Journal of Pharmaceutical and Scientific Innovation
www.jpsionline.com
Review Article

TASTE MASKING: A NOVEL APPROACH FOR BETTER PATIENT COMPLIANCE

Bhati Savita *, Arora Vandana Sethi,Nigarish Mizna
Student, Lloyd Institute of Management &Technology, Noida, U.P, India
*Email - savitabhati1987@gmail.com

Received on: 22/04/12 Revised on: 20/05/12 Accepted on: 11/06/12

ABSTRACT
Taste is one of the most important parameters for improve the patient compliance especially in the pediatric and geriatric, bedridden & non-cooperative patients. Masking the bitter taste is potential tools for the development of the dosage form. Several approaches have been developed which not improved the taste of a drug, but also the palatability, formulation and performance of the drug.
The present review articles attempts to brief account of many technologies of taste masking and novel evaluation parameter that are used by pharmaceuticals scientists for taste-masking.
KEY WORDS: Taste masking, Bitter, Palatability, Technologies, Evaluation parameters, Pediatric, Geriatric.

INTRODUCTION

Taste of a drug is a potential tool for governing patient compliance and the quality of treatment especially in paediatrics. Undesirable taste is one of the important formulation problems that are encountered with many drugs. Administration of bitter drugs orally with acceptable level of palatability is a key issue for health care providers. Proven methods for bitterness reduction and inhibition have resulted in improved palatability of oral pharmaceuticals.[1]

Two approaches are commonly utilized to overcome bad taste of the drug[2]

[1] Reduction of drug solubility in saliva, where a balance between reduced solubility and bioavailability must be achieved.

[2] Second approach is to alter the ability of the drug to interact with taste receptor.

The American Academy of Pediatrics estimates that compliance in children is as low as 53%, indicating that children frequently fail to take medications properly. Noncompliance can lead to**:** Persistent symptoms, Need for additional doctor visits or even hospitalizations, worsening of Condition, Need for additional medications, increased healthcare costs and Development of drug-resistant organisms in cases of infectious diseases.[3]

PHYSIOLOGY OF TASTE

Physiologically, taste is a sensory response resulting from a chemical stimulation of taste buds On the tongue. The sense of taste is conducted to the brain by a process called taste transduction. This process begins with the interaction of tastant (i.e., food or medicine) with taste receptor cells in the taste buds.The tastant binds with G-protein coupled receptors in the cells, triggering the release of a G-protein called gustducin. Taste sensation begins when gustducin activates the effector enzymes phosphodiesterase 1A or phospholipase C b-2. The effector enzymes then change the intracellular levels of second messengers such as cyclic adenosine monophosphate (cAMP), inositol 1, 4,5-triphosphate (IP3), and idacylglycerol (DAG). The second messengers activate ion channels, including calcium channels inside the cell, and sodium, potassium and calcium channels on the extracellular membrane. This ionization depolarizes the cell, causing the release of neurotransmitters that send a nerve impulse to the brain that carries the signal of taste.[4]

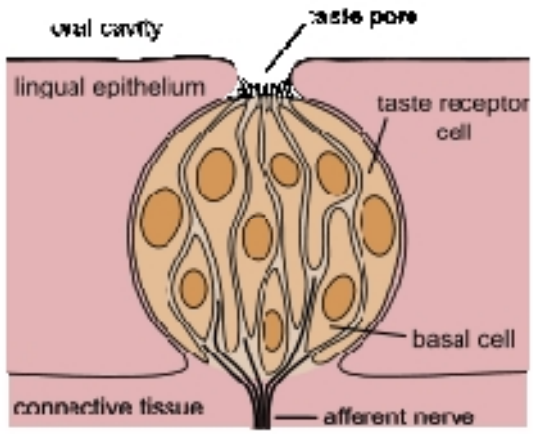

Figure 1. Structure of a taste buds.

Taste constitutes four primary taste sensations namely-sour, bitter, sweet, salty. Recently, a fifth basic taste umamai has been discovered.[5]

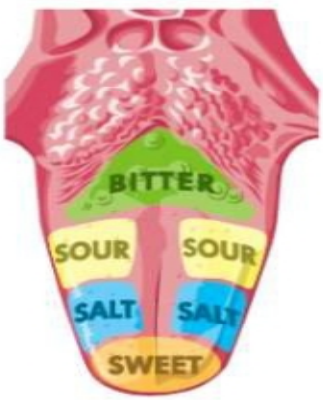

Figure 2.Taste points of tongue.

There are four different kinds of taste buds. These sensations are elicited by the tongue and interpreted by the brain. Certain areas of the tongue respond more readily to specific tastes than others. Sweet sensations are most easily detected at the tip, whereas bitterness at the back of the tongue, but salty sensations are usually detected at the tip and the sides of the tongue. During ingestion, taste buds react to soluble

substances. The resulting sensations are transmitted to the brain by the ninth cranial nerve and tastes are detected. The sensitivity of the tongue to different sensations varies widely among individuals.

Masking of taste is not an easy and simple procedure efforts are required before bitter drugs are acceptable for market trials. Number of steps are needed it. Pharmaceutical industries invest money time and resources into developing palatable and pleasant tasting products and industries adopt various taste-masking techniques to develop an appropriate formulation. So to avoid unwanted wastage time and money.

We concluded that ideal taste masking formulation should have the following properties[6]

- Involve least number of equipments and processing steps.
- Require minimum number of excipients for an optimum formulation.
- No adverse effect on drug bioavailability.
- Require excipients that are economical and easily available.
- Least manufacturing cost.
- Can be carried out at room temperature.
- Require excipients that have high margin of safety.
- Rapid and easy to prepare.

Patients now expect and demand formulations that are pleasantly, or at least tolerably, flavored. Flavor enhancers are **the** simplest and oldest method used but this method fail to mask 90% of moieties. When these methods fail then some new conventional methods were adopted such as microencapsulation which includes coating, spray drying techniques, by chemicals, inclusion complexes with cyclodextrins, use of ion exchange resins, prodrugs and other Different techniques like liposomes, multiple emulsions etc.

TASTE MASKING TECHNOLOGIES

Various methods are available to physically mask the undesirable taste of drugs, some of which are described below:

- Taste masking with flavors and sweeteners
- Polymer coating of drug
- Microencapsulation
- Mass extrusion
- Multiple Emulsions
- Ion exchange resin complexes
- Granulation
- Solid dispersion
- Prodrug concept
- Development of Liposome
- Taste masking by spraydrying technique
- Taste masking by adsorption
- Formation of inclusion complexes

TASTE MASKING WITH FLAVORS AND SWEETENERS:

Maskng of taste with flavors and sweeteners of bitter drugs is a good application found in a pharmaceuticles field. This is the foremost and simplest option to achieve taste masking. flavors are classified as natural, artificial, or natural and artificial which are obtained by mixing the natural & synthetic flavors. 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.[7] 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.

Unlike natural flavors are usually stable. These flavors are also used in formulations to mask the bitter taste and give pleasant mouth feel. Mannitol and Aspartame are most widely used excipients in formulating oral disintegrating tablet. Synthetic sweeteners such as sucralose are commonly used in most taste masked products. Now some novel sweeteners derived from plant parts have been evaluated for taste masking efficiency. For example, stevia was used to prepare the taste masked ibuprofen.[8]

POLYMER COATING OF DRUG

Most important factor to be considered in taste masking by coating is selection of coating polymers various inert coating agents can be used to coat bitter drugs. They include:

Water soluble polymers: Cellulose acetate, cellulose butyrate, polyvinylpyrollidone, Hydroxyethyle cellulose etc.

Water insoluble polymers: Cellulose ether, cellulose esters, polyvinyl acetate etc.

These coating agents simply provide a physical barrier over the drug particles. One of the most efficient methods of drug particle coating is the fluidized bed processor. In this approach, powders as fine as 50 mm are fluidized in an 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 a spray through a nozzle. The coated granules are dried with warm air.[9]

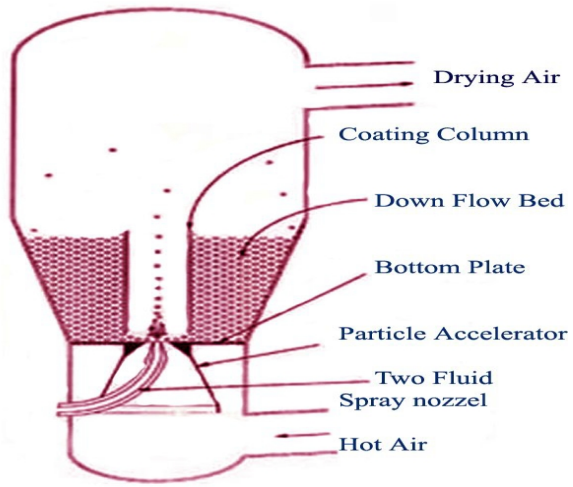

Figure 3:Fludized bed dryer.

TASTE MASKING BY MICROENCAPSULATION:

Microencapsulation techniques can be used for taste masking of bitter drugs microencapsulating drug particles with various coating agents. Coating agents employed includes gelatin, povidone, HPMC, ethyl cellulose, Bees wax, carnauba wax, acrylics and shellac. In this method bitter drugs are first encapsulated to give free flowing microcapsules which are then blended with excipients and compressed into tablet. Microencapsulation can be accomplished by any of the following techniques.

- Air suspension coating
- Coacervation - phase separation
- Spray drying and spray congealing
- Solvent evaporation

- Multiorifice - centrifugal process
- Pan coating
- Interfacial polymerization

Some advantages of taste making by microencapsulation[10]

- Taste masking can be achieved with the desirable fast or controlled drug release.
- Bitter liquids may be coated to convert them to solid particles.
- The coated bitter particles can adapt to a wide variety of dosage forms and product applications.

MASS EXTRUSION

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.

MULTIPLE EMULSION

A novel technique for taste masking of drugs employing multiple emulsions has been prepared by dissolving drug in the inner aqueous phase of w/o/w emulsion under conditions of good shelf stability. The formulation is designed to release the drug through the oil phase in the presence of gastrointestinal fluid.[11]

ION EXCHANGE RESINS COMPLEX

Taste masking by ion exchange resin is one of most extensively Used method to overcome this problem. Ion-exchange resins (IER) have received considerable attention from pharmaceutical scientists because of their versatile properties as drug-delivery vehicles. Bitter tasting drugs can be absorbed onto ion exchange resins, thus effectively removing them from solution during the transit through the mouth, at salivary pH 6.7, remains in intact form making the drug unavailable for the taste sensation. Various studies have revealed that ion exchange resins are equally suitable for drug delivery technology. Some ion exchange resins used widely for taste masking purpose in industries are Amberlite IRP64, Amberlite IRP69, Indion 204, Indion 214, Kyron T-114 and Kyron T-104.

Classification of ion exchange resins

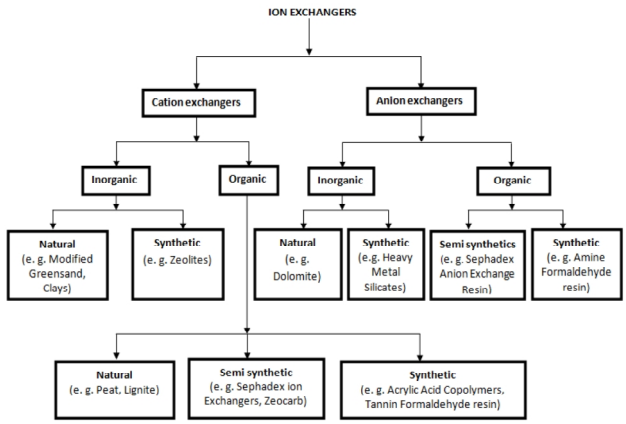

Figure 4: Classification of ion exchange resin

Selection of suitable ion exchange resins: The selection of IER for taste masking is primarily governed by the functional-group properties of the IER. Following points need to be considered during selection:

- Capacity of the IER.
- Degree of cross linking in the resin matrix.
- Particle size of resin.
- Nature of drug and site of drug delivery. It is also important to evaluate the resin in the pH- and ionic-strength environment, simulating the *in vivo* situation.
- Swelling ratio.
- Biocompatibility and biodegradability.
- Regulatory status of the IER.

Charged drugs are normally loaded on to ion exchange resins by two methods,[12]

- Column method
- Batch method

TASTE MASKING BY GRANULATION

Taste masking by granulation is an inexpensive, quick operation and an easily scalable taste masking technology. Granulation lowers the effective surface area of the bitter substance that come in contact with the tongue upon oral intake. Taste masked granules, prepared from saliva insoluble polymer can be formulated in different type of tablet dosage form. Liquid and low melting point waxes such as glycerol palmitostearate, glyceryl behenate and hydrogenated castor oil are commonly used ingredients during the granulation to achieve taste masking.

TASTE MASKING BY SOLID DISPERSIONS

Solid dispersion defined as dispersion of more active ingredients in an inert carrier or matrix at solid state prepared by fusion solvent method. Solid dispersion can also be prepared by co-precipitate method for that preparation obtained by solvent method such as coprecipitate of sulphasalazine and povidone. In this insoluble matrices or blend matrices may be used to mask the taste of drugs.[13]

Various approaches for preparation of solid dispersion are described below.

Melting method: In this method, the drug or drug mixture and a carrier are melted together by heating. The melted mixture is cooled and solidified rapidly in an ice bath with vigorous stirring. The final solid mass is crushed and pulverized.

Solvent method: In this method, the active drug and carrier are dissolved in a common solvent, followed by solvent evaporation and recovery of the solid dispersion.

Melting-solvent method: In this method the drug in solution is incorporated into a molten mass of polyethylene glycol at a temperature below 70oC without removing the solvent.

Some example of Natural polymers such as shellac and zein, and enteric polymers like derivatives of acrylic acid polymers and phthalate are good choices to develop the taste masked solid dispersions.

TASTE MASKING BY PRODRUG APPROACH

A prodrug is a chemically modified inert drug precursor, which upon biotransformation liberates the pharmacologically active parent drug. Prodrugs can be used to increase or decrease the aqueous solubility, mask bitterness, increase lipophilicity, improve absorption, decrease local side effects, and alter membrane permeability of the parent molecule . Tasteless/bitterless prodrugs of opioid analgesics and antagonists were formulated for improved buccal delivery, when administered as prodrugs; the bioavailability was improved without visible adverse effects.[14]

TASTE MASKING USING LIPOSOMES

Another approach of masking the obnoxious taste of therapeutic agent is to entrap them into Liposomes. Liposomes are simple microscopic vesicles in which an

aqueous volume is entirely closed by a membrane composed of lipid molecules, lipid bilayers mainly composed of natural or synthetic phospholipids.[15] The bitter taste of Chloroquine phosphate in HEPES (N-2-hydroxyetylpiperzine-N'- 2-ethane sulfonic acid) buffer was masked at pH 7.2. by incorporating into a liposomal formulation prepared with egg phosphatidyl choline.[15]

TASTE MASKING BY SPRAY DRYING TECHNIQUE

In the present investigation, bitter taste of drug is masked by preparing microparticles of drug with certain hydrophilic polymers such as Hydroxypropylmethylcellulose (HPMC) and polyvinyl pyrrolidone (PVP) by using spray drying technique.[16]

TASTE MASKING BY ADSORPTION

Adsorbates are commonly in taste masking technologies. The drug may be adsorbed or/and entrapped in the matrix of the porous component, which may result in a delayed release of the bitter active during the transit through the oral cavity thereby achieving taste masking.Loperamide and phenyl propanolamine have been adsorbed on magnesium aluminium silicates also known as Veegum F to prepare bitter taste masked suspension of these drugs.

TASTE MASKING BY FORMULATION OF INCLUSION COMPLEX

The complexing agents is capable of taste masking of bitter drug by either 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.[17]Cyclodextrin is most widely used complexing agent for inclusion type complexes. It is sweet, non toxic, cyclic oligosaccharide obtained from starch.[19]

EVALUATION TECHNIQUES

Sensory evaluation

Taste, to think of, is a very subjective perception. Depending on individuals, the perceived taste may vary to different degrees. If we have well controlled experimental set up, it is possible to accurately and reproducibly measures taste thresholds. To quantitatively evaluate taste sensation, following methods have been reported in literature.

- Panel testing (human subjects)
- Measurement of frog taste nerve responses.
- Multichannel taste sensor/ magic tongue
- Spectrophotometric evaluation/ D30's value

Panel Testing[20]

The panel testing is a psychophysical rating of the gustatory stimuli. In this method, a group of about 5-10 human volunteers is trained for taste evaluation by using reference solutions ranging in taste from tasteless to very bitter. Numerical values are then assigned to these levels of bitterness (eg.,0-5). Subsequently, test solution is tasted and rated on the same scale to assess its bitterness.

Measurement of Frog Taste Nerve Responses[21]

In this method, adult bull frogs are anaesthetized intraperitoneally and the glossopharyngeal nerve is then located and dissected from the surrounding tissue and cut proximally. An ac-amplifier and an electronic integrator are used to respectively amplify and integrate the nerve impulses. The peak height of the integrated response is then taken as the magnitude of response.

Multichannel Taste Sensor / Magic tongue/E-tongue[22]

This is an automated taste sensing device to detect the magnitude of bitterness of a drug substance. This sensor consists of transducer, which is composed of several kinds of lipid/polymer membrane with different characteristics. Taste information is transformed into a pattern composed of electrical signals of membrane potential of the receptor part. Multichannel taste sensor provide a fast, objective and simple assessment of oral formulations such as chewable tablets, liquid, rapid dissolve tablets and films, oral dispersive lozenges, sublingual delivery methods, and nasal delivery products which is highly correlated with the organoleptic taste panel methods.

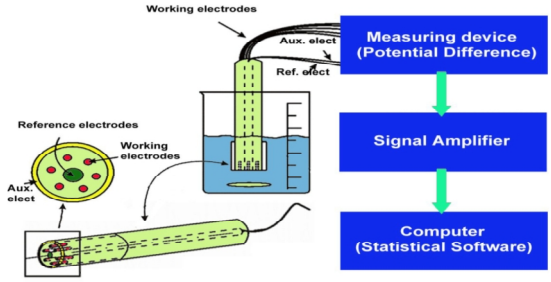

Figure 5: Evaluation of taste using e-tongue

Spectrophotometric Method[23]

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 sparfloxacin, with threshold concentration being 100µg/ml.

CONCLUSION

For better taste masking, number of technologies available which effectively altered bitterness of drug, better patient compliance but dose not affect the bioavailability of drug.The pharmaceutical industry have realized the importance of taste masking so developed of a universal method,which can applied to all drug for concealing the objectionable taste of the drug and lead to better patient compliance but with an ultimate clinical output.

REFERENCES

1. Gowthamarajan K, Kulkarni TG, Kumar NM. Pop the pills without bitterness:Taste masking technologies for bitter drug.Resonance general. 2004: 25-32.
2. Jha KS, Sharma RU, Surendra V. Taste masking in pharmaceuticals:An update.J of pharmacy research.2008; 1(2):126-130.
3. Suthar MA, Patel MM.. Ion exchange resin an imposing method for taste masking: a review.Int J of pharm science.2010;1(2):6-12.
4. Das S, Srikanth L, Saha S. Taste making of ciprofloxacin by ion exchange resin.Int J of preclinical and pharmaceutical research.2010; 1(1):7-13.
5. Triphati A, Parmar D, Patel U, Daslaniya D, Bhimani B. Taste masking:a novel approach for bitter and obnoxious drugs.JPSBR.2011; 1(3):136-142.
6. Wadhwa J, Puri S. Taste masking:a novel approach for bitter and obnoxious drugs. IJBTR.2011; 1(1):47-60.
7. Sharma V, Chopra H. Role of taste and taste masking of bitter drugs in pharmaceutical industries-an overview.Int J of pharmaceutical sciences.2010;2(4):14-18.

8. Ayenew Z, Puri V, Kumar L, Bansal KA. Trends in pharmaceutical taste masking technologies:a patent review. Bentham Science Publishers Ltd.2009;3:26-39.
9. Sikandar KM, Malviya R, Sharma KP. Taste masking:an important pharmaceutical technology for the improvement of organoleptic property of pharmaceutical active agents.European J of biological sciences.2011; 3(3):67-71.
10. Sharma S, Lewis S. Taste masking technologies:a review. Int J of pharmacy and pharmaceutical sciences.2010;2(2):6-12.
11. Jangde R, Saraf S, Daharwal S, Saraf S. Taste masking method for bitter drug and tasteless dispersible tablet:an overview.
12. Suhagiya VK, Goyani NA, Gupta NR. Taste masking by ion exchange resin and its new application:a review.Int J of pharmaceutical sciencse and research.2010;1(4):22-37.
13. Pandey S, Kumar S, Prajapati KS, Madhav SVN. An overview on taste physiology and masking of bitter drugs.Int J of pharma and bio science.2010;1(3):1-11.
14. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharmacokinetics,1st edition, vallabh prakashan,New delhi, 1995:162-163.
15. Y.Kasturgi,Sugiura Y.C.,Lee K,Kurihara Otsugi.Selective inhibition of bitter taste of various drugs by lipoprotein.Pharm.Res.1995;11:658-662.
16. Gedam SS,Tapar KK.Taste masking and characterization of diphenydramine hydrochloride by spray drying techniques.Int J of pharmaceutical research.2010;1(12):article 3.
17. Mendes WR,Anaebonam AO,Daruwala JB.In Lachman L,Liberman HA and Kanig JL.Theory and practice of industrial pharmacy,third edition.1976:346.
18. Stier ER. Masking bitter taste of pharmaceutical actives.
19. Patel RA, Vavia RP. Preparation and evaluation of taste masked famotidine formulation using drug/B-cyclodextrin ternary complexation approach.AAPS Pharm sci tech.2008;9(2):544-550.
20. Swarbrik J, Boylan S.C. (Eds.) Flavors and flavors modifier. In Encyclopedia of Pharmaceutical Technology (Vol. 6). New York:Marcel Dekker Inc.; 1990: 117-137.
21. Katsurgi Y., Kashiwayanagi M. Specific inhibitor for bitter taste inhibition of taste nerve responses and human taste sensation to bitter stimuli. Brain Res Protocols.1997**;** 1: 292-298.
22. Takagi S., Toka, K. Detection of suppression of bitterness by sweet substance using a multichannel taste sensor. J. Pharm.Sci. 1998; 87: 552-555.
23. Ibuprofen. Eur. Pat. Appl. EP 05,60,207 to Aziende chemiche Riunite Angelini Francesco (ACRAF) S.P.A.;1993.