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Review Article

Advances in taste masking of drug: a review study

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Abstract



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Taste is the ability to determine the flavor of substances like food, drug, etc. The aspect of taste only occurs when the drug get soluble in saliva. Firstly the drug gets dispersible in saliva then they show interaction with taste bud and then perception of taste is occurred. The above test receptor get binds to the molecules of saliva and generates the electrical impulses from the area of brain that area is cranial nerves 7th, 9th 10th and then perception of taste occurs. Currently varieties of drugs are available like cardiac, analgesic, anti-inflammatory, opioid analgesic, anti-epileptic, anticoagulant, oral vaccine and sex hormone. Due to bitter formulation it tends to patient complain the problem of bitter and unpleasant taste of drug in the pediatrics and geriatric formulation is provocation to the pharmacist in the current scenario. Bitter taste masking become important to solve patient complain. This is become most important issue regards with pharmaceutical therapies. Taste masking get broadly classify into physical, chemical, biochemical and organoleptic methods. There are different types of method are available to mask the unpleasant taste of drug. The physical method involves the use of sweeteners and flavor enhancers. The chemical method involves Ion exchange resin, solid dispersions, spray drying, Inclusion complex, Microencapsulation, coating. The biochemical method involves Prodrug, Hot melt extrusion. The most abundantly used method involves are spray drying, Inclusion complex, Microencapsulation, coating, hot-melt extrusion, and organoleptic methods.

Keywords: Obnoxious, Hot melt Extrusion, Ion exchange resin, coating, palatability.

INTRODUCTION

In biological sense, definition of taste (gustation) is a chemical reaction derived from a Sensory response from the four main taste perceptions; salt, sour, bitter, and Sweet. Taste is the ability of the human body to discover the flavor of substances like food, drugs, etc. It gained its attention as most of the drugs

are administered through the oral route. The unpleasant taste of the drug creates a huge problem in drug administration, particularly in the case of pediatrics and geriatrics. Humans detect taste with taste receptor cells which get combined to form an onion-shaped organ called taste buds. Each taste bud has a pore that opens out to the surface of the tongue through which molecule and ion reach the receptor cell inside.

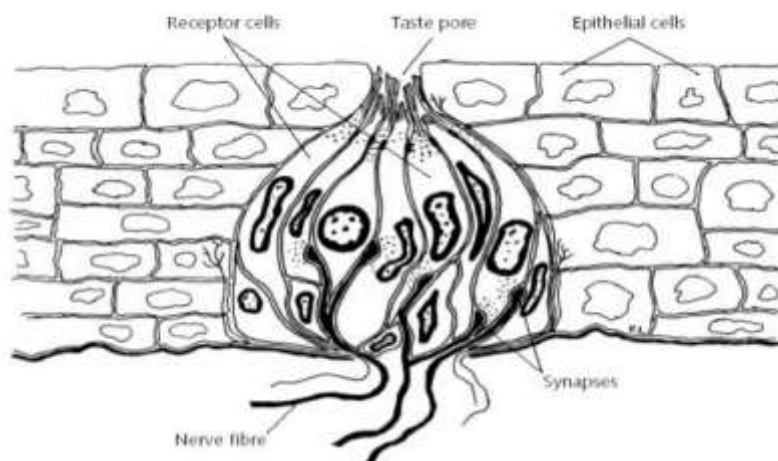


Figure 1: Microscopic image of Taste bud¹

There are about 10000 taste bud in human and in foetus condition 50 -100 taste bud present in single cell. Taste cell receptors are transmembrane proteins that bind to the molecule and ion giving rise to four primary sensations of taste. The sensitive nerves ending present over taste bud produce and pass on electrical instinct to the brain. once the substances are dissolved in salt solubilized and commune with taste bud and perception of taste occurs. Oral administration of medicine is Convenient and economical. Several oral pharmaceutical preparations countless food, and beverage product, and bulking agent have annoying, tart-tasting components. So pharmaceutical formulation with pleasant taste is more preferential today to compete with over a competitor's products and its provide better therapeutic values for patient and business also. Some properties are followed by ideal taste masking process and formulation

- 1.) Few equipment and processing step is required.
- 2.) Least usage of different excipients for formulation.
- 3.) No inauspicious effect on the bioavailability of the drug.
- 4.) Economical and easily available excipient must be in use
- 5.) Manufacturing cost should be minimal
- 6.) required excipient having the safety of high margins.
- 7.) Perform formulation at room temperature.
- 8.) Easy and expeditious to prepare

The fifth independent taste unani, recently discover the monosodium glutamate present in seaweed and disodium insoniate in fish and meant. The taste receptor binds to the molecule by saliva and transmits electrical instinct by the 7th, 9th, and 10th cranial nerves to the area of the brain which participates in detection of taste.¹

Need of taste masking

- One of the important character of good oral form is pleasant taste. Significant development has been attained in the taste-masked formulation over the past decades.
- use of a proven method for inhibition and bitterness deduction has resulted in improved palatability of these preparations.
- 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.
- 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.²
- A central challenge of administrating medicine to children is a "matter of taste" drugs 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.
- 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.
- 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 of all age categories.³

- Hence effort is directed to make the preparation sweet to a different degree for controlling the taste qualities.⁴

Advantage of taste masking

- For the pediatric population, pediatricians have reported obnoxious taste as the biggest barrier in the treatment.⁵ Unless the active ingredient does not have any unpleasant taste or must be pleasant tasting thus this barrier can be braked by using certain taste-masking techniques.
- The industry will continue to see improvement and development in taste masking of dosage form for the geriatric and pediatric patient population. It is need of present world hence it will give large amounts of employment for people in this field who will work just to cover the taste of bitter drug thus makes it more palatable

The 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.
- 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'.
- 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 its research and testing.
- 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.⁶

Method of taste Masking

There are different kinds of methods used for taste masking of drug. This is an problem of increasing importance in the area of patient palatability with drug therapy recommendations. 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.⁴

1. Conventional method

1. Use of flavor enhancer
2. Uses of sweetener

2. Recent method

1. Granulation
2. Prodrug
3. Ion exchange resin
4. Solid dispersions
5. Organoleptic method
6. Hot melt Extrusion
7. Spray drying
8. Inclusion complex
9. Microencapsulation
10. Coating.

Use of sweetener

Sweeteners are frequently utilized in pharmaceutical formulation for a variety of purposes (eg, diluents in tablet) in combination to their critical role in taste masking nutritive sweetener, polyols, and hydrogenated starch hydrolysates, and high-intensity sweetener are three types. They have different organoleptic and functional qualities as no specific individual sweetener is suitable for everyone. This this can be overcome by using a mixture of sweeteners that lower the ingestion rate of a specific sweetener. Example saccharin is 500 times sweeter than sucrose but can be Carcinogenic Aspartame. ⁷

Use of flavors enhancer

- The material used for taste masking is frequently categorized based on the basic flavor that is hidden. Natural and manmade sources of flavoring and perfuming agents are available.
- Some example of natural products are distilled fraction of fruit juice, aromatic oils such as peppermint and lemon oil ,herbs species. They are accessible as concerned extracts, alcoholic, aqueous solutions, and other forms.
- By adding some traditional material like alkaline earth oxide ,alkaline earth hydroxide has proved effective for masking the bitter nature of chemical.⁸
- Natural flavors are the most common type of taste found in food and pharmaceutical products. They are however being phased out in the flavor of synthetic flavor due to numerous drawbacks, including unpredictability in standard due to natural origin, unreliability, expense, and reachability.

Granulation

- Granulation is a flavor masking method that is less expensive, quick, and scalable. To conceal the taste of bitter medicine, polymer, flavor, and waxes have been utilized as granulating agents.
- Liquid having low melting point waxes such as glycerol palmitosterate, glyceryl behenate and hydrogenated castor oil are used.
- The practical coating may be incomplete during granulation. Swelling of the matrix, on the other hand, can reduce the diffusion of the bitter active. As a result, when compared to non-swellable polymer, a swellable polymer can provide greater taste masking in granulation. ⁶
- It's a common procedure in the manufacturing of tablet dosage forms. As a binding agent, several saliva insoluble polymers are utilized. The taste of granules made of these polymers is muted because they are less solubilized in saliva. The productive surface area of the bitter chemical that contacts the tongue during oral consumption is reduced by granulation. ⁹
- Taste masked granules made from saliva insoluble polymer cab be made into a variety of tablet dosage forms, including chewable and rapidly dissolving tablets. To produce the taste masking liquid and waxes of low melting point such as glycerol palmitate stearate, glyceryl behenate, and hydrogenated castor oil is typically utilized in process of granulation. ¹⁰

Prodrug

- They are therapeutic compounds that are indolent moieties but release pharmaceutically active parent metabolic after biotransformation. The degree of bitter taste reaction of the taste receptor.

- Substrate adsorption constant can be altered by modifying the parent molecule chemical configuration.
- When opioid analgesic and antagonist were delivered as prodrug tasteless /bitterness prodrug was created for enhancing buccal distribution, bioavailability was improved without obvious side effect. ¹

Ion Exchange Resin

- Ion exchange resin (IERS) are polymers having a cationic and anionic functional group that has a high molecular weight. A copolymer of styrene and divinylbenzene is the most commonly used polymeric network.
- Drugs can be bonded to the resin through repeated exposure to the drug in a chromate graph column or extended touch with the solution of drug. Drugs bind to the oppositely charged substrate of resin, generating insoluble adsorbates or resonance by weak ionic interaction, preventing the drug-resin complex from dissociating under salivary pH conditions. ⁶

In ion-exchange resin is divided into four categories.

IERS has been intensively investigated in the evolution of novel drug delivery system and other medical application over the last few years. For immediate releases and peroral administration, several ion exchange resin preparations have been devolved for the goal of long-term release.

- Ion exchange resins have been shown in many investigations to be equally suitable for drug delivery technology. ¹¹

Solid Dispersion

- Specific interaction between weakly soluble pharmaceutical and hydrophilic polymer can improve the drug solubility, conversely, specific interaction between the drug and hydrophobic polymer can reduce the drug solubility.
- A large number of recipients are required in this method. ⁴
- Natural polymers like shellac and zein as well as an enteric polymer like acrylic acid polymer derivative and phthalate are the ideal alternative for creating taste-masked solid dispersion.

Taste techniques on an industrial scale

The taste-masking technique is frequently used in conjunction with formulation technologies. In a nutshell, they must be compatible with one another. Coated particles created from the fluid-bed coating, for example, should be capable to hold out against the compression process employed in the fabrication of the final dosage form. The organoleptic method is one of the most often utilized industrial taste-masking methods. Organoleptic approaches, polymer coating, hot-melt extrusion, microencapsulation, complexation, and spray drying are some of the most regularly utilized industrial taste-masking techniques. ¹²

Organoleptic methods

- This is the most straightforward way to hide your taste. To disguise the disagreeable taste of low to moderate bitter actives, a aggregate of sweeteners and flavors is used.
- To improve the mouthfeel, effervescent substances can also be added. A bitterness blocking agent may be included in some preparations to disguise the tart taste.
- The addition of sodium chloride to a formulation to conceal bitterness has also been discovered, as in the

manufacturing of pioglitazone hydrochloride orally disintegrating tablets.¹³

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.¹³

Spray drying

- By using a physical barrier coating spray drying is an alternative method to taste masking.
- The bitter medication is either dissolved or dispersed in a suitable solvent with a polymer, then spray dried.
- Three steps are commonly involved in the procedure:
 1. Atomization of feed into a spray
 2. Before drying spray air.
 3. estrangement of dried product from the air
- Spray drying has several advantages, including
 - a) A shorter processing time as it is a one-step process.
 - b) The capacity to level up.
 - c) A broad range of solvent and polymer options.¹⁰

Inclusion complex

- In the formulation of inclusion complex, the drug molecules get trapped into the cavity of the complexing agent, i.e. host cell, forming a stable complex.¹⁴

- 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.
- By adding *Gymnema Sylvestre*, a tart and astringent tasting sweetener for diabetic control, with β -cyclodextrin, the disagreeable taste of medication can be disguised.²

Microencapsulation

- In this process, there is a coating of polymeric material on the active moiety.
- The flavor of bitter drug particles can be concealed by coating the drug particles, which established a physical obstacle between the drug and taste buds. Microencapsulation has a polymeric skin or wall that surrounds a core.¹⁵ Microencapsulation comes in a variety of forms, such as:
 1. Coating for air suspension.
 2. Separation of coacervation phase.
 3. Drying using a spray gun.
 4. Evaporation of solvent.
 5. Coating the pan.
 6. Polymerization at the interface.⁸

Coating

- The number of coating layers, the kind of coating substance, the coating material, and the coating solvents system is all used to classify coatings.
- To accomplish flavor masking via aqueous or organic-based coating method, hydrophobic polymers, lipids, sweeteners, and hydrophilic polymer can be employed as coating materials, either alone or in combination, as a single or layered coat.¹⁶
- However, this approach may be ineffective for the oral liquid dosage forms such as suspension because of gradual decrease of taste masking efficiency upon storage in a liquid dosage form.
- This method can provide an effective taste-masked suspension over a long prolonged storage time.⁶

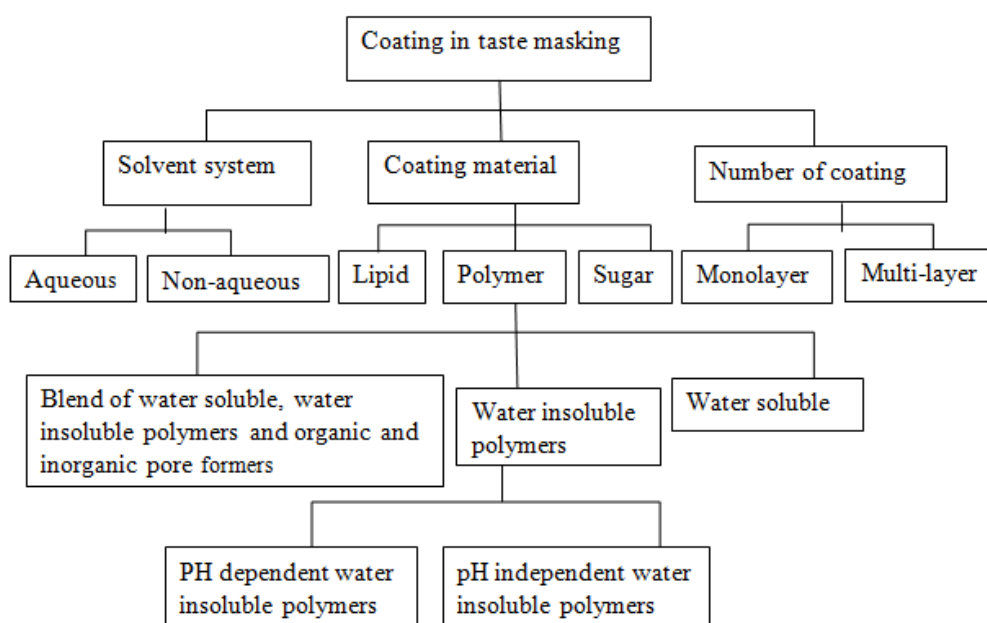


Figure 2: Coating¹

Techniques employed for taste masking of different dosage forms

• Tablets:-

- The flavor of most tablets can be effectively concealed by using an inert polymer covering that prevents the medication ingredient from connecting with the taste buds.
- Nonetheless, various professionals have attempted to examine and discover the usage of modern elements in poor flavor abatement and excellent taste improvement on numerous occasions.¹⁷

• Granules/Powders:-

- Sachets sprinkle capsules, and powders for reconstituting as liquid account for a large portion of the pediatric and geriatric market.
- The importance of the topic is demonstrated by a huge number of patients on the subject. The procedure entails covering the drug cores with many aqueous copolymer dispersions layers.
- The invention's granules could be utilized to make chewable tablets with high palatability and bioavailability.

• Liquids:-

- Because the bulk of pediatric medicines is syrups and suspensions, they pose a significant problem in flavor masking. However, the aforementioned methods have also been employed to enhance the liquid taste, and a few patents in the area are worth highlighting.
- Meyer et al. employed prolamine as a single coating at a weight ratio of 5%-100% relative to the active compound being coated, resulting in a liquid solution that successfully concealed the taste of extremely bitter orally delivered medicines.
- The active substance's initial bioavailability is unaffected by the prolamine coating. antibiotics, vitamins, dietary fiber, analgesics, enzymes, and hormones can be effectively coated by prolamine coating.

Method of evaluation of taste masking effect

- Sensory analysis has long been used to characterize flavors, smells, and scents in industrialized countries. In the past, experts offered subjective data on the composition of one product compared to another to formulation scientists.
- Nowadays, the sensory analysis incorporates both objective and subjective or hedonic methodologies. Sotakagi et al. developed a multichannel taste sensor with varied properties that can identify flavor in a way that is similar to human gustatory sensibility.
- Taste information is covered into patterns made up of electrical signals from the receptor's membrane potential. It was claimed that utilizing a multichannel taste sensor, the bitterness suppression of Quinine and a pharmacological ingredient by sugar could be detected.¹⁸
- It is anticipated that the current method will give several automated methods for determining the strength of a drug ingredient. The rate of release of medicine from the microsphere can be used to access the taste-masking effect of coated microspheres.
- The drug release rate can be used as a measure of the degree of taste masking accomplished when analyzing the flavor masking effect of ion exchange resin.

- A trained flavor profile panel and the time-intensity approach, in which a sample comparable to a regular dose was retained in the mouth for 10 seconds are two more methods the level of bitterness is immediately recorded and assigned value ranges from 0-319.
- Continuous Multipurpose Melt (CMT) Technology and Wet Spherical Agglomeration (WSA) Technique to hide the bitter taste of enoxacin, a novel microencapsulation procedure was combined with the wet spherical agglomeration (WSA) technology.
- The continuous granulation and coating of pharmacologically active compounds were established using the CMT approach.⁵

CONCLUSION

There is a variety of technologies that can disguise the unpleasant taste of medication but they must be used with care so that the pharmacokinetics of the drug is not harmed. These approach, combined with proper assesment of the taste masking effect, can significantly improve product preferences. New technologies for effective taste masking are also discussed in the review. With the use of these strategies, one can significantly enhance the product preference the flavor hide the fact that the medication was being delivered. For the quality of care delivered to patients, particularly children, and adolescents, research is becoming increasingly important. All these procedures vary in their applicability from drug to drug and are dependent on the type of dosage form required. The universal inhibitor of all bitter taste compounds that do not influence other taste modalities such as sweetness would be the ultimate solution to bitterness reduction or inhibition. However, no single ingredient has yet been discovered that functions as a universal bitter taste inhibitor.

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