

Review on Taste Masking Approaches and Evaluations

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Submitted: 15-07-2022

Accepted: 30-07-2022

ABSTRACT

Taste is one of the most important factors which effects on the development of oral dosage form especially in paediatrics and geriatrics. Taste is the ability of taste buds present on tongue to detect the flavour of various substances, food and drugs. For better compliance of patients & quality of pharmaceutical products good taste is an important parameter. Bitter or unpleasant taste is the main barrier in administration of oral dosage form. To mask the bitter taste of drug there is various test masking technologies are used. This review paper contains various taste masking technologies not only for overcome the bitter taste but also maintaining bioavailability of the drugs. It also may explore a evaluation techniques, current and future scope.

Oral administration of bitter or noxious drugs With an acceptable degree of palatability is a key issue For health care providers & pharmacist especially for paediatric Patient.

Keyword: Taste masking, IER's, flavours, paediatrics, Medical product

I. INTRODUCTION

Taste is an important factor in the development of a oral dosage form. Taste masking becomes a essential for undesirable or noxious drugs to improve the patient's acceptance specially in the paediatric and geriatric Patients. Some of the orally administered drugs contain bitter taste. Mainly two approaches are commonly used to overcome the bitter taste of the drug. The first approach the reduce the drug solubility in the saliva and second is to alter the ability of the drug to interact with taste receptors. There are various techniques are available to mask the unpleasant taste of the drugs.

II. TYPES AND MECHANISM OF TASTE

Taste is the ability of taste receptor to detect the flavour of substances such As food, minerals, Drugs, & poison substance etc. by sensory organs,

taste buds. It also stimulates the reflexes for secretion of saliva, Gastric juices, and pancreatic juices & selection of food.

There are mainly five taste which are mentioned below:

- Sweet
- Saltish
- Sour
- Bitter
- Umami

Humans receive tastes through gustatory Calyculi (taste buds, Sensory organs) present on the upper surface of the tongue.

Tastebuds

Taste buds are a small organ located primarily on the tongue. The adult human tongue contains between 2,000 and 8,000 taste buds, each of which are made up of 50 to 150 taste receptor cells. Taste receptor cells are responsible for reporting the sense of taste to the brain

Mechanismoftaste

The gustatory system is the sensory system which is partly responsible for the perception of any flavour or tastes. Taste is the perception which is produced when an any substance or food introduce into oral cavity and chemically contact with the taste receptor present on the tongue. Humans contain taste receptors on taste buds and other areas including the upper surface of the tongue and the epiglottis. Mainly the gustatory cortex is responsible for the perception of taste or flavour of food. Tongue is covered with thousands of small bumps called as papillae, which are seen by the naked eyes. All papillae contain hundreds of taste buds on their surface. The taste buds which are located on the back and front of the tongue. Remaining taste buds are present on the roof, sides and back of the oral cavity, and in throat. Each and every taste bud contains 50 to 100 taste receptor cells. There are five main taste which are determined by tastes buds: Sweet,saltish, sour, bitter, umami.

III. MECHANISM OF TASTE MASKING

The mechanisms of taste-masking techniques based on two major approaches.

- A. The first is to add sweeteners, flavours, and effervescent agents to mask the unpleasant taste.
- B. The second is to avoid the contact of bitter or unpleasant drugs with taste buds.

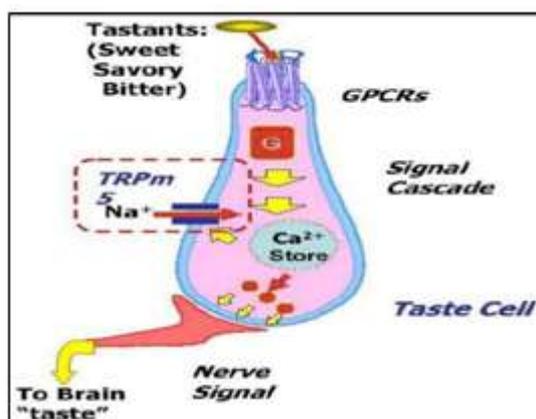


Fig. Taste blocking mechanism

A. Taste Masking Technology

Taste Masking is very essential & important technology for masking the unpleasant taste of drugs. There are various techniques available in this literature review there are some of the following techniques are mentioned:

1. Taste masking with Flavours and Sweeteners

This is one of the simple methods to mask the taste of bitter drug. This method includes the sweetener, flavour & amino acid to mask the taste. But this is not more successful for bitter drugs.

- **Flavours**

Flavour is defined as the sensory impression of a food or other substance, and it is detected by the chemical senses of taste and smell. The trigeminal senses, which may also occasionally determine flavours. The flavours can alter the bitter taste of drugs by using natural or synthetic Sweeteners or flavour.

- **Natural Flavours**

Natural flavours are those flavour which are obtained from natural source like plant and animal which includes flowers, buds, fresh etc. Raspberry Juices, Liqueurices, Extract of Lemon & Orange Spirits & Cinnamon Aromatic Waters, Peppermint & Lemon Aromatic Oils.

- **Synthetic Flavours**

It is an artificial flavour designed to mask the taste. Alcohol has a bitter and medicinal taste, ester is fruity, ketones and pyrazines taste like caramel etc.

- **Sweeteners**

A sweetener is a substance which may be added to food, drink, or medicine to impart the flavour of sweetness. Complementary flavours associated with sweetness provide a soothing effect on the membranes of the throat.

- **Natural Sweetener**

According to the FDA, all sweeteners “derived from a natural source” are called natural, no matter how highly refined and processed they might be. Sucrose, Glucose, Fructose, Sorbitol, Mannitol, Honey, Glycerol, etc.

- **Artificial Sweetener**

Following are some artificial sweeteners added to mask the taste:

Nutritive Sweeteners- Sucrose, Fructose, Glucose
 Non-Nutritive Sweeteners- Sucralose, Saccharine, Aspartame

2. Polymer coating of drug

This is the simplest and most convenient option to achieve taste masking. The coating acts as a physical barrier to the drug particle, thereby minimizing interaction between the drug and taste buds. Coating of chewable tablets provides excellent taste masking and provides acceptable bioavailability. In this method, taking powders as fine as 50 µm are fluidized in an expansion chamber heated with high-velocity air and the drug particles are coated with a coating solution introduced usually from the top as a spray through a nozzle. Any polymer which is insoluble at pH 7.4 and soluble at acidic pH, is an acceptable alternative for the taste masking.

The agents which are mostly used for coating are Carbohydrates (Cellulose), Synthetic polymers Proteins, Gelatine, and Prolamins. There are three types of classification under this category, namely, Natural, Synthetic, and Semi-synthetic Polymers which are used to mask taste.

Sr. No.	Drugs	Techniques	Polymer Used
1	Pinaverium bromide	Coating	Cellulose or shellac
2	Propranolol hydrochloride	Coating	L-HPC, EC
3	Ibuprofen	Air-suspension coating	Methacrylic acid copolymer
4	Triprolidine HCL	Dispersion coating	HPMC
5	Dimenhydrinate	-	Eudragit or CMC

3. Ionexchangeresincomplexes

The Ion-exchange resins are highly molecular weight Polymers which contain cationic and anionic functional groups attached to the water insoluble polymer backbone. These Groups of polymers have an ability to exchange for oppositely Charged counter ions, thus it absorbing the ions into the Polymer matrix since the most of the drugs possess ionic sites in their molecule. The resin's charge complexes provide Weak ionic bonding Hence the dissociation of the drug- resin complex does not occur under the salivary pH Conditions it results into taste masking. For the taste Masking Approaches Weak cationic exchange or weak anionic exchange resin are used based on the drugs nature.

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)
Chloroquine phosphate	Indion 234(weak cation exchange resin)

4. Soliddispersion

The term solid dispersion defined as the dispersion of one or more active ingredients in a hydrophilic inert carrier matrix at molecular level. It is prepared by the melt (fusion) method and solvent evaporation technique. However, the process is depending on the interaction between drug and carrier. Solid dispersion of the drug With the help of polymers, sugar and other suitable Agent used to Mask the taste. Some of the Carriers which is Used in solid dispersion systems include: Polyethylene glycols, hydroxypropyl methylcellulose, urea, mannitol and ethyl cellulose. Various methods are used for solid dispersion of drug are mentioned below

- **Melting method**

In this type of method, the drug or drug mixture melted with carrier by the process of heating. The melted mixture is cooled and solidified rapidly in an ice bath with vigorous stirring. The final solid mass is crushed and triturate.

- **Solvent method**

In this method, the active drug and carrier are dissolved in a same solvent, by the process of solvent evaporation and recovery of the solid dispersion.

- **Melting solvent method**

In this method drug in solutions is incorporated into molten mass of polyethylene glycol at a temperature 70°C without removing the solvent.

5. Microencapsulation

Microencapsulation is the modified form of film coating differentiating only in the size of the particle to be coated and the Methods by which coating is achieved. Microencapsulation is a process in which tiny particles or droplets are surrounded by a coating with coating agent such as gelatine ethyl cellulose, bees wax etc to give small capsules, with useful medicinal properties. Microencapsulation can also be used to enclose solids, liquids, or gases inside a micrometric wall made up of hard or soft soluble film, in order to reduce dosing frequency and also prevent the degradation of pharmaceutical products.

The soluble portion of the drug only can generate the sensation of taste. Hence coating of active pharmaceutical ingredients with selected polymer coating can reduce the solubility in the saliva present in oral cavity thus resulting into taste could be masked. Coating act as the barrier between the drugs and the taste buds.

Polymers have been used as Coating materials, either alone or in combination in the taste masking of bitter drugs.

Types of microencapsulation include:

- Air suspension coating
- Spray drying
- Spray congealing
- Solvent evaporation
- Pan Coating

6. MultipleEmulsions

Multiple emulsions are the complex polydisperse systems where both oil in water and water in oil emulsion exists simultaneously which are stabilized by lipophilic and hydrophilic surfactants.

The w/o/w or o/w/o type multiple emulsion are Vesicular systems in which active pharmaceutical ingredients can be Entrapped in an internal phase. These entrapped substances Can be transferred from internal phase to the external Phase through the membrane phase. This phase Controls the release of drug the system. If the system is enough stable for their self-life, then the formulation may mask the taste

7. Development of Liposome

Liposomes are the round bubbles consisting of an aqueous core encapsulated by natural or synthetic phospholipids layer. This liposome structure act as ideal drug carriers, since hydrophilic drugs tend to be entrapped in the core; while hydrophobic drug will be entrapped within the lipid bilayers. Oils, surfactants, polyalcohol's, and lipids effectively increase the viscosity in the mouth due to which the time Of contact between the bitter drug and taste receptors is decreases, thus improving the overall taste masking efficiency. Masking the bitterness of drugs by phospholipids such as phosphatidic acid, phosphatidylinositol, soya lecithin etc has been reported. For example, the bitterness of Chloroquine phosphate in HEPES buffer (PH 7.2) is masked development of liposome.

8. Prodrugapproach

Prodrugs are therapeutic or medicine that are inactive but after administration it is metabolized into Pharmacologically active compounds. Prodrugs are designed to improve a bioavailability of drugs as well as for Masking bitter taste of drug. This may also reduce adverse or unintended effects of a drug, especially important in treatments like chemotherapy. 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 drug.

Parent Drug	Prodrug
Erythromycin	Erythromycin Propionate
Clindamycin	Clindamycin palmitate ester
Chloramphenicol	Chloramphenicol palmitate ester
Morphine	N-oxide derivatives of all morphine

9. Tastemaskingusinginclusioncomplex

This is the one of the latest and current technique for the taste masking with advantage of enhanced solubility Of poorly soluble drug. Complexation of drug by complexing agent that enhances li Drug dissolution rate and thus it masks the bitterness of the drug.

In the inclusion complex formation, the drug molecule fits Into the cavity of a complexing agent (host Molecule) forming a stable complex, a low stability Constant would lead to a rapid release of

free drug in the oral cavity, results into taste Masking.

10. Taste Masking with Lipophilic Vehicles

It is one of the effective methods for taste Masking by using lipid & lecithin & lecithin like substances.

• Lipids

Taste Masking mechanism generally done by increasing viscosity of saliva in oral cavity. Oils, surfactants, polyalcohol's, and lipids effectively increase the viscosity in the mouth and coated the Taste buds may effectively use is Taste Masking. For example, Gabapentin (acyclic amino Acid) a drug used for treatment of seizure has improved taste when it Coated with gelatine and then mixed with partially Hydrogenated soybean oil and glyceryl monostearate.

• Lecithin and Lecithin-like Substances

For controlling bitter Taste of medicines formulation with large excess of lecithin and lecithin like substances are used. Magnesium aluminium silicate With soybean lecithin is used to mask the unpleasant Taste of talampicillin HCl. The drug is dissolved in or dispersed into an organic solvent such as chloroform.

Drug	Complexing Agent	Dosage form
Benexate Hydrochloride	Cyclodextrin	Granules
Caebepentane citrate	Cyclodextrin	Oral liquid
Chloroquine Phosphate	Tannic acid	Syrup
Dimenhydrinate	Eudragit S 100	Chewable Tablet
Gymnema Sylvestra	Chitosan	Oral liquid
Ibuprofen	Hydroxy propyl-cyclodextrin	Solution

IV. EVALUATIONTECHNIQUES

• Sensory evaluation

Taste is a very subjective & critical perception it may vary depending on individual. For selection of appropriate method of Taste masking sensory evaluation is very important parameters. For Quantitatively evaluate taste sensation, following methods have been reported.

• Panel testing

In this Method, a group of about 5 to 10 human volunteers is trained for taste evaluation by using Reference solutions ranging in taste from tasteless to very bitter. Then numerical values are assigned

the levels of bitterness. Subsequently, test solution is tasted And rated on the same scale to assess its bitterness.

- **Measurement of frog taste nerve responses.**

In frog testing nerve response method, adult bull frogs are anaesthetized within peritoneal cavity and the Glossopharyngeal nerve is dissected from the surrounding tissue and cut Proximally. Nerve impulses of frog are measured by using an amplifier & electronic integrated.

- **Multichannel taste sensor or magic tongue**

Invention of E-Tongue, electronic sensor array Technology overcomes this problem of evaluation of taste. It is a device For recognition, quantitative multicomponent analysis and artificial assessment of taste and flavour. It determines three levels of biological taste including Receptor level (Taste buds in humans, probe Membranes in E-Tongue), circuit level (neural Transmission in humans, transducer in E-Tongue), Perceptual level (cognition in the thalamus humans, computer and statistical analysis in the E-tongue).

- **Spectrophotometric evaluation (D30's value)**

This technique has been used to evaluate the taste masked Granules of sparfloxacin, with threshold concentration being 100µg/ml.Spectrophotometric method. In this method a known quantity of the taste-masked formulation is mixed With 10ml of distilled water in 10ml syringe by revolving the Syringe, end to end, five times in 30 seconds. Then the test medium is filtered through a membrane filter, Followed by spectrophotometric determination of concentration of the drug in the filtrate.

V. CURRENT & FUTURE DEVELOPMENTS

Medicine word is like synonyms to bad taste for children.Oral pharmaceutical companies continually enhanced the taste of medicine for betterment of products. Taste masking is a viable strategy to improve the patient compliance, especially for geriatrics & paediatrics consumer. In present scenario the patients demand for pleasant taste drugs. Hence taste masking is an important factor for the success of any pharmaceutical products. This is the key challenge to pharmacist. Now there are various taste masking technology are evolved in for betterment. For success of company's product & better results taste masking is an important for current & future.

VI. CONCLUSION

The taste masking of unpleasant or bitter drug has been challenged to a pharmacist and scientists in the present scenario especially in paediatrics and geriatrics.

Taste masking can be achieved by using various recent taste masking technologies. There are various taste masking technology are available which effectively Mask the unacceptable taste of drug as well as product acceptance at large extent without affecting bioavailability of drug. For appropriate selection of taste masking technology Evaluation parameters are essential.

This study helps us to develop a new Approaches of taste masking for the better patient compliance. After considering all of factors it is concluded that taste masking formulation required following parameters. It may involve least number of equipment and processing steps. It may require minimum number of economical excipients. Not required any kind of adverse reactions on bioavailability of drugs due to these technologies.

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