximum intensity for each parameter) on provided score sheets. To develop temporal profiles, the intensity of adjectives is determined at different time points.

Animal preference tests

Bottle preference and conditioned taste aversion tests are used for determining taste preference and concentration-response properties of tastants by animals [3,4]. Rats, mice, cats and dogs can be used for conducting such preference determination tests. Attempts have been made to develop methodologies that can produce robust behavioral tests, capable of providing data comparable with those obtained from physiological investigations. A brief contact procedure has been studied to evaluate the ability of rats to detect the presence of a weak bitter compound dissolved in a strong sucrose solution. These results demonstrate the acute ability of rats to discriminate, by taste, not only the presence but also the concentration of a dilute bitter compound dissolved in a strong sucrose solution [5]. Rat behavioral avoidance models that identify bitter-tasting compounds have been validated and might well serve as a useful surrogate test to identify compounds that illicit a bitter taste [6].

Electrophysiological methods

Electrophysiological recordings from animals [7], primate [8] and human taste nerves [9] have provided insights into the physiology of taste sensation. Responses of tastants from single glossopharangeal or chorda tympani nerve fibers or nerve bundles can be utilized for taste assessment [10]. Mice [11], bull frogs *(Rana ctesbeiana)* [12,13] or gerbils (*Meriones unguiculatus*) [2] have all been described in the literature in this respect. In these tests, the animal is anaesthetized, following which electrodes are implanted in the chorda tympani nerve bundle and/or glossopharyngeal nerve. Tastant solutions are then passed over the tongue for a controlled period. Electrophysiological recordings from the chorda tympani and/or glossopharyngeal nerve provide a means of directly measuring the temporal profiles or dose response curves of taste stimuli [11]. Taking recordings from single taste nerve fibers is useful for gathering information about the taste quality of the samples. Following exposure to the tastant, the animal tongue is rinsed with deionized water to measure the recovery from the stimulant.

In vitro approaches for taste assessment

Release studies are commonly used in taste assessment to measure the effectiveness of coating and complexation within a formulation (Figure 1a). They are indirect methods for assessing taste because the methods do not contribute to the evaluation of taste and sweetness of the drug product. Novel drug release apparatus and pharmacopoeial apparatus have both been adapted to simulate buccal dissolution of dosage forms so as to compare taste in different pharmaceutical formulations. Such novel apparatus and

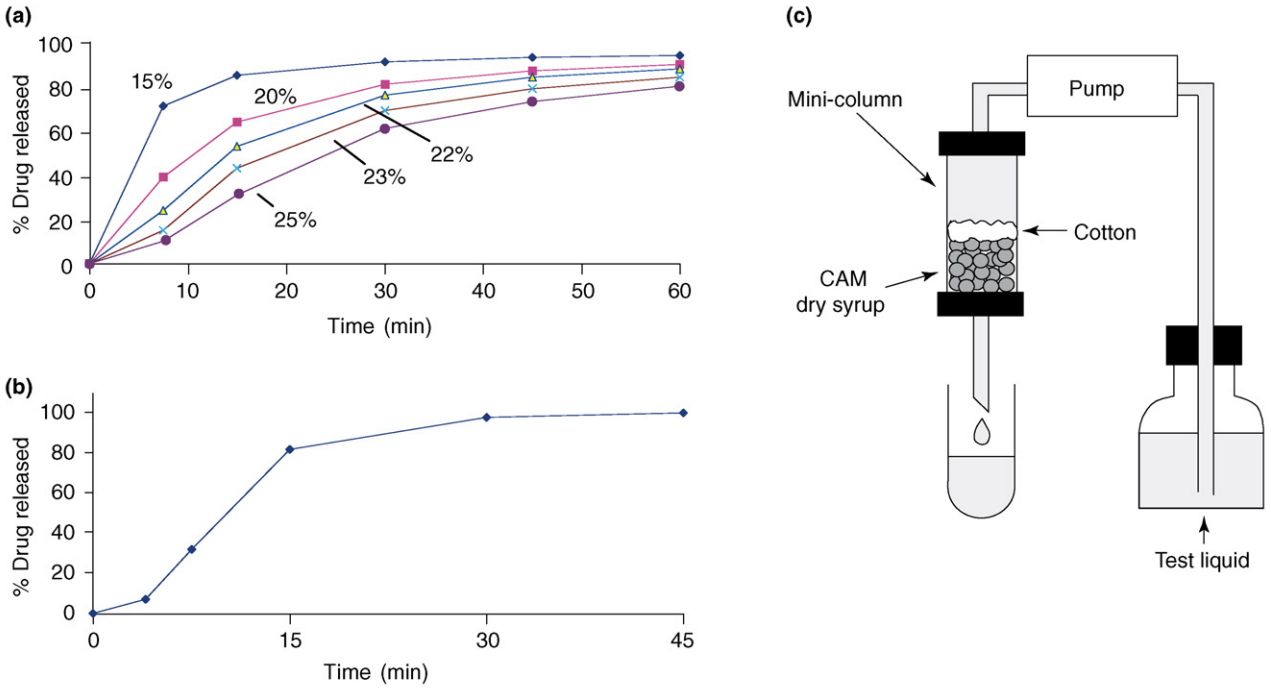

FIGURE 1

Taste assessment by performing *in vitro* drug release studies **(a)** The dependence of dissolution on taste mask-coating thickness for bulk, taste-masked pseudoephedrine HCl particles. The percentage of drug released is indicated by diamonds (15%); squares (20%); triangles (22%); crosses (23%) and circles (25%). **(b)** Early time-point analysis in a simulated ideal dissolution profile for taste masked product. **(c)** A novel mini-column apparatus for evaluating the bitterness of dry syrups. Reproduced, with permission, from Ref. [21] (a,b) and Ref. [15] (c).

methods for drug dissolution or release studies tend to simulate the release of bitter or undesirable tasting drug in the mouth. The *in vitro* biochemical assay of gustducin and/or transducin can also be used for the high-throughput taste assessment of new molecular entities (NMEs).

In vitro drug release studies

Pharmacopoeial release tests have been modified by altering the chemical composition of the dissolution media (e.g. artificial saliva) and reducing the size of the basket screen size (screen size <0.381 mm square opening) to prevent particles from escaping. Taste masking is achieved when, in the early time points from 0 to 5 min, the drug substance in the dissolution medium is either not detected or the detected amount is below the threshold for identifying its taste (Figure 1b). Drugs can be analyzed either spectrophotometrically or using HPLC. Of these, HPLC is generally preferred, especially when testing is performed in the presence of UV-absorbing components, such as flavourings and sweeteners. Furthermore, the drug signal is frequently indistinguishable from background in the UV estimation when there is a high excipient:-drug ratio in the taste-masked formulations.

The degree of masking of bitter taste from fine granules has been evaluated using a simplified *in vitro* dissolution test [14–16]. Either fine granules, dry syrup or powder containing drug are gently mixed with a small amount of distilled water in a syringe by revolving the syringe. Thereafter, concentrations of drug in the ultrafiltrate, obtained by passing through a pore size of 0.45 μm, are determined either spectrophotometrically or using HPLC.

An HPLC method has been developed and validated to determine the coating integrity of topiramate sprinkle formulations [17]. The sprinkles are placed in a specially designed stainless steel basket equipped with a 25-mesh screen at the bottom. Water is used to solubilize any incompletely coated drug. The aqueous solution is analyzed for topiramate using a phenyl column in the reversed-phase mode, using isocratic elution, and refractive index detection. Drug release studies have been performed using mini-columns (Figure 1c) to determine the taste-masking efficiency of dry syrup [15].

A novel *in vitro* buccal dissolution testing apparatus and method for the assessment of taste masking in oral dosage forms have recently been invented [18]. The apparatus consists of a single, stirred, flow-through filtration cell including a dip tube designed to remove fine solid particles. Simulated saliva is used as the dissolution medium. The filtered solution is removed from the apparatus continuously and used to analyze the dissolved drug. The method enables the relative prediction of taste intensity of dosage forms. The method is rapid, taking only 20 minutes to complete, and is repeatable.

A taste recognition system and method has been devised that is, in principle, a flow-through system [19]. The system comprises a holding section, for holding the object to be recognized, a delivery flow path, for delivering the solvent to the holding section, and a taste sensor, for measuring the taste of the solvent that has flowed through the holding section. Both the holding section and taste sensor are maintained at constant temperature. Simulated saliva is passed through the holding section at a rate of ~1 ml min^{-1}. The

holding section consists of a chamber that holds the substance, that is, powder, granules or microcapsules, to be characterized for taste. The dosage form is dissolved or suspended in simulated saliva. The taste of the substance can be assessed using lipid membrane taste sensors (LMTSs), ion-sensitive field effect transistors (FETs) or other newly developed taste sensors that measure the taste characteristics of simulated fluid that has flowed through the holding section. Thus, the taste characteristics of the drug product can be measured in a solid state when it is unnecessary to dissolve drug product in the solvent.

According to FIP/AAPS guidelines [20], specifically for coated particles or granules in orally disintegrating tablets (ODTs), the relative assessment of taste is performed using release studies in a neutral pH medium to establish an approximate baseline for early time-point (e.g. $\leq$5 min) dissolution values (Figure 1b). 'Such a dissolution criterion (typical example: $\leq$10% dissolved in five minutes) would largely depend on the taste intensity of the drug and might enable the *in vitro* evaluation of the taste masking properties while avoiding organoleptic measurements' [20]. Taste-masked ODTs should be formulated in a manner such that the delay in drug release needs only to be long enough to pass through the oral cavity, followed by fast and complete release as for any immediate release dosage form [21].

In vitro assay methods

Gustducin and transducin are guanine nucleotide-binding regulatory proteins (G proteins) expressed in taste receptor cells (TRCs). Gustducin is selectively expressed in 20–30% of TRCs in the palate and all taste papillae, and in apparent chemosensory cells in the gut and the vomeronasal organ [22]. Most bitter stimuli can activate both transducin and gustducin, and this activation depends upon receptors in the taste-bud membrane [23]. The activation of gustducin and/or transducin in the presence of the taste-bud membrane can be measured to identify certain bitter tastants, determine molecular mode of action, quantitatively determine potency profiles and screen chemical libraries for potential bitterness inhibitors [24]. Not all the bitter compounds demonstrate *in vitro* activity (gustducin-independent taste modifiers, e.g. caffeine and aristolochic acid), which could be due to the presence of multiple transduction pathways. Furthermore, gustducin and/or transducin are not activated in the presence of sucrose, glycine, monosodium glutamate, citric acid or potassium chloride.

Biomimetic taste sensing systems (BMTSSs)

The use of multivariate data analysis (MVDA), combined with sensors that have partially overlapping selectivities, has become an incredibly powerful tool in taste measurement technology. Such systems, often referred to as artificial senses, emulate biological taste reception at the receptor level, the circuit level and the perceptual level (Figure 2). BMTSSs have been marketed as taste sensors, or electronic tongues or e-tongues [25,26]. These instruments employ electrochemical sensors coupled with chemometric methodologies to perform qualitative and quantitative analyses of organoleptic and chemical properties of substances and products. The data can be processed using MVDA, either to search for correlation within the data or to develop predictive models. BMTSSs have been shown to be globally selective for detecting and quantifying specific classes of chemical compounds [27]. They do not discriminate minute differences in the structure of compounds but can transform molecular information from interactions with biological membranes into several types of group, that is, taste intensities and qualities [28]. Taste sensors therefore act as intelligent sensors to reproduce the complex and comprehensive taste sense of humans. Global selectivity signifies the quantification of a combination or mixture of various types of substances that result in a compound effect, such as a synergistic effect or suppression effect amongst the substances. Flavour, odour and contamination by organic substances (such as humic substances) are some examples of this compound effect. Furthermore, taste sensors have the ability of molecular recognition to distinguish chemical substances even in the same group of taste; for example, the patterns for hydrochloric acid, citric acid and acetic acid are slightly different [27]. Thus, the global selectivity concept is based on the recognition of the response patterns that characterize different classes of chemical compounds through the use of electronic sensor(s).

Lipid membrane taste sensors

LMTSs capitalise upon the properties of lipids, which participate in the natural process of taste. The sensors are formed by dispersing the lipid compound responsible for transducing the signal on to a polymeric matrix that is normally non-conducting, such as polyvinyl chloride [28–33]. Such sensors analyze, in a nonspecific manner, detected signals and hence can extract the inherent taste characteristics of substances [26].

Taste substances cause changes in the electric charge density of the lipid–polymer membrane surface and/or ion distribution near the surface of the membrane of the sensor. The total electric change is given as the response membrane electric potential for the substance tested. The sensor output shows different patterns for chemical substances that have different taste qualities, such as saltiness and bitterness, whereas it shows similar patterns for chemical substances with similar tastes. LMTSs have been used for the evaluation of taste, water quality and pollution in rivers [32,33]. They have been extensively studied and used for analysing beers, mineral water, coffee, milk, food products, drug products [34–40], bitterness inhibitors [41–43] and for environmental monitoring [27,28,44].

The taste-sensing systems SA401 and SA402

Two specific LMTSs, SA401 and SA402, have been developed by Anritsu Corporation together with researchers at Kyushu University in Japan. The detecting sensor part of the systems consists of seven (SA401; Anritsu Co., Ltd, Japan; Figure 3a) or eight (SA402; Intelligent Sensor Technology, Inc., Japan; http://www.insent.co.jp; Figure 3b) electrodes made of lipid–polymer membranes. Different types of lipid are used for preparing the membrane (e.g. oleic acid, oleyl amine, decyl alcohol and so on) depending upon the material being measured. Each lipid is mixed in a test tube containing polyvinyl chloride and dioctyl phenyl phosphonate as a plasticizer, dissolved in tetrahydrofuran, and dried on a glass plate at 30 °C to form a transparent thin film, almost 200 μm thick.

Lipid or polymer membranes are fitted on a multichannel electrode that acts as the detecting electrode. The detecting electrode of each channel is made up of silver wires plated with Ag/AgCl, which is kept in holes filled with 3 M KCl solution. The electrode is connected to a scanner through high-input impedance

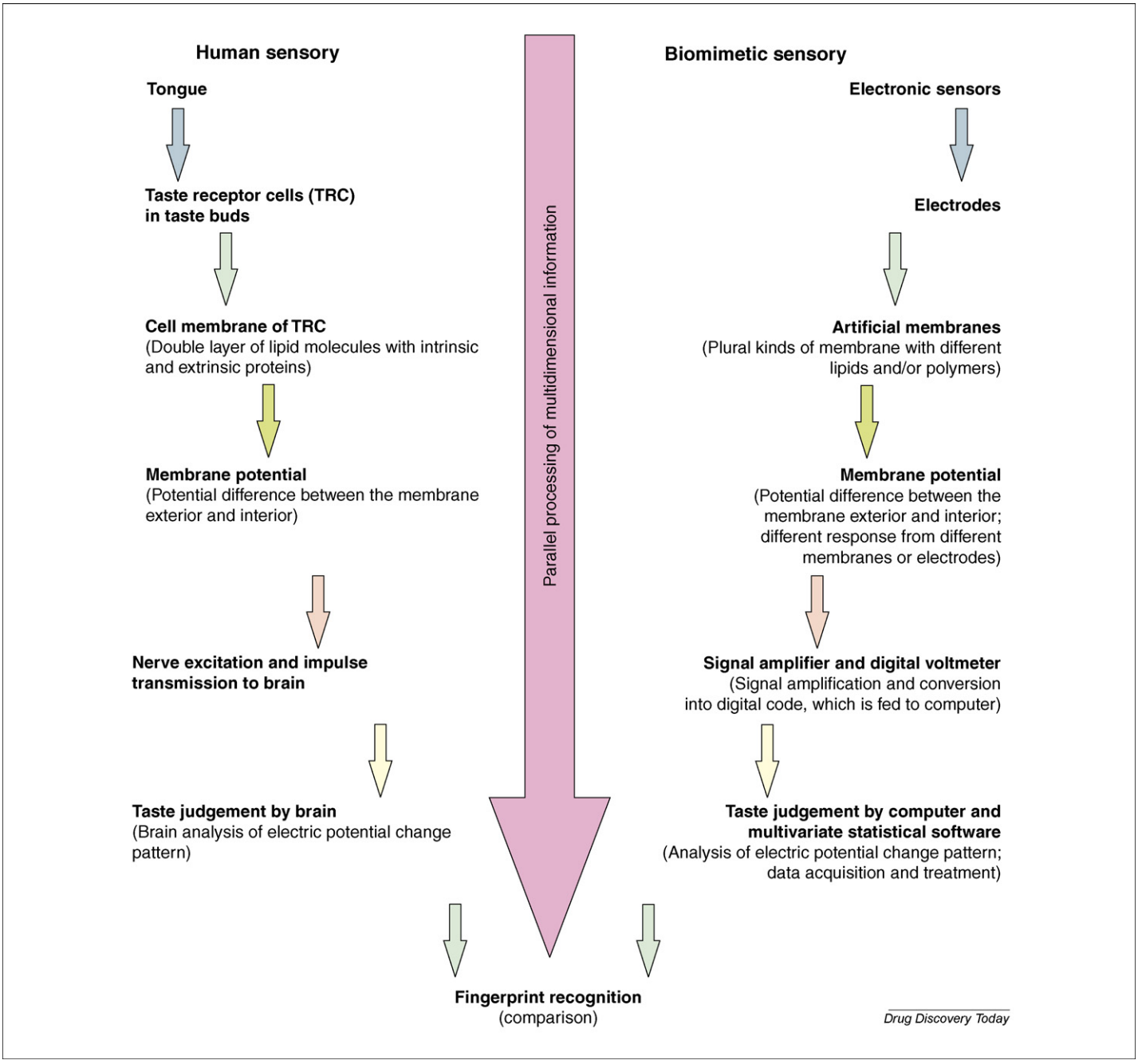

FIGURE 2

Development of taste sensors on the basis of mechanisms found in biological systems.

amplifiers. The voltage difference between the multichannel detecting electrode and an Ag/AgCl reference electrode is measured with active and placebo formulations. The potentiometric response data from all probes for active formulations and placebo formulations are compared using principal component analysis (PCA) mapping. Thus, lipid membranes immobilized with a polymer act as transducers, converting the taste sensation into an electronic potential pattern [26–28].

Ion-sensitive field effect transistors

FET taste sensors are prepared by pasting artificial lipid–polymer membranes of the same composition, as in LMTS above, on to the gate of a FET. The FET taste sensor has the same sensitivity to taste substances as LMTS, but the potential reproducibility is less than that for LMTS and the lifetime is shorter for miniaturized devices [27]. Ion-sensitive FET sensors determine ions present in solution (e.g. mineral water and wines). They detect ions in solutions through the use of selective membranes containing dispersed amorphous semi-conductors (i.e. polyvinyl chloride membranes containing dispersed semiconductors) and conventional electrodes [37,45,46]. Such sensors do not permit the detection of non-polar substances, such as coffee, for example, or those that do not form electrolytes, such as saccharose. Ion-selective electrodes have been proved to be useful in studies of masking mechanisms of bitter taste, in estimating appropriate concentrations of masking agents and in the screening of masking agents [41].

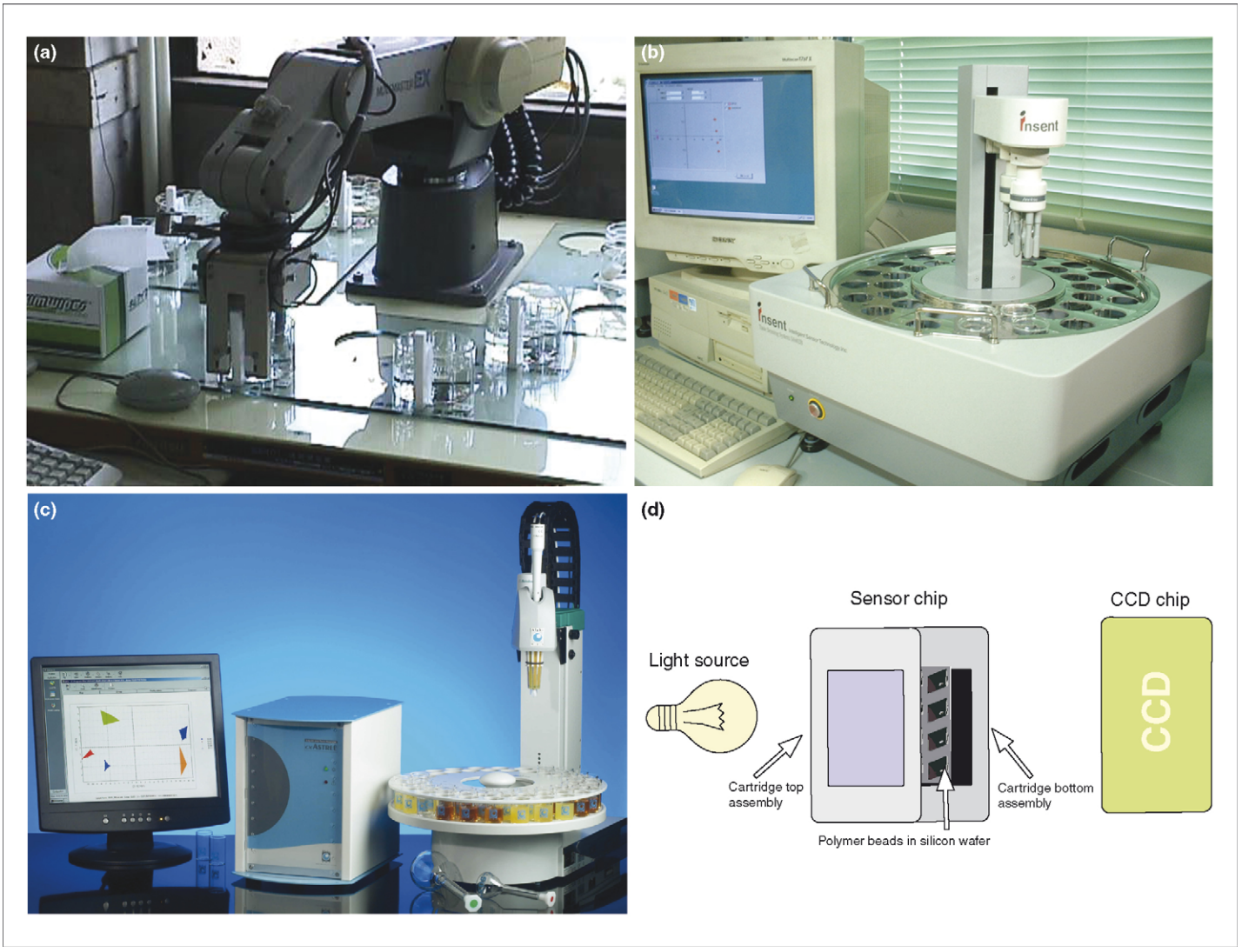

FIGURE 3

Commercially developed and developing taste sensors. **(a)** Taste sensor SA 401 developed by Anritsu Corp. **(b)** Taste sensor SA 402 B developed by Intelligent Sensor Technology. **(c)** Astree electronic tongue developed by Alpha M.O.S. **(d)** A schematic of the electronic tongue developed by the University of Texas and Vusion. Reproduced with permission from http://ultrabio.ed.kyushu-u.ac.jp/A9912/katudo/sensor_e.html (a,b); http://www.alpha-mos.com/en/pharma/pharma_astree.php (c).

Astree electronic tongue

The Astree electronic tongue system (Alpha M.O.S.; http://www.alpha-mos.com; Figure 3c) is a taste-sensing instrument equipped with a seven-sensor probe assembly for qualitative and quantitative analysis [47]. It is fully automated, with 16 or 48 positions for formulation samples. The probes consist of a silicon transistor with proprietary organic coatings that govern the sensitivity and selectivity of the probe. Tastant molecules in the sample interact with the proprietary organic coating, which modifies the physical properties of the sensor, resulting in potential variations. The measurement is potentiometric, with readings taken against an Ag/AgCl reference electrode. Each probe is cross-selective to enable coverage of the full taste profile. The system samples, quantifies, digitizes, records and processes potentiometer readings with multivariate statistical tools integrated with software.

The system can be combined with a solid foam dynamic analyzer (S-FDA) to measure, dynamically, the taste of drug in solid dosage forms during their dissolution phase for simulation of the buccal dissolution mechanism, to measure tablet coating dissolution and to check the effectiveness and homogeneity of the coating on different dosage forms when dissolving. Thus, the system provides methods for obtaining taste and dissolution data simultaneously.

Voltammetric electronic tongue

The voltammetric electronic tongue, developed by S-Sence, consists of four working metal electrodes made of gold, iridium, platinum and rhodium, an Ag/AgCl reference electrode and a stainless steel counter electrode [48]. A relay box enables the working electrodes to be connected consecutively, to form four standard three-electrode configurations. The potential pulses/steps are applied by a potentiostat which is controlled by a personal computer (PC). The PC is used to set and control the pulses, measure and store current responses, and to operate the relay box. Voltage pulses are applied to the working electrode and the resulting current is measured. A hybrid electronic tongue has

TABLE 2

Features of commercially available BMTSSs and their applications in the pharmaceutical industries

Features	Lipid membrane taste sensors	Ion selective field effect transistors
Sensors	Potentiometric sensors with thick film polymer membrane based on polyvinylchloride	Liquid sensors based on ChemFET technologies
Principle of detection	Potential variations	Potential variations
Compounds detected	Dissolved	Dissolved
Sensitivity	Inorganic and Organic	Inorganic not organic
Sampling	Autosampler	Autosampler with 16 or 48 beaker positions
Commercial apparatus	Taste sensing system SA 401 and SA 402	Astree electronic tongue
Applications		
Bitterness measurement of new molecular entities, drugs, excipients and various formulations thereof		
Determination of bitterness masking efficiency and screening of best excipients, additives, and taste agents (sweetener, flavor and taste-masking agent)		
Placebo development with the same taste as the formulation		
Optimization of taste masked formulations and scale-up of formulation process		
Comparison with competitor products (benchmark analysis)		
Simulation of buccal dissolution and tablet-coating dissolution		
Homogeneity and effectiveness of coating during dissolution		
Measuring efficiency of complexation within formulation		

also been developed, based on the combination of the measurement techniques potentiometry, voltametry and conductivity [49–51]. It has many useful applications, including the continuous monitoring of milk in the dairy industry, in the water-cleaning process, in dishwater processes, to follow fermentation during yoghurt fabrication, as an instrument to detect trace amounts of, for example, cadmium, lead or copper in soil, and for the continuous monitoring of the chemical oxygen demand (COD) in the paper and pulp industry.

Electronic tongue developed by the University of Texas and Vusion, Inc.

The electronic tongue initially developed by the University of Texas consists of a light source, a sensor array and a detector [52]. The light source shines onto chemically adapted polymer beads arranged on a small silicon wafer, which is known as a sensor chip. These beads change colour on the basis of the presence and quantity of specific chemicals. The change in colour is captured by a digital camera and the resulting signal converted into data using a video capture board and a computer (Figure 3d). The technology can be applied to the measurement of a range of chemical compounds, from the simple, such as calcium carbonate in water (which effects water hardness), through to complex organic compounds, such as haemoglobin in blood and proteins in food. Moreover, it is helpful in discriminating mixtures of analytes, toxins and/or bacteria in medical, food/beverage and environmental solutions. As a result, the electronic tongue has many potential uses in the food, beverage, chemical and pharmaceutical industries. Vusion, Inc. (http://www.businessplans.org/Vusion/Vusion00.html) is developing a chemical analyzer and sensor cartridge, based upon the electronic tongue technology of University of Texas, that can instantly analyze complex chemical solutions. The analyzer consists of a customized housing into which the sensor cartridge can be placed and exposed to liquid chemicals within a process plant.

BMTSSs have been used extensively to evaluate the taste-masking efficiency in solution formulation to compare the bitterness intensity of formulations and drug substances during pharmaceutical research and product development [53,54]. These sensors are safe, sensitive, reproducible, durable, fast and cost-effective, and require almost no sample preparation. The methodology is easy to speed up and optimize, and is well accepted and established for almost all dosage forms [55]*. The taste sensor is of great value to both the food and pharmaceutical industries, in quality control and in assisting the automation of production [26]. Commercially available taste sensors and their applications in pharmaceutical industries are compared in Table 2. The results from these systems correlate well with human tongue and HPLC analysis. The systems do not fatigue, particularly with respect to bitterness, as is found with the human tongue. Taste sensors have been found to be useful in screening new substances for bitterness when human tasting is not possible because the requisite toxicological data are not available [53]. In most of the studies, the electronic tongue can differentiate between tastes, but in a very few cases it ranked masking agents in a different order than that determined by human volunteers [56]. When the taste of an oral medicine, other than a liquid medicine, is recognized by using such a taste sensor, the taste is measured by completely dissolving or suspending the oral medicine in water, which is impractical and undesirable.

The potentiometric e-tongue, incorporating an array of artificial lipid–polymer membranes as a fingerprint device, has been developed as a promising tool for use in the quality control of

* Murray, O. *et al.* (2004) Utilizing the Astree electronic tongue to quantify taste masking approaches in the development of Zydis® orally disintegrating tablets (ODTs). *AAPS Annual Exposition* (http://www.alpha-mos.com/docs/pharma/2004_aaps_cardinal_health_poster.pdf.) and (http://www.cardinal.com/pts/content/aboutus/whoweare/posters/AAPS%202004%20-%20OJM.pdf).

phytomedicines [38]. The miniaturization of taste sensors is of particular interest for the food and pharmaceutical industries. A portable, low-cost sensing system has been made that interfaces to a voltammetric electronic tongue sensor [57]. Screen printing technology has been used to develop a disposable taste sensor [58]. The use of the sequential injection analysis (SIA) technique in a potentiometric e-tongue, operated as a virtual instrument implemented in LabVIEW6.1 (software), has been reported to achieve improvements in complete automation, ease of handling, time saving, reliability and modularity [59].

Conclusions

Human taste panels are preferred for assessing the taste of drugs or formulations, but their use is limited because of the subjectivity of panel members, potential toxicity and liability issues. Further problems are found in recruiting, motivating and maintaining taste panellists, which becomes a particularly difficult task when working with unpleasant molecules, drugs or drug products. NMEs cannot be ethically tasted by human beings because of the lack of appropriate toxicological data. Even in the case of new nontoxic drugs, finding human volunteers for taste assessment is an arduous mission. Moreover, animal preference tests might be of little use in assessing the taste of NMEs. The results from such tests are extrapolated, which might or might not be accurate because it is assumed that a molecule disliked by the animal might be bitter. Electrophysiological methods involving animals are difficult and costly because of the requirement for surgery and they are not amenable to the screening of a large number of samples. The *in vitro* biochemical assay of gustducin and/or transducin can be used to identify and determine the concentration response function of many bitter compounds. It can also be used for the rapid-throughput screening of high-potency bitterness inhibitors. *In vitro* buccal dissolution methods and other *in vitro* drug release studies enable the relative prediction of the taste intensity of dosage forms.

The advancement of electronic sensing of taste and the development of taste sensors has reduced the tension associated with the taste assessment of new molecules. Furthermore, the burden on taste panels and animals for taste assessment is reduced. New regulatory guidelines, for testing and evaluation of age-adapted dosage forms meant for geriatric and pediatrics, will emphasize the need to conducting taste studies in special populations. The overall impact will limit the use of humans in taste assessment. There has been an increase in the number of *in vitro* studies using either taste sensor or innovative apparatus for drug release studies. Taste-sensor output is similar to that of the biological gustatory system, which further advocates its application to the taste assessment of not only drugs and formulations, but also new molecular entities. *In vitro* approaches should therefore be useful both in the development of more desirable and palatable dosage forms and in high-throughput taste assessment.

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