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A BRIEF STUDY ON NOVEL AND ADVANCES IN TASTE MASKING TECHNOLOGY IN THE FIELD OF PHARMACEUTICAL INDUSTRY: AS REVIEW ARTICLE

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ABSTRACT

The present review article highlights different technologies of taste masking with respect to dosage form and novel methods of evaluation of taste masking effect. According to year 2003 survey of pediatrician by association of pediatrics unpleasant taste was the biggest barrier for completing treatment in pediatrics. Acceptability of any dosage form are mainly depends over its taste i.e. mouth feel. Drug molecule interacts with taste receptor on the tongue to give bitter, sweet or salty taste sensation, when they dissolve in saliva. This sensation of the taste is the result of signal transduction from the receptor organs for taste, commonly known as taste buds. In market, there are numbers of pharmaceutical preparations available in which actives are bitter in taste. l To overcome this problem, many techniques have been developed to mask the bitter taste of drugs. These techniques are not only masking the bitter taste of drug but also enhance the bioavailability and performance of drug dosage form. It includes adding sugars, flavors, sweeteners, use of lipoproteins, numbing taste buds, granulation, use of adsorbents' ,coating drug, microencapsulation, multiple emulsion, viscosity modifier, vesicles and liposomes, Prodrug and salt formation, inclusion and molecular complexes, solid dispersion and Ion Exchange Resins (IERs) which have been tried by the formulators to mask the unpleasant taste of the bitter drugs. Test masking of obnoxious drugs has gained the important as the most of them are administered orally. By development of taste masking technology of dosage form characteristics is improve and good patient compliesis achieved.

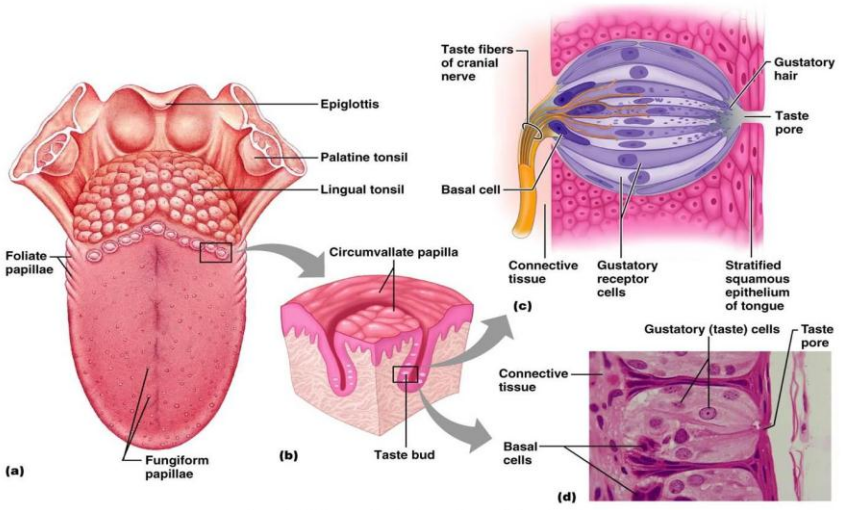
KEYWORDS: Taste, Bitter drugs, Taste buds, Taste masking, Taste masking technology.

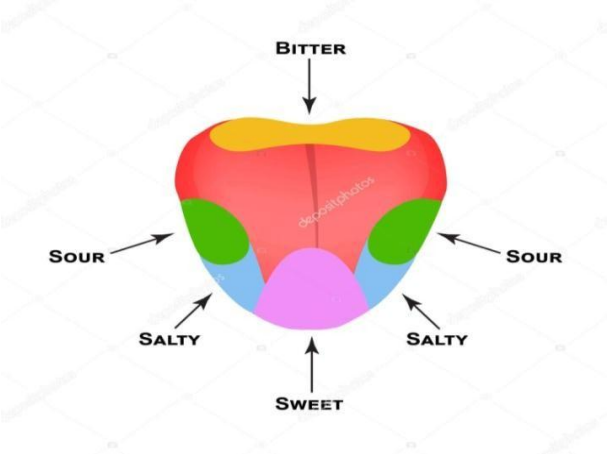
INTRODUCTION

Organoleptic properties are important considerations for development of a solid oral dosage form that can influence consumer preference and compliance. In the case of bitter drugs, taste is one of the most important parameter governing patient compliance.[1] Taste, smell, texture and after taste are important factors in the development of dosage forms and oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers especially for pediatric and geriatric.[2] The methods most commonly involved for achieving taste masking include various chemical and physical methods that prevent the drug substance from interaction with taste buds.[3] Masking of the unpleasant taste of a drug improves the compliance of the patient and product value Pharmaceutical companies are investing much time, money and resources in developing palatable, pleasant tasting products because good tasting products not only enhance the patient compliance but also provide a competitive advantage when a therapeutic category is crowded with similar products (e.g. anti-infective) and provide brand recognition to combat private-label competition.[4] Taste masking is defined as a perceived reduction of an undesirable taste that would otherwise exist. The ideal solution to reduce or inhibit bitterness is the discovery of a universal inhibitor of all bitter tasting substances that does not affect the other taste modalities such as sweetness or saltiness.[5] Thus in the present days, taste masking of bitter agents in the pharmaceutical industry has become commercially motivated activity for huge success of the product. Recent years have seen a tremendous progress in the techniques of masking the unacceptable taste of orally administered pharmaceuticals. Filling in capsules, adding flavors and sweeteners, use of lipoproteins for inhibiting bitterness, numbing of taste buds, coating of drug with inert agents, microencapsulation, multiple emulsion, viscosity modifiers, vesicles and liposomes, Prodrug formation, salt formation, formation of inclusion and molecular complexes, solid dispersion system and application of ion exchange resins are various approaches available to the formulator.[6] The present review deals in detail about all those approaches used for masking the taste of the bitter drugs.

Physiology of taste

The sense of taste is mediated by taste bud, which are group of taste receptor cell (50 – 100 cells), bundled together in clusters like bananas and gives sensation of taste via sensory neurons to central nervous system (CNS) in the brainstem Taste buds are chemoreceptor stimulated by chemicals dissolved in saliva from oral ingested medicaments and enter via the taste pore followed by interaction with surface proteins known as taste receptors causing electrical changes within taste cells, which cause the transmission of signals to the brain.[7]





[Physiology of taste]

Types of Taste and Its mechanism

Taste is one of the five senses and is the ability to detect the flavor of substances such as food, certain minerals, and poisons, etc. It determines the selection of food, its palatability and stimulation of reflexes for secretion of saliva, gastric juices and pancreatic juices.

Salty taste (Edge, Upper portion)

The salty taste is one among the four taste receptors of tongue. They are located on the edge and upper front portion of the tongue.

Sweet taste (Tip)

The sweet taste is one among the four taste receptors in the tongue. They are found on the tip of the tongue.

Sour taste (Along sides in back)

The sour taste is also one of the four taste receptors of the tongue. They occur at sides of the tongue and are stimulated mainly by acids.

Bitter taste (Back)

The bitter taste is the last and one of the four taste receptors in the tongue. That is located toward the back of the tongue. It is stimulated by a variety of chemical substances, most of which are organic compounds, although some inorganic compounds such as magnesium and calcium also produce bitter sensations.[8]

Ideal properties of taste masking process

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

a) Involve least number of equipments and processing steps.
b) Require excipients that have high margin of safety

c) Least manufacturing cost.
d) No adverse effect on drug bioavailability.
e) Require minimum number of excipients for an optimumformulation.
f) Require excipients that are economical and easily available.
g) Can be carried out at room temperature.[9]

Disadvantage of taste masking

- In some case adding a flavor or sweetener is a sample in others, applying some type of barrier membrane is used. Taste masker that seizes the API from taste receptors may recently fully affect PK, leading to efficacious taste-masking but leading to a decrease in bioavailability.
- Babies to teenagers are all the parts of the pediatric community, each with its demand. Full filling this requirement will be required a huge amount of time and money for itsresearch and testing.
- Destitute correlation of in vitro taste models frequently results in playability and sub-optimal taste masking. There is also increasing regulatory pressure to decrease the number of excipient usage in pediatric formulation, leading to the bioavailability of lack of regulatory clarity and fewer on how specifically to approach pediatric formulation. Advancement "rather than ascribing a defined process for the most part, agencies have adopted an approach of 'proposed and justify'.
- Due to progressive loss of taste masking efficiency upon storage in the liquid from polymer coating appears less effective for the oral liquid dosage form such as suspension.[10]

Need of taste masking

(a) One of the important characters of good oral form is pleasant taste. Significant development has been attained in the taste-masked formulation over the past decades.
(b) The active ingredient of numerous pharmaceuticals is bitter. Now a day most of the drugs that may be analgesic, cardiac, anti-inflammatory, diuretic, opioid analgesic, antiepileptic, anticoagulant, oral vaccines and sex hormones are bitter-like.
(c) Use of a proven method for inhibition and bitterness deduction has resulted in improved palatability of these preparations.
(d) The challenge of the obnoxious and disgruntled taste of drugs in the geriatric and pediatric formulation is a huge trouble for pharmacist in the current scene. Bitter taste- masking becomes essential to ensure patient compliance.[11]
(e) The medicine has the potential to be poisonous when consumed in enough quantity as numbers of drugs interrupt with physiological process with in cell. The bitter taste is thought to have been involved as a biggest barrier against consumed poisonous substances; this thing explains the bitter taste of the drug.
(f) A central challenge of administrating medicine to children is a "matter of taste" drug by their very nature, often taste unpleasant, with bitter taste a primary culprit. 95% of pediatricians describes that the greatest barrier to completing treatment are playability and drug taste.
(g) The basic biology of the pediatrics, as reviewed here, explain the reason adults and Children reject the bitter- tasting drug. Bitter compounds are very efficacious in preventing pediatric poisoning when synergized with different preventive excipients, such as child-resistant closure. Sweet taste is very loved by our species it was found out in a survey of the taste preference of humans ofall age categories.
(h) Hence effort is directed to make the preparation sweet to a different degree for controlling the taste qualities.[12]

Factor affecting the selection of taste masking technology

1. Bitter taste of (API)

Bad tasting medicaments even a little exposure is sufficient to perceive the bad taste. For example, sweeteners could not achieve taste masking of oral formulation of ibuprofen due to its dominating taste. Coating is more efficient technology for aggressively bitter drugs even though coating imperfections, if present, reduce the efficiency of the technique.[13]

Conventional taste masking techniques such as the use of sweeteners, amino acids and flavoring agents alone are often inadequate in masking the taste of highly bitter drugs such as quinine, Etoricoxib etc.[14]

2. Drug particle Shape and Size distribution

Particle characteristics of the drug would affect the taste masking process efficiency. Core materials with irregular shapes and small particle size lead to poor taste masking efficiency and varying dissolution of coated particles. Fines,abrasion and variable coating thickness can lead to situations wherein the taste mask coating is compromised. Multilayer coating using inner spacing layer to sequester the drug from taste masking layer helps to reduce or eliminate such coating imperfections. Taste masked granules of gatifloxacin and dextro methorphan were formulated by multilayer coating consisting of inner spacing layer followed by outer taste masking layer. [15]

3. Dose of active pharmaceuticals

Dose of a drug may dictate whether a particular formulation strategy would be suitable to achieve taste masking. In pediatric formulations, the dose is small enough so as to allow the usage of flavoring agents to mask the taste of the medicine. For example, low dose palatable pediatric aspirin oral formulation was developed by adding sweeteners, but the same approach failed to address the problem of drugs like acetaminophen because of its high dose. In such cases, coating is preferred to achieve taste masking along with

sweeteners to attain an acceptable final dosage form size.[16]

4. Dosage forms

It is estimated that 50% of the population have problem of swallowing tablets, especially the pediatric and geriatric population. Chewable tablets and liquid oral dosage forms have been used to address these problems. However, it is difficult to formulate some drugs in these dosage forms due to their poor palatability.[17]

5. Drug solubility

Physicochemical properties of the drug play an important role in the selection of taste masking technology. For example, ondansetron has a relatively lower water solubility at higher pH, based on which a rapidly disintegrating taste masked composition of ondansetron was formulated by adding an alkalizing agent(sodium bicarbonate) to reduce the water solubility and the consequent taste perception.[18]

6. Ionic characteristics of the drug

Ionic characteristics of drugs govern the selection of ion exchange resin polymers and the suitability of the drug candidate for this technology. For example, anionic polymers (e.g. alginic acid) are good candidates for cationic drugs like donepezil hydrochloride, and the cationic polymers are choice of excipients for anionic drugs like sildenafil.[19]

Method of taste masking

There are different kinds of methods used for taste masking of drug. This method of masking of taste can be divided into large parts into physical-chemical, biochemical and Organoleptic methods. Various methods are available to disguise the unnecessary taste of medicine. Some of them are as shown below.

(a) Use of flavor enhancer

(b) Conventional method

(a) Uses of sweetener

Sweeteners

Complement flavors associated with sweetness.

Soothing effect on the membrane of throat.

Natural sweetener: Sucrose, glucose, fructose, Sorbitol, mannitol, glycerol, Honey, liquorices.

Artificial sweetener-Saccharin, Saccharin sodium Aspartame.

Nutritive- Sucrose, Fructose and Glucose

Polyols- Mannitol, Sorbitol, Xylitol, Erythritol, Maltitol.

Non-Nutritive-Aspartame, Sucralose, Neotame and Saccharine.

Novel sweetener-Trehalose, Tagatose.

(b) Flavors

Natural flavors

- Juices - Raspberry
- Extracts - Liquorices
- Spirits - Lemon & Orange
- Syrups – Blackcurrant
- Tinctures -Ginger
- Aromatic waters - Anise & Cinnamon
- Aromatic Oils – Peppermint & Lemon.

Synthetic flavors

- Alcoholic solutions
- Aqueous solutions
- Powders.[20]

Microencapsulation

Microencapsulation is a process by which very tiny droplets or particles of liquid or solid material are surrounded or coated with a film or polymeric material. The goal of Microencapsulation may be accomplished by any of thefollowing techniques.

- Air suspension coating
- Coacervation - phase separation
- Spray drying and spray congealing
- Solvent evaporation
- Multiorifice - centrifugal process
- Pan coating
- Interfacial polymerization

Granulation

Granulation is a common processing step in the production of tablet dosage form. This step can be exploited as a mean for taste masking of slightly bitter tastingdrug. Some saliva insoluble polymers can also act as binding agent, granules prepared from these polymers show less solubility in saliva and thus taste could be masked. Granulation lowers the effective surface area of the bitter substance that come in contact with the tongue upon oral intake. But this reduction in surface area of bitter substance may or may not be effective in masking the bad taste.

Prodrug

Prodrug are defined as therapeutic agents that are inactive moieties but on biotransformation liberate the pharmaceutically active parent metabolites. By changing the molecular configuration of the parent molecule, the magnitude of a bitter taste response or taste receptor-substrate adsorption constant may be modified. Prodrug 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.[21]

Ion exchange resin

Another popular approach in the development of taste masking is based on ion exchange resin. Ion exchange resins are solid and suitably insoluble high molecular weight polyelectrolyte's that can exchange their mobile ions of equal charge with the surrounding medium. The resulting ion exchange is reversible and stiochiometric with the displacement of one ionic species by another. Synthetic ion exchange resins have been used in pharmacy and medicine for taste masking or controlled release of drug as early as 1950.

Solid dispersions

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.[22]

Melting method: In this method, the drug or drug mixture and 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

Organoleptic method

This is the most straightforward way to hide your taste. To disguise the disagreeable taste of low to moderate bitter actives, an aggregate of sweeteners and flavors is used.

To improve the mouth feel, effervescent substances can also be added. A bitterness blocking agent may be included in some preparations to disguise the tart taste.

Hot melt extrusion

Hot-melt extrusion (HME) is a novel approach to mask the drug also having several disadvantages, including no organic solvent in the process, fewer processing stages, continuous operations, and scale-up potential. The bitter active is combined with other substances in dry conditions to disguise the taste. A hopper holds the mixture, which is then transported, combined, and melted by an extruder. To make the taste-masked extrudates, the components go through a heating procedure with a lot of mixing. It is then micronized to make taste-masked granules which are then added to an appropriate dosage form.[23]

Spray drying

The bitter medication is either dissolved or dispersed in a suitable solvent with a polymer, and then spray dried. Three steps are commonly involved in the procedure:

Atomization of feed into a spray

Before drying spray air.

Estrangement of dried product from the air.[24]

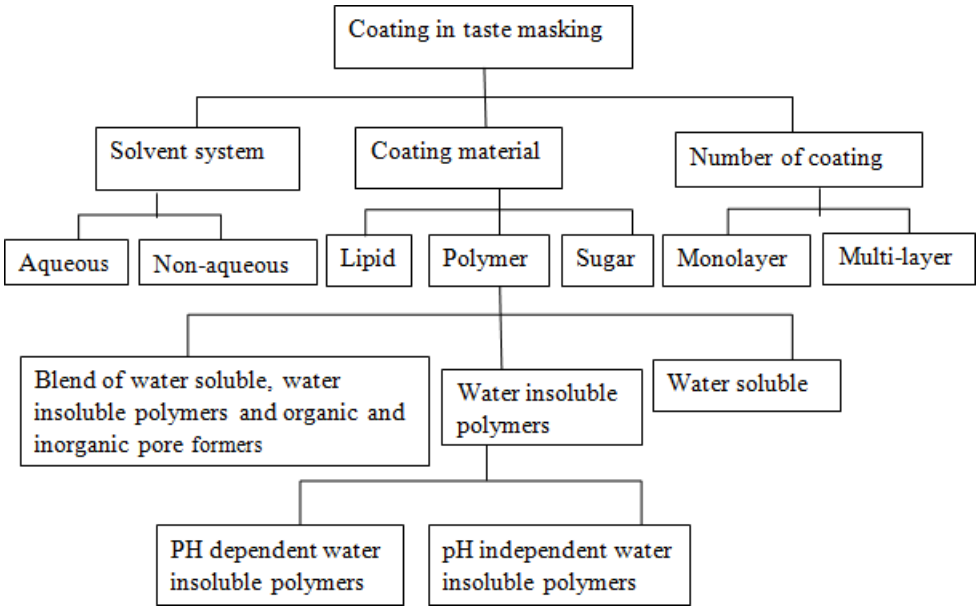
Inclusion complex

In the formulation of inclusion complex, the drug molecules get trap into cavity of complexing agent I.e. host cell forming a stable complex. The complexing agent can disguise the medicine's bitter taste by lowering its oral solubility after consumption or reducing the number of drug particles exposed to taste buds, hence lessening the bitter taste perception.

Recent method

Coating

To accomplish flavor masking via aqueous or organic-based coating method, hydrophobic polymers, lipids, sweeteners, and hydrophilic polymer can be employed as coating materials, eighter alone or in combination, as a single or layered coat.[25]



CONCLUSION

Taste masking of drugs has been challenge to the scientist. Taste of drugs requires skillful application which does not affect the bioavailability of drug There are number of technology available which effectively mask the objectionable test of drugs. Selection of technology depends upon the bitterness of drugs and their compatibility with the taste masking agent. Test masking of bitter drugs has significantly improved the quality of treatment provided to suffering patients especially children. Use of sweeteners is an age old and most popular tool for disguising bitterness, the present trend has been towards exploring intense sweeteners of natural origin that can hasten commercialization The

development of taste masking methodology requires great technical skills and the need of massive experimentation Several approaches namely sensory, barrier, chemical and complication have been tried to mask the unpleasant taste of formulation. Palatability is recognized as being a critical factor in patient compliance, particularly for children in whom the acceptability of medicament and hence its ease of administration.

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