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Review Article

Recent Trends on Achieving Taste Masking of Bitter Drug

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Abstract

Taste is most important organoleptic aspects about the acceptance of oral drugs. Bitter and unpalatable taste is a major problem of certain drugs in formulations. In market, there are numbers of pharmaceutical preparations available in which actives are bitter in taste. The improved palatability in these products has prompted the development of numerous formulations, which improved performance and acceptability. The bitterness of preparation also leads to patient incompliance. So masking of bitterness becomes essential and done by masking the bitter taste of drugs by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste buds thereby reducing the perception of bitter taste. Methods commonly used for taste masking involves various physical and chemical method that prevent the interaction of taste bud with drugs and are based on coatings, solid dispersion system and ion exchange resin, entrapment method etc. Taste masking of bitter drugs become necessity in case of oral administration and selection of technology depends upon the bitterness of drugs and their compatibility with taste masking agents that does not affect the bioavailability of drug.

Keywords: Taste buds, Taste masking, Microencapsulation.

1. Introduction

Taste is an important factor in the development of dosage form. Although it is overlooked it is the part of product development. The problem of bitter and obnoxious taste is challenge to the pharmacist in the present scenario. Many different oral pharmaceuticals and bulking agents have unpleasant, bitter-tasting components. So many different formulations are developed with a desire to improve the palatability by improving performance and acceptability. Current state of the art taste masking technology uses microencapsulation techniques which rely primarily on polymer coating materials. These polymers are known to be permeable to aqueous solvents. Upon exposure to an aqueous environment, drug leaching is a frequent occurrence with these coatings since they are greatly porous and therefore permeable to water.

In addition, their effectiveness for taste-masking purposes is acknowledged as being less than perfect.[1] The biological definition of taste (gustation) is a chemical reaction derived from sensory responses from the four main taste perceptions: salt, sour, bitter, and sweet. Two other perceptions (umami and trigeminal) should be included when considering taste. Umami is derived from the presence of glutamate, such as monosodium glutamate, resulting in the fullness sensation from certain foods. Trigeminal is the burning sensation derived from such foods as spices and peppers. Fig. 1 shows the location of the sensors for these four perceptions around the tongue.

Fig. 1: Diagram of the tongue surface showing localized taste buds.

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1.1 Mechanism of action

Molecule interacts with taste receptor on the tongue to give bitter, sweet or other taste sensation, when they dissolve in saliva. This sensation is the result of signal transduction from the receptor organs for taste, commonly known as taste buds. These taste buds contain very sensitive nerve endings, which produce and transmit electrical impulses via the seventh, ninth and tenth cranial nerves to those areas of the brain, which are devoted to the perception of taste.[2]

Table 1: Compound categorization for taste perception.

Taste perception	Compounds
Sweet	Sugars, saccharin, alcohols,
Sour	Acids (dissociation of H_ in solution)
Salt	Metal ions (inorganic salts)
Umani	Amino acids (glutamate)
Bitter	Alkaloids (quinine, nicotine, caffeine, morphine) and non alkaloids. Donepezil, Ofloxacin etc.

1.2 Taste signalling pathways

Taste transduction begins with the interaction of attractant (eg. medicine or food) with taste receptor cells in the taste buds. The tastant binds with G-Protein coupled receptors (GPCRS) in the cells triggering the release the release of G-Protein called Gustducin.

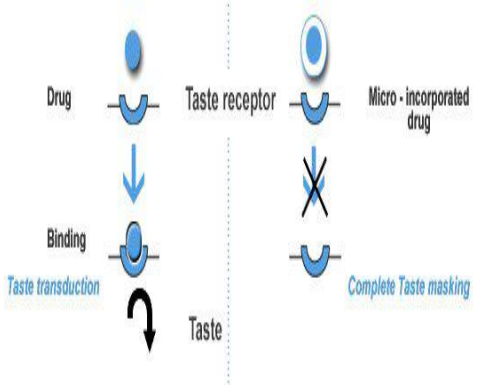


Fig. 2: Taste Signalling Pathway.

The process of taste sensation begins when Gustducin activates the effector enzymes phosphodiesterase IA (PDE) or phospholipase C beta-2(PLC). The effector enzyme then changes the intracellular level of second messenger such as cyclic adenosine monophosphate (cAMP), Inositol, 1, 4, 5-triphosphate (IP3) and diacylglycerol (DAG). The second messengers activate ion channel including calcium channel inside the cell and sodium, potassium and calcium channel on extra cellular membrane. This ionization depolarizes the cell causing the release of neurotransmitters that send nerve impulses to the brain that carries the signal of bitter taste and taste blockers work by interfering with taste transduction

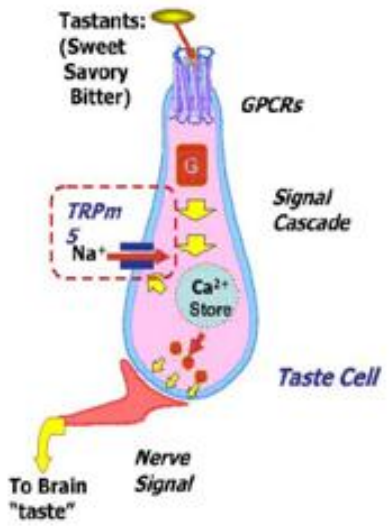


Fig. 3: Taste Signalling Pathway.

1.3 Need for taste masking

There are numerous pharmaceuticals that contain active ingredients which are bitter in taste .now a day most of the drug that may be cardiac, analgesic, anti-inflammatory, diuretic, opioid analgesic, anti-epileptic, anticoagulant, oral vaccine and sex harmones. Most of them bitter in taste With respect to OTC preparations, such as cough and cold syrups, the bitterness of the preparation lead to lack of patient compliance. The problem of bitter and obnoxious taste of drug in pediatric and geriatric formulations is a challenge to the pharmacist in the present scenario. In order to ensure patient compliance bitter taste masking becomes essential.

Approaches to overcome bad taste

Two approaches are commonly utilized to overcome bad taste of the drug.

1. Reduction of drug solubility in saliva, where a balance between reduced solubility and bioavailability must be achieved.
2. Alter the ability of the drug to interact with taste receptor.

1.4 Ideal taste masking properties

An ideal taste masking process and formulation should have the following properties**.**

1. Involve least number of equipments and processing steps.
2. Require minimum number of excipients for an optimum formulation.
3. No adverse effect on drug bioavailability.
4. Require excipients that are economical and easily available.
5. Least manufacturing cost.
6. Can be carried out at room temperature.
7. Rapid and easy to prepar.[3]

1.5 Therapeutic agent with unpleasant taste

Table 2: Therapeutic agent with unpleasant taste.

Class	Drug
Antibiotics	Ampicillin, Cloxacillin, Pivampicillin, Azithromycin, Chloramphenicol, Erythromycin, Clarithromycin
Antitussives	Codeine phosphate or sulphate, Dextromethromethorphan
Laxatives	Dioctyl sodium Sulphosuccinate
Antihistamines	Azatidenameliate, Brompheniraminen maleate, Bromdipheniramine HCl, Chlorpheniramine maleate,
NSAIDs	Fenbufen, Fenoprofen, Flubifronate, Ibuprofen, Meclofenamate
Antimalarial	Chloroquine phosphate, Quinine hydrochloride

2. Methods of taste masking

A number of methods are known for masking the taste of drugs. This is an increasingly important issue in the area of patient compliance with recommended pharmaceutical therapies. Taste masking techniques may be broadly divided into physical, chemical, biochemical and organoleptic methods. The technique to be adopted will depend on several factors, but primarily on the extent of bitterness of the drug to be incorporated into an oral pharmaceutical formulation. Different methods are available to mask undesirable taste of the drugs. Some of these are as given below.

2.1 Conventional method

1. Use of flavor enhancers.
2. Use of sweeteners.

2.2 Recent methods

1. Applying Polymer Coating
2. Taste Masking by formation of inclusion complexes
3. Ion Exchange Resin
4. Microencapsulation
5. Multiple Emulsions
6. Using Liposomes
7. Prodrugs
8. Mass Extrusion Method (Dispersion Coating)

2.1.1. Use of flavors enhancers

The materials for taste masking purpose have often been classified depending upon the basic taste that is masked. Flavoring and perfuming agents can be obtained from either natural or synthetic sources. Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices and distilled fractions of these. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups or spirit. Apart from these conventional materials many compositions have been found to show effective taste masking abilities with improved flavor such as alkaline earth oxide, alkaline earth hydroxide or an alkaline hydroxide. Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and their mixtures. Anethole effectively masked bitter taste as well as the aftertaste of zinc, which is use in treating the

common cold. Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution.

Example: Lansoprazole is strawberry flavored delayed-release oral drug.

2.1.2. Definitions and classes of flavors

Flavors determine identity. In pharmaceutical formulation, the identifying flavors are often chosen on the basis of market studies, age of user, mode of use, product characteristics, composition and other product-specific requirements. As in food formulation, flavors may be added to complement or depress others. Flavoring agents should act in synergy with the other ingredients in the system. Several parameters should also be considered in choosing the correct flavor, including the required concentration, pH, processing temperature, compatibility with components, storage conditions, and shelf life. Flavors fall into three classes: Natural, artificial, and natural and artificial (N&A) flavors.

Natural flavors are the oldest class of flavors to be used in food and pharmaceutical formulations. However, they are being replaced by synthetic flavors and their use alone in pharmaceutical formulations is very limited due to several disadvantages, including unpredictable quality due to the natural origin, instability, cost, and availability.

Table 3: Masking agents used to mask basic taste.

Basic Taste	Masking agents
Sweet	Vanilla, Bubble gum, Grapefruit
Acid	Lemon, Lime, Orange, Cherry, Grapefruit
Metallic	Grape, Marsh, Mellow, Gurana, Berries, Mints
Bitter	Liquorice, Coffee, Chocolate, Mint, Grapefruit, Cherry, Peach, Raspberry, Orange, Lemon, Lime.

2.1.2. Use of sweeteners

Definition and Classes

In pharmaceutical formulation, sweeteners are widely used for several functional reasons (e.g., diluents in tablets), in addition to their essential role in taste masking. They can be classified as nutritive sweeteners; polyols and hydrogenated starch hydrolysates; and high-intensity sweeteners. They differ in their organoleptic and functional properties, and no single sweetener works for every situation. This can be overcome by using a blend of sweeteners which reduces the ingestion level of one specific sweetener.

1. Nutritive Sweeteners

Nutritive sweeteners are simple carbohydrates generally present in food. Sucrose, a disaccharide of glucose and fructose, is the most commonly used sweetener.

2. Polyols (Sugar Alcohols) and Hydrogenated Starch Hydrolysates

Polyols are the hydrogenated derivatives of a corresponding sugar (e.g., mannitol from mannose). Compared to their parent sugars, polyols are lower in calories, less reactive, do not promote dental cavities, and have greater stability and longer shelf life

3. High–Intensity Sweeteners

High-intensity sweeteners are artificial sweeteners with very low caloric content and high sweetness intensity. They are used in small concentrations in many dosage forms (e.g., chewable tablets, powder for suspension, etc

Example

- Saccharin which is 500 times sweeter than sucrose but can be carcinogenic.
- Aspartame**.**

Disadvantages

1. Sweeteners differ in their organoleptic and functional properties, and no single sweetener works for every situation.
2. Most of the times a blend of sweeteners which reduces the ingestion level of one specific sweetener has to be used.

2.2.1. Applying Polymer Coating

Coating is an extremely useful technique for number of applications in the pharmaceutical field. By coordinating the right type of coating material it is possible to completely mask the taste of a bitter drug, while at the same time, not adversely affecting the intended drug release profile. Any nontoxic polymer that is insoluble at pH 7.4 and soluble at acidic pH, would be an acceptable alternative for taste masking. Coating of drugs using a suitable polymer offer an excellent method of concealing the drug from the taste buds. The coated composition may be incorporated into much number of pharmaceutical formulations, including chewable tablet, effervescent tablets, powder and liquid dispersion. Taste masking of ibuprofen has been successfully achieved by using the air suspension coating technique to form microcapsules, which comprises a pharmaceutical core of a crystalline ibuprofen and methacrylic acid copolymer coating that provides chewable taste masked characteristics. Various inert coating agents like starch; povidone, gelatin, methylcellulose, ethyl cellulose etc. are used for coating drug particles. One of the most efficient methods of drug particle coating is the fluidized bed processor. In this approach powder's as fine as 50µm, are fluidized in expansion chamber by means of heated, high velocity air and the drug particles are coated with a coating solution introduced usually from the top as spray through nozzle. The coated granules are dried with warm air**.**

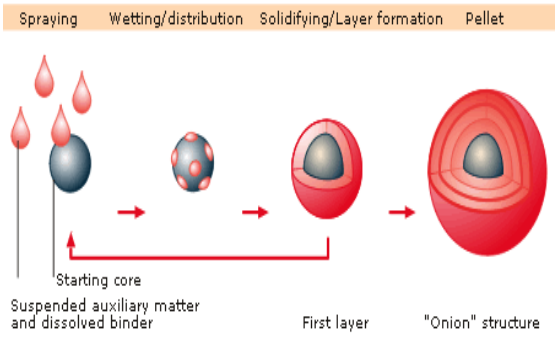


Fig. 4: Applying polymer coating.

2.2.2. Marketed Taste Masked Drug By Drug Partial Coating

Table 4: Marketed Taste Masked Drug By Drug Partial Coating.

Technique	Polymer	Taste Masked Drug
Air Suspension Coating	Methacrylic acid copolymer	Ibuprofen
Phase separation Coacervation	Eudragit E-100, Chitosan	Clarithromycin, Paracetamol
Fluidized Bed / Spray Coating	Hydrogenated Oil and Surfactant	Indeloxazine
Solvent Evaporation Method	Eudrgit E, PEG, Ethyl Cellulose	Pseudoephedrine Ranitidine
Extrusion Coating	Eudragit E-100	Oxybutinin ofloxacin, pirezepin

Advantages

1. The triglyceride/polymer combination prevents the drug coating from dissolving while still in the patient's mouth. The coated drug remains intact until reaching the stomach where it is immediately released upon contacting the gastric fluid.
2. It dissolves at body temperature.
3. It can be easily applied, economical in manufacture, and efficient in use.

Disadvantages

Polymers are known to be permeable to aqueous solvents. Upon exposure to an aqueous environment, drug leaching is a frequent occurrence with these coatings since they are greatly porous and therefore permeable to water.

2.2.2. Microencapsulation

Microencapsulation is essentially a process by which coatings are applied to small particles of solids, droplets of liquids or dispersions, so as to form microcapsules; the technique differs from other coating procedures in that the size of the particles generally ranges from several tenths of a µm to 5000 µm in diameter It is a coacervation-phase separation process which involves utilization of three phases[12]

- “Core material" phase of the drug to be encapsulated
- "Coating material" phase of the substance which will ultimately form the coating
- “Liquid phase” in which the core and coating materials are dispersed or dissolved

The coating is then deposited on the core material, and a desolvation process is used to remove the liquid phase and isolate the microcapsules. This makes use of materials and process parameters which enable preparation of uniform, impervious coatings, and involves preparation of formulations having high coating levels. In this way it provides for extremely effective taste masking while also providing for release of drug shortly after the drug passes through the mouth.

Method

The microcapsules are prepared by first admixing the selected drug, a first polymeric material to serve as the coating, and a second polymeric material to promote phase separation, in a nonpolar organic solvent. Mixing is preferably conducted along with stirring or agitation using any number of conventional means A variation on the aforementioned procedure provides a valuable alternative method which may be preferred for heat-sensitive drugs. This alternative procedure involves dissolving the first and second polymeric materials in the selected nonpolar organic solvent, without addition of drug, followed by heating to a temperature effective to dissolve the polymers. Drug is then added, the mixture is then allowed to cool, and the remainder of the procedure described above is carried out.

Advantages

1. Microencapsulation provides the means of converting liquids to solids.
2. Can be used for altering colloidal and surface properties.
3. Provides environmental protection and controls the release characteristics or availability of coated materials.
4. The small size of the particles can be widely distributed throughout the gastrointestinal tract thus potentially improving drug absorption.

2.2.3. Taste Masking By Host And Guest Complex

In inclusion complex formation, the drug molecule fits into the cavity of a complexing agent i.e., the host molecule forming a stable complex. The complexing agent is capable of masking the bitter taste of the drug by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste buds thereby reducing the perception of bitter taste. Vander Waals forces are mainly involved in inclusion complexes. Cyclodextrin is the most widely used complexing agent for inclusion complex formation. The use of cyclodextrins as pharmaceutical excipients for various applications such as solubility, bioavailability and stability enhancement of various drugs. “Cyclodextrins” are cyclic oligosaccharides consisting of multiple (α, D1-4) linked glucopyranose units that display amphoteric properties of a lipophilic central cavity and hydrophilic outer surface. Cyclodextrins are crystalline, homogenous and non-hygroscopic substance, which are tours-like macro ring shape.[4]

Mechanism of Action

The hydrophilic exterior surface of the cyclodextrin molecules makes them water soluble, but the hydrophobic cavity provides a microenvironment for appropriately sized non-polar molecules.

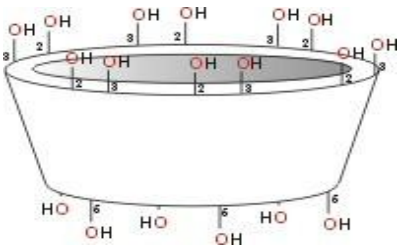


Fig. 5: Schematic representations of hydrophobic cavity and hydrophilic outer surface of Cyclodextrin

1. Cyclodextrin complexation

Inclusion complexation with cyclodextrin is like a “host-guest interaction”. In this interaction cyclodextrin act as host molecule and the drug molecule to be entrapped in host cavity act as guest molecule. Comparing to other encapsulation methods, which involve entrapment of more than one guest, cyclodextrin complexation involve entrapment

of one molecule of guest in cyclodextrin cavity. For formation of complex with cyclodextrin, variety of non-covalent forces like Vander wall forces, hydrophobic interaction, and dipole movement are responsible. In majority of cases only a single guest molecules is entrapped in the cavity. For High molecular weight molecules, more than one molecule of cyclodextrins can bind to the guest.

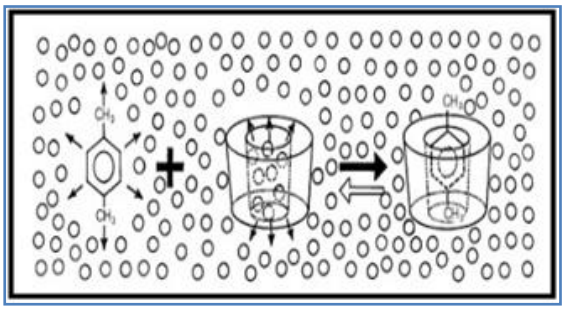


Fig. 6: Schematic representation of host-guest interaction.

For the preparation of complex, many solvents are used, but generally water is preferred as a solvent for complexation. The cavity of cyclodextrin is non-polar and it favours non-polar area of guest molecule. Water gives driving force for formation of complexation. Not all guests are sufficiently soluble in water. It is not necessary that complete solubilization of drug should be done. Small amount of drug must be soluble to form a complex. Sometimes water miscible solvents in small quantities are helpful for dissolution of drug, which enhances complexation reaction. After addition of the dissolved drug to the solution of cyclodextrin, either guest may be dissolved or suspended in the form of high precipitate.

Example: Bitter taste of ibuprofen and gymnima sylvestre has been effectively masked by cyclodextrin.

Advantages

1. Bioavailability enhancement: Drugs having limited oral bioavailability due to poor dissolution rate and solubility can be complexed with cyclodextrins to improve their absorption. Complexation reduces active recrystalization of drugs, which may help to increase their aqueous solubility.
2. Reduction in drug irritation: Drugs, which are irritant to mucus membrane and skin are complexed with cyclodextrins to minimize the irritation.
3. Stability of active ingredients: Cyclodextrins can prevent the deterioration of active pharmaceutical ingredients due to light, temperature and atmospheric oxidation.
4. Improve patient compliance by taste masking of bitter drugs

2. Molecular Complexes of Drug with Other Chemicals

The solubility and adsorption of drug can be modified by formation of molecular complexes. Consequently lowering drug solubility through molecular complex formation can decrease the intensity of bitterness of drug. Higuchi and Pitman reported that caffeine forms complexes with organic acids that are less soluble than xanthane and as such can be used to decrease the bitter taste of caffeine.

3. Chitosan: An Attractive Biocompatible Polymer

Chitosan comes from *chitin* a natural biopolymer originating from crustacean shells. Chitin is similar to cellulose in morphology; a bountiful natural polysaccharide that contains amino sugars. Partial deacetylation of chitin gives rise to chitosan, a linear polysaccharide with interspersed D-glucosamine, and acetyl-D-glucosamine units. The preponderance and distribution of acetyl-D-glucosamine residues lead to differing physicochemical properties and biological response.

Chitosan is a biocompatible, biodegradable, and nontoxic natural polymer that exhibits excellent film-forming ability. As a result of its cationic character, chitosan is able to react with polyanions giving rise to polyelectrolyte complexes. Therefore, because of these interesting properties, it has become the subject of numerous scientific reports and patents on the preparation of microspheres and microcapsules. The techniques employed to microencapsulate with chitosan include, among others, ionotropic gelation, spray drying, emulsion phase separation, simple and complex coacervation, and polymerization of a vinyl monomer in the presence of chitosan. The aim of this work is to review is for a taste masking by various methods.

Chitosan polymer and drug are dissolved in suitable solvent. Sonication done by ultracentrifuge, after stirring 24 hrs with magnetic stirrer, after completely loading polymer to drug, it way from sprays drying the complexes and evaluate for taste masking, threshold concentration of bitterness was determine and complexes was characterization with the help of XRPD, FT-IR, DSC and SEM. If Complexation was achieve, % of drug content was determine and equivalent weight of complexes taken and formulate it. Dissolution of the chitosan – drug complexes tablet give sustain released effect.

Example:

Metaclopramide and Glipizide loaded chitosan microspheres

2.2.4. Solid dispersion system

Solid dispersion has been defined as dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting (fusion) solvent or melting solvent method. Solid dispersion is also called as co precipitates for those preparation obtained by solvent method such as co precipitates of sulphathiazale and povidone. Solid dispersions using insoluble matrices or bland matrices may be used to mask the bitter taste of drugs. Also using them as absorbates on various carriers may increase the stability of certain drugs.[5, 6]

Example:

The preparation of orally administrable formulations of quinolone- or naphthyridonecarboxylic acids specifically relates to quinolone- or naphthyridonecarboxylic acids in a solid phase dispersion, which masks their bitter taste.

2.2.5. Multiple emulsions

Multiple emulsions are complex polydispersed systems where both oil in water and water in oil emulsion exists simultaneously which are stabilized by lipophillic and hydrophilic surfactants respectively. The ratio of these surfactants is important in achieving stable multiple emulsions. Among water-in-oil-in-water (w/o/w) and oil-in-water-in-oil (o/w/o) type multiple emulsions; the former has wider areas of application. The formulation is designed to release the drug through the oil phase in the presence of gastrointestinal fluid.

Example: polyvinylacetal diethylaminoacetate microspheres containing trimebutine[7, 8]

To produce acid soluble, polyvinylacetal diethyl aminoacetate microspheres containing trimebutine (as maleate) using a water-in-oil-in-water (w/o/w) emulsion solvent evaporation method is used to characterize their in-vitro release properties. The pH of the external aqueous phase was the critical factor in achieving a high loading efficiency for trimebutine in the microencapsulation process; nearly 90% (w/w) loading efficiency was obtained at above pH 10. Trimebutine was completely released from AEA microspheres within 10 min in a dissolution test at pH 1.2, simulating conditions in the stomach, whereas at pH 6.8, the pH in the mouth, only small quantities of trimebutine were released in the initial 1–2 min. The results of a gustatory sensation test in healthy volunteers confirmed the taste-masking effects of the AEA microspheres. Finally, an attempt was made to encapsulate the salts of other basic drugs (lidocaine, imipramine, desipramine, amitriptyline, promethazine and chlorpheniramine) into AEA microspheres using the w/o/w emulsion evaporation method. The loading efficiencies were ranked in almost inverse proportion with the solubility of the drugs in the external aqueous phase. This study demonstrated the possibility of masking the taste of salts of basic drugs by microencapsulation with AEA using a w/o/w emulsion solvent evaporation method.

2.2.6. Using Liposomes

The unpleasant taste of therapeutic agent can be masked by entrapping them into liposome. Liposomes are microscopic, fluid-filled pouch whose walls are made of layers of phospholipids identical to the phospholipids that make up cell membranes. Liposomes are used to deliver certain vaccines, enzymes, or drugs (e.g., insulin and some cancer drugs) to the body. When used in the delivery of certain cancer drugs, liposomes help to shield healthy cells from the drugs' toxicity and prevent their concentration in vulnerable tissues (e.g., the kidneys, and liver), lessening or eliminating the common side effects of nausea, fatigue, and hair loss. Liposomes are especially effective in treating diseases that affect the phagocytes of the

immune system because they tend to accumulate in the phagocytes, which recognize them as foreign invaders. They have also been used experimentally to carry normal genes into a cell in order to replace defective, disease-causing genes. Liposomes are sometimes used in cosmetics because of their moisturizing qualities.

Example:

Incorporating into a liposomal formulation prepared with egg phosphatidyl choline masked the bitter taste of chloroquine phosphate in buffer at pH 7.2.

2.2.7. Mass Extrusion Method (Dispersion Coating)

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

Example:

Characterization of solid dispersions of paracetamol and eudragit ((R)) E prepared by hot-melt extrusion using thermal, microthermal and spectroscopic analysis.

2.2.8. Ion Exchange Resin

Being high molecular weight water insoluble polymers, the resins are not absorbed by the body and are therefore inert. The long-term safety of ion exchange resins, even while ingesting large doses as in the use of cholestyramine to reduce cholesterol is established unique advantage of ion exchange resins is due to the fixed positively or negatively charged functional groups attached to water insoluble polymer backbone. Antibacterial belonging to quinolone category like ciprofloxacin was loaded on cation exchanger and administered to animals. Binding to a cation exchange resin like Amberlite IRP-69 masked the taste of peripheral vasodilator buflomid. Manek S.P.et al. evaluated resins like Indion CRP 244 and CRP 254 as taste masking agents. Some bitter drugs whose taste has been masked by using ion exchange resin.

Table 5: Bitter Drugs masked by ion exchange resin.

Drug	Ion exchange resin
Norfloxacin	Indion 204 (weak cation exchange resin)
Ciprofloxacin	Indion 234 (weak cation exchange resin)
Roxithromycin	Indion 204 (weak cation exchange resin)

Ion exchange resins (IER) have received considerable attention from pharmaceutical scientists because of their versatile properties as drug delivery vehicles. In past few years, IER have been extensively studied in the development of Novel drug delivery system and other biomedical applications. Several ion exchange resin products for oral and peroral administration have been developed for immediate release and sustained release purposes. Research over last few years has revealed that IER are equally suitable for drug delivery technologies, including controlled release, transdermal, nasal, topical, and taste masking.[15]

3. Evaluation of taste masking effect

3.1 Electronic taste sensing system

The main elements of an electronic taste sensing system are a different number of various sensor types which can be attached to a robot arm, a sample table, an amplifier and a computer system for data recording.

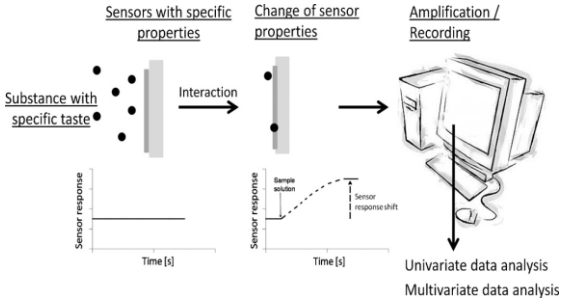


Fig. 7: Electronic taste sensing system.

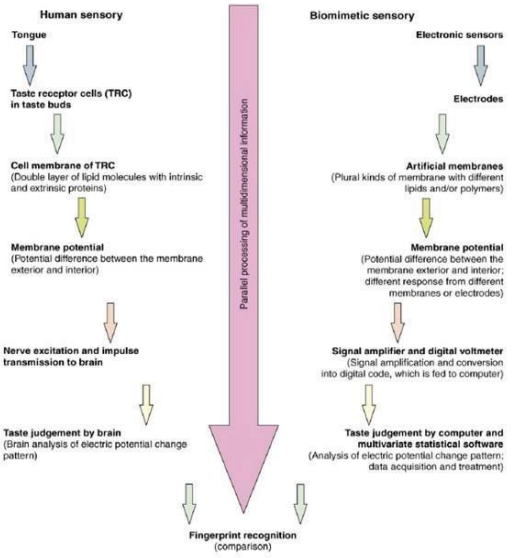
3.2 Lipid membrane taste sensors (lmtss)

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 nonconducting, such as polyvinyl

chloride. Such sensors analyze, in a non-specific manner, detected signals and hence can extract the inherent taste characteristics of substances.

3.3 Biomimetic taste sensing systems (bmtsss

The use of multivariate data analysis (MVDA) combined with sensors that have partially overlapping selectivity, has been demonstrated to be a 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. BMTSSs have been marketed as taste sensors, or electronic tongues or e-tongues. These instruments employ electrochemical sensors coupled with chemometric methodologies to perform qualitative and quantitative analysis.



3.4. Astree electronic tongue

The Astree electronic tongue system (Alpha M.O.S.) is a taste-sensing instrument equipped with a seven-sensor probe assembly for qualitative and quantitative analysis. 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.

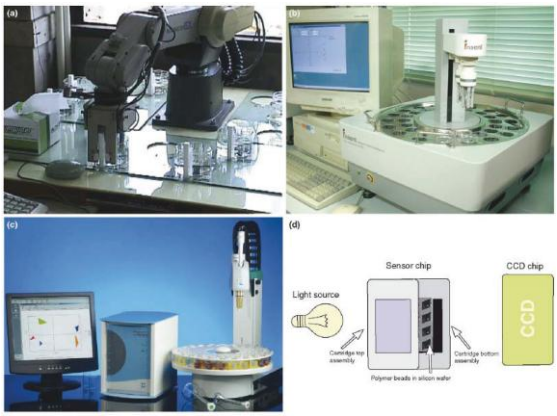


Fig. 8: Commercially developed and developing taste sensors. (a) Taste sensor SA401 developed by Anritsu Corp. (b) Taste sensor SA402B developed by Intelligent Sensor Technology (Insent Corp). (c) Astree electronic tongue developed by Alpha M.O.S. (d) a schematic of the electronic tongue developed by the University of Texas and usion.

3.5. Spectrophotometric method

A known quantity of the taste-masked formulation is mixed with 10 ml of distilled water in 10 ml syringe by revolving the syringe, end to end; five times in 30 seconds. The test medium is then filtered through a membrane filter, followed by spectrophotometric determination of the concentration of the drug in the filtrate. If this concentration is below the threshold concentration, it may be concluded that the bitter taste would be masked *in vivo*. This technique has been applied to evalute the taste masked granules of oflaxacin with threshold concentration being 100µg/ml.

Conclusion

Some drugs have relatively no taste, and simply adding a suitable flavor or sweeteners can “hide” any slightly unpleasant sensations. However, most drugs do require taste masking if they are to be incorporated into an ODT (orally disintegrating tables). Numerous methods exist to achieve this includes simply spray drying or dispersion coating or using multiple emulsions especially for liquids.

If further taste masking is needed, the resultant particles can be sealed with a suitable coating material. The choice of polymer system will determine the mechanism of taste masking. For example, whether dissolution of the active is slowed down in the oral cavity or behaves in a more complex behavior, such as pH-dependent dissolution. In addition, the quantity of coat applied, how it is applied, and whether other excipients are included in the coating will all affect the quality of the taste masking. Some drugs may be formulated for target delivery in the form of liposomes or some may be used in the form of prodrugs.

Cyclodextrins (cyclic-linked oligosaccharides) have been shown to provide some measure of taste masking by trapping the drug within its cyclic structure long enough to retard initial dissolution. In fact, because cyclodextrins can help solubilize many drugs, this method of taste masking may actually give higher blood levels than non-taste-masked active. Other taste-mask methods exist, namely by coating with other chemicals. Encapsulation using coacervation has also been employed to encapsulate certain flavors. Ion exchange resin is one of ideal method for taste masking of bitter drug. In this method drug molecule form a complex with resin and mask the bitter taste of drug, this method is ideal because resin does not release the drug in mouth but it releases the drug in stomach and does not affect on drug release profile. Ion exchange resin is also one of the ideal methods of taste masking of bitter drug, in which weak cation resin is most suitable for taste masking, this method do not affecting on their bioavailability of drug. The pharmaceutical industry have to realised the importance of taste masking so to develop universal method which can applied for all drug.

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