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A Review on Taste Masking of Mouth Dissolving Tablet Using Central Composite Design

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Abstract: The gold standard in the pharmaceutical industry is oral delivery because it is a simple, safe, cost-effective and convenient method of drug delivery. Oral contraceptives have become a very popular application over the past few decades and in the pharmaceutical industry the industry has become a fast-growing area. Melting pills when put into the mouth should be dispersed or dispersed in the mouth within 15 to 3 minutes without the help or need of any drinking agent such as water.

The acceptance of any type of drug is largely dependent on its taste, namely, oral sensation. The drug molecule interacts with the taste receptor in the tongue to provide a bitter, sweet or other taste, when dissolved in saliva. This sense of taste is the result of signal transmission from the taste buds, commonly known as taste buds. Nowadays most days powerful drugs that can be cardiac, analgesics, anti-hypertensive, anti-inflammatory, anti-tubercular, anthalmentics, antibacterial, anticoagulants, anti-epileptics, antimalarials, anti neoplastics, anti-thyroids, antiprotozoal, diuretics, histamine receptor antagonists, nutrient agents, opioid analgesics, oral contraceptives and sex hormones, many of which are bitter in taste. It is therefore necessary to develop such a dose of what should be acceptable to taste in the patient especially if it is children or the elderly.

Hiding the taste becomes a requirement for spicy drugs to improve patient compliance especially in children and the elderly. To overcome this problem there are so many ways to hide the bitter taste of drugs. These processes not only block the taste of the drug but also enhance the bioavailability of the drug dosage form. The most widely used techniques for the production of large doses of pharmaceutical form are the use of flavors, the coating of drug particles with non-functional properties, the formation of inclusion complexes, molecular complexes of drugs and other chemicals, Microencapsulation, Mulsion Multiple Emulsions, Drugs, use. liposomes, Dispersion coating and Ion Exchange Resin method.

Keywords: Mouth dissolving tablet, Taste masking, Ion exchange resin, Central composite design.

I. INTRODUCTION

For drug use, the oral route is considered the most widely used route. [1] In this way the main limitation of the delivery of commonly used oral medications such as pills and pills is having difficulty swallowing (dysphasia) especially if pediatric and adult patients feel very unfit to take pills and pills. Preparing patients for the administration of these dosage forms plays an important role in the development and development of dosage forms.

To overcome this problem and make the oral route easier for patients a new drug delivery system has been developed known as oral, orodispersible or oral-melt delivery system etc. These MDTs should be dispersed or dispersed in the mouth within a few minutes without the need for water, chewing with the help of saliva in the mouth.

In forming a melting tablet in the mouth, the main measure is to eliminate the tablet's bitterness by adding a sweetening agent or by adding sugar to the tablets.

To increase tablet dispersion, super disintegrants are added to it, which greatly helps to increase tablet bioavailability and increase tablet dispersion properties. Disintegrants are mainly applied to tablets in three ways. These methods are extra-granular, intragranular and partially extra-granular and intragranular. The dispersal time of MDT is generally considered to be less than 1 minute.

Patients may experience a typical duration of MDT duration ranging from 5-30sec. MDT's are mainly prepared in a variety of ways such as direct compression, wet granular, solid dispersion and tablet formulation etc. Direct pressure method is the most widely used and simple or inexpensive method of MDT compared to other methods.

MDT are widely used in critical situations such as:

- Motion Sickness [2]
- Parkinsonism
- Pediatric patients and patients
- Fainting
- Patients with a mental disability

- Lack of water

MDT: These pills dissolve or dissolve rapidly in the saliva to show their action in a few seconds without help when wet. The mouth-melting tablet is mainly soluble in the mouth between 15sec-3mins. Especially MDT superdisintegrants and masking agents.

Advantages of MDT:
MDT should have the following symptoms:

- MDT should be dissolved or dispersed in the mouth for a few seconds.
- No liquid or water should be required to demonstrate its action.
- Do not leave any residue in the mouth after handling the tablet.
- It should not be too expensive.
- It should not function properly in natural conditions such as humidity, temperature etc.

Benefits of MDT:

- It is easy to use in patients who are unable to swallow pills such as children and in patients who are young, unconscious and mentally disabled. [3]
- You do not need water to drink the tablet during the trip.
- Rapid dispersion and termination of the drug tablet to produce rapid action.
- The bioavailability of the drug can be increased by avoiding the passage of the drug into the pharynx and esophagus.
- It has a good mouth that helps to take medicine more easily than bitter pills in pediatric patients.
- There is no risk of constipation and severity during taking MDT.
- It is useful for other conditions such as motion sickness, coughing etc.
- These MDTs are stable for a long time, until they are consumed.

II. TASTE

Whenever we met someone at a restaurant table and those bodies asked about the taste of any food, then we would tell anyone in any of the four flavors whether it was sweet, sour, spicy or salty. Although it is a matter of debate about the type of taste but in general these four are taken for granted. Now the point is how we forgive about the taste of any food. All of this is done in our language. Our tongue, which is made up of many cells, helps to release the taste buds, called taste buds. In 1908 the Japanese researcher KIKUAE IKEDA discovered the fifth new flavor of glutamate called UMAMI, meaning meat. [4-7]

TASTE BUDS

The taste buds are a small sensory organ in many vertebrates, which help in gaining taste. Thus a collection of cells, found mainly on the tongue Taste buds have been found in the soft palate, pharynx, epiglottis, allowing different types of flavors to be seen. [4]

Salty Taste (edge, top section)
One salty taste between the four taste buds of the tongue. They are found on the edge and top of the tongue part. [4-5]

Sweet taste (tip)
Delicious taste is one of the four flavors in the language. They are found in the language title. [4-5]

Sour taste (with later side effects)
The sour taste is also one of the four taste buds of the tongue. They occur on the sides of the tongue and are mainly stimulated by acids. [4-5]

Bitter taste (back)
The bitter taste is the last and is one of the four senses of taste in the tongue. That is found behind the language. It is stimulated by a variety of chemical substances, many of which are organic compounds, although other inorganic compounds such as magnesium and calcium also produce bitter emotions. [4-5]
Performance of taste buds [4 - 7]
Taste buds work by transmitting information about different types of taste to the brain through nerve fibers. Taste buds for all four types of flavors namely, sweet, sour, salty and spicy show different distribution patterns on the surface of the human tongue Taste seedlings have been seen in the soft palate, pharynx, epiglottis e. The tongue, soft palate, and epiglottis contain taste buds, which allow a person to see a distinct taste in the food he eats. The taste buds are chemo receptor, which means they transmit chemical signals from food into electrical signals. These signals travel to the brain through the nervous system to sense taste.

It should be noted that the taste buds in fish are spread throughout the body to provide information about the environment. [4-7]
Impact of age on taste buds [8]
The cells that make up the taste buds grow old, as a result of which the taste buds begin to disappear from the roof and sides of the mouth without the taste buds placed on the tongue. The remaining pieces of flavor are a little more sensitive. Studies have shown that smoking and eating hot foods can be harmful to taste. This lack of taste can lead to loss of appetite and junk food. Taste is a kind of medium to discover the world of infants and toddlers. It seems that children are more sensitive to certain

tastes than any adults. but because the taste can be subjective. the mechanism that causes taste sensation in teens may be difficult to reverse.

Causes of infected taste buds

Taste buds infections often occur due to a lack of complex vitamin B, long-term antimicrobial treatment followed by radiation, smoking, severe tooth decay and muscle stiffness in the elderly and fungal infections in those with low fever. [4-7]

Methods of taste testing [9 - 10]

To do this research, we need the following-

* Food color

The process

1. With the help of cotton place the food coloring over the title of your tongue.
2. Place a tightening ring on the tongue.
3. Start counting the pink dots inside the ring using a magnifying glass.

These pink spots are fungi that form papillae. These have the property of not taking food coloring. These papillae are small bumps similar to our tongue which is to put your taste buds on top the amount of papillae means greater sensitivity against taste. If any person has less than 15 papillae on average they are called tasteless while those with more than 30 papillae are called supertasters. [9-10]

III. TASTE MASKING

Children, the elderly, and many other people, including patients with disabilities or disabilities, often have difficulty swallowing pills or pills. In these cases, it is desirable to prescribe the drug in a solid chewing form or in the form of a liquid. [24] Unwanted taste is one of the few important structural problems associated with certain drugs. Oral administration of spicy medicines with an acceptable level of taste is an important issue for health care providers, especially in pediatric patients. [13] Concealing the bitter taste of drugs is an important parameter for improving patient compliance. [11] The problem of bitter taste and the abhorrence of the drug in the formulation of children and adults is a challenge for the pharmacist in the current situation. [14]

Chemoreceptors on the Tongue

Taste is the way the brain defines the chemicals that cause receptors in the tongue, stored in taste buds. The cell works with the taste receptor on the tongue to give a sense of taste, as it dissolves in the saliva. This sensation is the result of signal fluctuations from taste-sensing organs, commonly known as taste buds. These taste buds contain extremely sensitive nerve endings, which produce and transmit electrical impulses through the seventh, ninth, and tenth cranial nerves in those areas of the brain, dedicated to visual perception. [14,15]

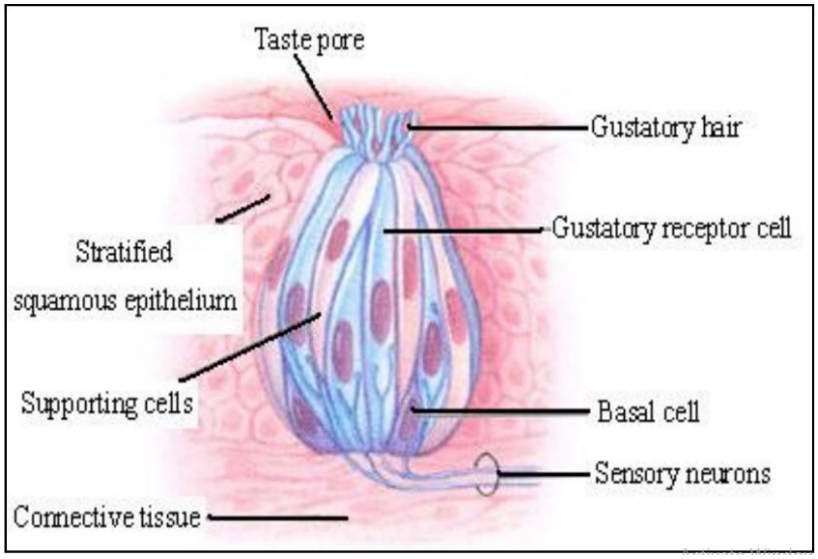

Fig.1 Physiology of Taste Bud

Four taste buds have been described: Sweet and salty, especially in the end. Sour, on the sides. Spicy, in the background. [15] and is the fifth most widely accepted flavor of Umami. [11]

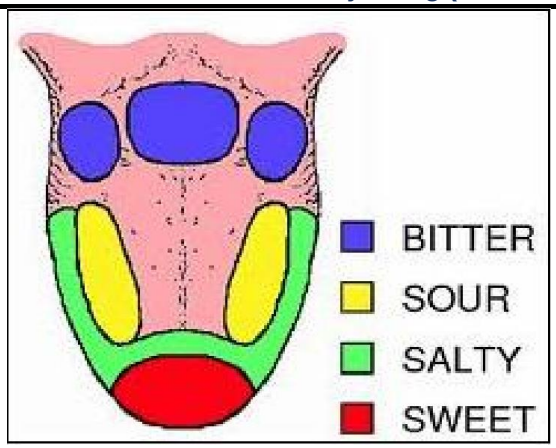

Fig. 2 Taste Points in Tongue

Taste Signaling Pathways

The exchange of taste begins with the interaction of a sweet substance (eg medicine or food) with taste receptor cells in taste buds (Fig. 3). Tastant binds to G-Protein coupled receptors (GPCRS) in cells that trigger the release of G-Protein called Gustducin. [11]

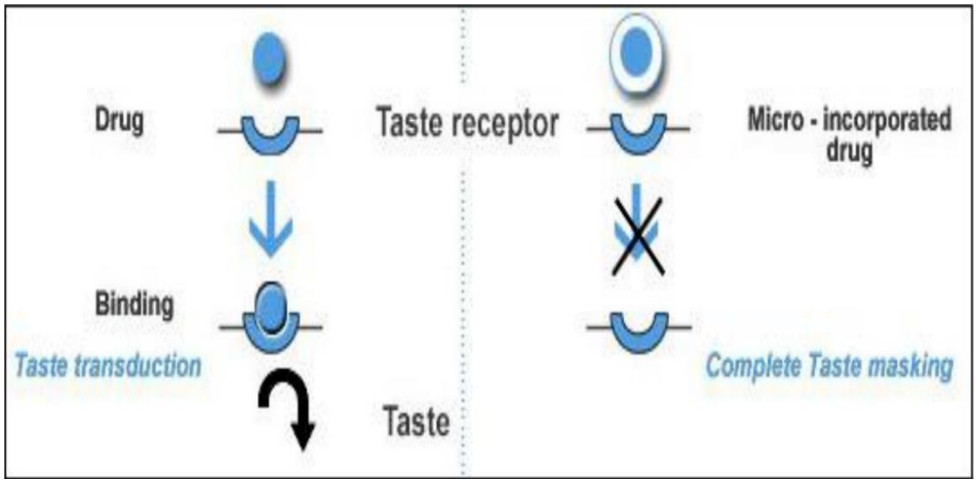

Fig. 3 Taste Signaling Pathways

Taste Blocking Mechanism

Taste sensation begins when Gustducin activates the effector enzymes phosphodiesterase IA (PDE) or phospholipase C beta-2(PLC)

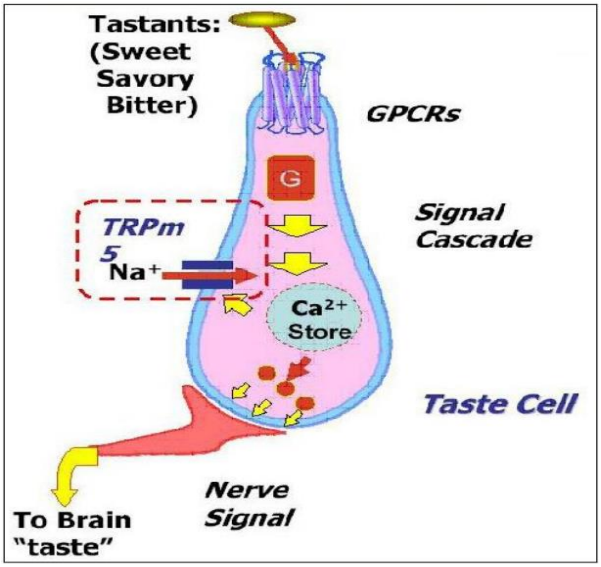

Fig. 3 Taste Blocking Mechanism

The active enzyme then alters the intracellular level of the second messenger such as cyclic adenosine monophosphate (cAMP), Inositol, 1, 4, 5- triphosphate (IP3) and diacylglycerol (DAG). The second messengers activate the calcium ion channel within the cell as well as the sodium, potassium and calcium channel in the cell membrane. Ionization causes the cell to slow down the cell that causes the release of neurotransmitters that send nerve impulses to the brain that carry the signal of a bitter taste and the taste buds work by interfering with the transfer of taste. [19]

TASTE MASKING TECHNOLOGIES:

Hiding a taste is defined as the perceived reduction of unwanted taste that could occur. [24] The most commonly used methods of concealing taste involve a variety of physiological and chemical mechanisms that inhibit the interaction of taste buds with drugs. Two methods are often used to overcome the bad taste of the drug.

1. By reducing the solubility of the drug to the pH of the saliva (5.6 - 6.8).
2. By changing the relationship and nature of the drug that will interact with the taste receptor. [17]

The process of concealing good taste and composition should have the following characteristics.

1) Include at least a small number of tools and processing steps.
2) Thoroughly coat the taste of a few rich and readily available additives.
3) There is no adverse effect on drug bioavailability.
4) Minimum production costs.
5) It can be done at room temperature.
6) Look for helpers with a high level of security.
7) Rapid and easy to prepare. [12,13,22]

Factors that are taken into consideration during the taste-masking formulation process include:

1) Extent of the bitter taste of the API.
2) Required dose load.
3) Drug particulate shape and size distribution.
4) Drug solubility and ionic characteristics.
5) Required disintegration and dissolution rate of the finished product.
6) Desired bioavailability.
7) Desired release profile.
8) Required dosage form. [13]

Factors affecting the selection of flavor secretory techniques Conventional flavoring methods such as the use of sugars, amino acids and flavor agents alone are often insufficient to conceal the taste of highly bitter drugs such as quinine, celecoxib, etoricoxib, antibiotics such as levofloxacin , Sweeteners could not. reach to hide the oral formulation of ibuprofen due to its dominant taste. Dressing is a very effective technology for very bitter drugs although the imperfections of the cover, if any, reduce the efficiency of the method. Similarly, microencapsulation of potent active agents such as azithromycin is insufficient to suppress the secretion of liquid oral suspension. [21]

Taste Masking Technologies

To achieve the goal of taste abatement of bitter or unpleasant taste of drug. Various techniques reported in the literature are as follows

1. Taste masking with flavors, sweeteners & amino acids
2. Polymer coating of drug
3. Formation of inclusion complexes
4. Ion exchange resin complexes
5. Solid dispersion
6. Microencapsulation
7. Multiple Emulsions
8. Development of Liposome
9. Prodrug approach
10. Taste masking by adsorption
11. Taste Masking with Lipophilic Vehicles like lipids and lecithins
12. Taste Suppressants and Potentiators
13. Taste masking by gelation
14. Formation of salt and derivative
15. Use of Amino Acids and Protein Hydrolysates
16. Miscellaneous.
    a) By effervescent agents
    b) Rheological modification
    c) Continuous multipurpose melt (CMT) technology
    d) Wet Spherical Agglomeration (WSA) [12,16]

Different taste masking patents and patent application filed in the period of year 1997 to 2007.

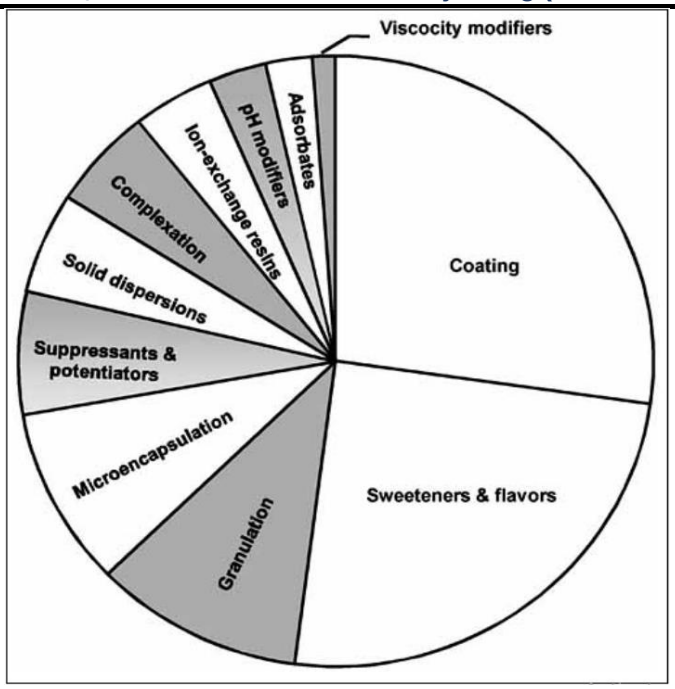

Fig. 4 Taste masking technology filed in the period of year 1997to 2007. [20]

About 49.34% of taste masking patents and patent applications are contributed from Asia. North America accounts for about 41.45% of which62.67% were filed in USA and about 9.30% from Europe. [20]

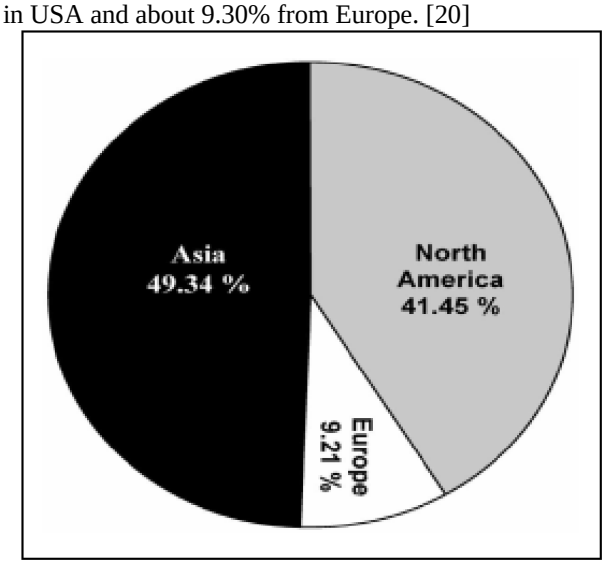

Fig. 5 Geographical distribution of taste masking patents and patent application filed in the period of year 1997 to 2007.

1. Taste masking with Flavors, Sweeteners and amino acids

This process is an easy way to hide flavor. But this treatment has not been very effective in very painful drugs. Synthetic sweeteners and flavors are often used alone with other flavors to enhance the effectiveness of these methods.

A. Flavors

Basis of Choosing a Flavor

1. Complementary to existing flavor of the drug
2. Known popularity of particular flavors
3. Age of patients
4. Allergy

Natural Vs Synthetic

1. Cheaper
2. More readily available
3. Less variable in chemical composition
4. More stable Flavoring agents for taste masking [14]

Natural Flavors-

Raspberry Juices; Liquorices Extract; Lemon & Orange Spirits; Blackcurrant Syrups; Ginger Tinctures; Anise & Cinnamon Aromatic waters; Peppermint & Lemon Aromatic Oils.

Synthetic Flavors-

Alcoholic solutions; Aqueous solutions; powders. [20]

B. Sweeteners

- Complement flavors associated with sweetness
- Soothing effect on the membranes of the throat [12]

Natural Sweetener- Sucrose, Glucose, Fructose, Sorbitol, Mannitol, Honey, Glycerol, Liquorice.
Artificial Sweetener- Saccharin, Saccharin Sodium, Aspartame.
Nutritive Sweeteners- Sucrose, Fructose, Glucose.
Non-Nutritive Sweeteners- Aspartame, Sucralose, Neotame, Saccharine.
Polyols- Mannitol, Sorbitol, Xylitol, Erythritol, Maltitol.
Novel Sweeteners- Trehalose, Tagatose. [13]

Sweeteners	Sweetness factor, Sucrose=1
Aspartame	180-200
Sucralose	600
Acesulfame	K 200
Neotame	7,000-13,000
Saccharin	300

Table 1. List of FDA approved Non-Nutritive Sweeteners [13,24]

A. Amino acids

Amino acids and their salts (alanine, taurine, glutamic acid, glycine) in combination with bitter drugs reduce drug overdose, for example, the taste of ampicillin is significantly improved by preparing its granules and glycine and mixing them with extra value. and glycine, sweeteners. , flavors and finally squeeze them into tablets. [11]

2. Polymer coating of drug

This is the easiest and most likely option for achieving flavor hide. Coating acts as a physical barrier to drug particles, thereby reducing the interaction between the drug and the taste buds. The coating of the chewing gum provides the best flavor mask while still providing acceptable bioavailability. [24] In this process, powders measuring 50 mm are injected into a hot air bubble, at high speed, and the drug particles are covered with a coated solution that is usually introduced from the top as a spray hose. [19] Any non-toxic polymer that does not dissolve in pH 7.4 and dissolves in acidic pH, may be another acceptable way to hide taste. Concentration of the taste of ibuprofen has been successfully achieved by using a combination of air suspension to form microcapsules, which include the medicinal core of crystalline ibuprofen and a methacrylic acid copolymer copolymer that provides hidden flavor features.[12]

Agents used for coating

- Carbohydrates (Cellulose)
- Synthetic polymers (Eudragits etc)
- Proteins, Gelatine, and Prolamines (Zein)
- Zeolites [24]

It is classified based on the type of coating material, the solvent coating system, and the number of coating layers. Hydrophobic polymers, lipids, sweeteners and hydrophilic polymers can be used as coatings, either alone or in combination. [20]

Multilayer coating has been used to overcome the challenges of covering imperfections, leading to a decrease in the effectiveness of concealing flavors, especially in highly bitter herbs. The core material was coated with a first smooth and uniform layer dividing the space, which could reduce coverage imperfections during the second coating layer and could serve as a quick barrier between taste receptors and the spinal cord. [20]

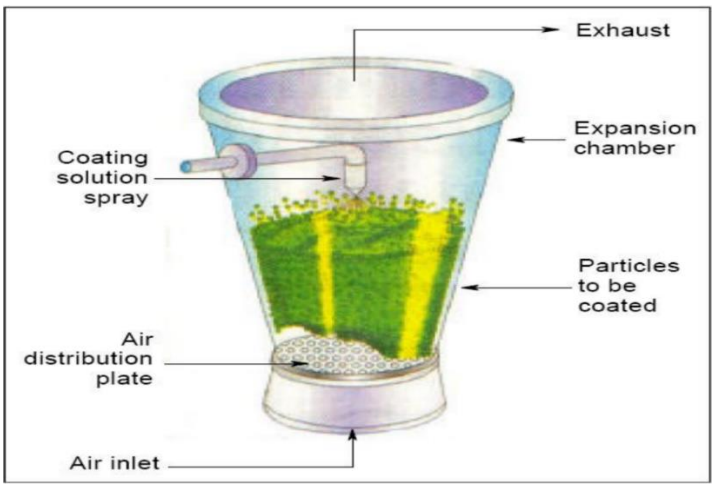

Fig. 6 Schematic representation of fluidized bed coating technique. [19]

3. Formation of inclusion complexes

In the complex formulation of the implant, the drug molecule enters the cavity of a complex agent, i.e. the host molecule, which forms a stable complexion, a constant low density that can lead to the rapid release of the free drug into the oral cavity, leading to obscure the unpleasant taste. . [19,25] The elimination of bitterness depends on the degree of complexity of the visitor and host molecule, the number of fixed molecules, the temperature and the host / host ratio. [11] The power of Vander Walls is strongly involved in inclusion complexes. The binding agent blocks the bitter taste of the drug by reducing its oral solubility or by reducing the number of drug particles exposed to the taste buds, thus reducing the perception of bitter taste. This method is most suitable only for low dose drugs. B-CD is a complex, widely used compound agent. It is a sweet, non-toxic, cyclic oligosaccharide found in starch. [14]

Hydrophobic drugs create complexity by adding 'embedded water' while evolving easily (hydrophilic, well-soluble) drugs form complex, replacing 'crystal water'.

Blending (PM), Mixing Method (KM), Solid dispersion / co-evaporated dispersion method, Precipitation method. [25]

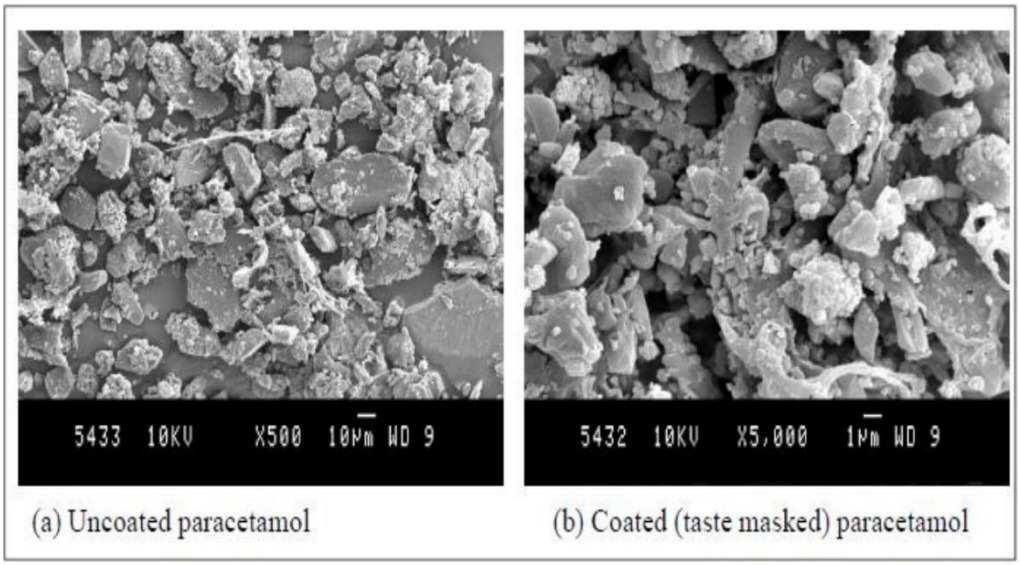

Fig. 7 Scanning electron micrograph of uncoated (bitter) and coated (taste masked) paracetamol particles. [19]

4. Ion exchange resin complexes

Ion-exchange resins (IERs) are high-density polymer molecules with active cationic and anionic groups attached to a water-soluble polymer core. These groups have the ability to exchange [26] ion counters charged in reverse, thus absorbing ions in the polymer matrix. Since many drugs have ionic properties in their molecule, resin charging provides a way for weak ionic accumulation so that the dissociation of the drug-resin complex does not occur under the pH conditions of the saliva, thus causing the taste to hide. For the purpose of masking the taste of weak cation or weak anion exchange resins are used, depending on the type of drug. [21]

Classification

Solid cation exchanger - sulfuric acid sites
Weak cation exchanger-components of carboxylic acid
Strong sites of anion exchanger- quaternary amine ionic
Weak anion exchanger - especially high-grade amines

Type	Functional group	Commercial resin	Taste masked drug
Weak cation	-COOH	Indion 204, Tulsion T-335, Amberlite IRC 50	Norfloxacin, Ofloxacin, Roxithromycin
Weak cation	-COO-K+	Tulsion T- 339, Indion 234, Amberlite IRP 88	Ciprofloxacin, Chloroquinine
Strong cation	-SO3H	Indion 244, Dowex 50, Amberlite IR 120	Chlorpheneram-ine maleate, Ephedrine Hydrochloride
Strong cation	-SO3Na	Tulsion T-344, Amberlite IRP 69 Indion 254	Dicyclomin, Rantidine, Dextromethorp-hen, Pseudoephedri-ne, Buflomedil.
Weak anion	N-R_2	Amberlite IR4B, Dowex 2	not used in taste masking
Strong anion	N-R_3	Amberlite IR400, Dowex 1, Indion 454, Duolite AP143	not used in taste masking

Table 2. Commonly used ion exchange resins [11]

5. Solid dispersion

Solid dispersion has been defined as the dissolution of one or more active ingredients in an inactive carrier or matrix in a solid state prepared by dissolving (composite) solvent or dissolving method. [13] A strong distribution of the drug with the help of polymers, sugars, or other suitable agents, is very helpful in concealing the taste. [24] Carriers used in solid dispersion systems include povidone, polyethylene glycols, hydroxypropyl methylcellulose, urea, mannitol and ethylcellulose. Different ways to prepare for a solid dispersion are described below. [14,19]

i) **Melting method**

In this way, the drug or drug mixture and the carrier melt together by heating. The melted mixture is cooled and hardened immediately in an ice bath with vigorous stirring. The final solid weight is crushed and crushed.

ii) **Solvent method**

In this way, the active substance and the carrier are dissolved in a normal solvent, followed by solvent evaporation and the restoration of solid dispersion.

iii) **Melting solvent Method**

In this way the solution in the solution is mixed with a molten mass of polyethylene glycol at a temperature of 70˚C without removing the solvent. The bitter taste of dimenhydrinate can be masked by preparing a solid dispersion of the drug with polyvinyl acetate phthalate.

6. Microencapsulation

Microencapsulation is a process of applying relatively thin coating to small particles of solids, droplets of liquids and dispersions, using various coating agents, such as gelatin, povidone, hydroxyethyl cellulose, ethyl cellulose, bees wax, carnauba wax acrylics and shellac. [14,15,19] It is important to understand that only soluble portion of the drug can generate the sensation of taste. Coating the active drug with a properly selected polymer film can reduce its solubility in saliva and thus taste could be masked. Coating the drug particles created a physical barrier between the drug and the taste buds and taste of active could be masked. [13] Polymers have been exclusively used as coating materials, either alone or in combination, as a single or multi-layer coat, in the taste masking of bitter medicaments. Combinations of pH independent water insoluble polymers such as cellulose ethers, cellulose ester, polyvinyl acetate and water-soluble polymers such as cellulose acetate butyrate, Polyvinylpyrrolidone, hydroxyethyl cellulose have been used to attain a balance between the taste masking and in vitro release.

The unpleasant taste of clarithromycin was masked when the drug was encapsulated in combination of gelatine and acrylic resins such as Eudragit L-100, Eudragit S-100 & E-100. [24]

TECHNIQUE	POLYMER	TASTE MASKED DRUGS
Air Suspension Coating	Methacrylic acid copolymer	Ibuprofen
Phase separation Coacervation	Eudragit E- 100, Chitosan	Clarithromycin, Paracetamol
Fluidized Bed /Sprayn Coating	Hydrogenated Oil and Surfactant	Indeloxazine
Solvent Evaporation Method	Eudrgit E, PEG, Ethyl Cellulose	Pseudoephedrine, Ranitidine
Extrusion Coating	Eudragit E- 100	Oxybutinin, ofloxacin, pirezepin.

Table 3. Marketed taste masked drugs by drug particle coating technique [11]

7. Multiple Emulsions

The w / o / w or o / w / o of most emulsion types are vesicular systems in which active ingredients can be trapped in the inner layer. Bonded material can be transferred from the inner layer to the outer layer through the membrane phase. This phase controls the release of the drug in the system. If the system is stable enough for a reasonable shelf life, the composition may also obscure the taste of the tree. Both w / o / w or o / w / o bulk chloroquine phosphate emulsion has been prepared and has been reported to be partially effective in masking the bitter taste of the drug. [16]

8. Development of Liposome

Liposomes are simple microscopic vesicles in which a fluid volume (drug or biological agent) is completely blocked by a membrane made up of lipid molecules, lipid bilayers mainly composed of natural or synthetic phospholipids. Bitter substances are usually hydrophobic by nature. Selected inhibition of the bitter taste of various drugs by phospholipids such as phosphatidic acid, phosphatidylinositol, soy lecithin, has been reported. Bitter taste of Chloroquine phosphate in HEPES (N-2-hydroxyetylpiperzine-Ní- 2- ethane sulfonic acid) buffer was secreted at pH 7.2. by combining in a liposomal formulation prepared with egg phosphatidyl choline [17] The bitter taste of polymyxin B sulfate and trimethoprim sulfamethoxazole is secreted by BMI 60 obtained by separating soy lecithin. [16]

9. Prodrug approach

Prodrug is a precursor to a chemically inactive drug that by means of biotransformation is released into a chemically active parent compound. [11,14,15] By changing the configuration of the parent molecule, the magnitude of the bitter taste response or the receptor-substrate adsorption constant may be altered. Drugs can be used to increase or decrease water solubility, mask irritation, increase lipophilicity, improve absorption, reduce local adverse effects, and alter the membrane that can penetrate the parent molecule. [13,17]

The flavorless prodrug of nalbuphine HCL, naltrexone, naloxone, oxymorphone HCL, butorphanonol, and levallorphan has been developed for use in buccal administration to enhance the bioavailability associated with oral dosing without the taste-free factor. [24]

10. Taste masking by adsorption

Adsorbate of the bitter medicine can be considered a small version of this saliva-soluble drug. Adsorption involves preparing the drug solution and mixing it with an insoluble powder that will adhere the drug, remove the solvent, dry the resulting powder, and use this dry adsorbate to prepare the final dosage form. [13,16] Many substrates such as veegum, bentonite, silica gel and silicates can be used for the adsorbate preparation of spicy drugs. Loperamide and phenyl propanolamine are advertised in magnesium aluminum silicates also known as Veegum F to correct the bitter secretion of these drugs. [12,16]

11. Taste Masking with Lipophilic Vehicles like lipids and lecithins

Fats, surfactants, polyalcohols, and lipids effectively increase viscosity in the mouth and cover taste buds, so they can hide the taste. Acetaminophen granules are sprayed with melted stearyl stearate, mixed with appropriate tablet ingredients, and combined with the composition of a hidden, chewable tablet. [12] Formulas with high levels of lecithin or substances such as lecithin are said to regulate the bitter taste of medicines. Magnesium aluminum silicate containing soy lecithin is used to mask the unpleasant taste of talampicillin HCl.. [15]

12. Taste Suppressants and Potentiators

Most Linguagenis antibodies (e.g., adenosine monophosphate) compete with the bitter substances to bind to the sites of G-protein-binding receptors (GPCR). In general, the hydrophobic nature of these bitter substances contributes significantly to their binding and activity with reception areas. Lipoproteins are the mainstays of the world's bitter taste. Animal experimental studies have shown that lipoproteins composed of phosphatidic acid and ,- lactoglobulin inhibit the sensory response of bitter substances without affecting those caused by sugar, amino acids, salts or acids. Venkatesh and Palepu (2002) described the use of flavor enhancers as phospholipid (BMI-60) in flavoring the bitter herbs. Neohesperidine phospholipids have properties that suppress bitter taste by interacting with chemicals and taste receptors. Cooling and warming agents suppress the unpleasant taste of medicines by injecting sensory receptors into extreme emotions in order to overcome the bitter taste and confuse the mind. A cooling mixture (e.g., eucalyptol) and heating agents (e.g. methyl salicylate) was used to disguise the taste of thymol. Potentiators enhance the taste buds of sweeteners and hide unpleasant after-tasting. Strong substances such as thaumatine, nehesperidine dihydrochalcone (NHDC) and glycyrrhizin can raise the profile of sodium or calcium saccharinates, saccharin, aspartyl-phenylalanine, acesulfame, cyclamate, and stevioside. Thaumatine was also used with sugar alcohol to achieve a hint of bromhexine flavor. Bitter taste inhibitors such as hydroxyl flavanones, adenosine monophosphate and „- aminobutanoic acid have been found to be effective in counteracting the taste of spicy drugs.. [20]

Desensitizing agents

Desensitizing agents like phenols, sodium phenolates desensitize the taste buds by interfering with taste transduction (Fig. 4), the process by which taste message from the mouth to the brain and thus mask the taste of drug. [11]

13. Taste masking by gelation

The water-soluble gelation on the surface of the tablet containing a bitter substance can be used to hide the taste. Sodium alginate has the potential to cause dissolving gelation in water in the presence of bivalentmetal ions. The amiprolose hydrochloride tablet has been flavored and secreted by the insertion of the lower coating of sodium alginate and the upper coating of calcium gluconate. In the presence of saliva, sodium alginate reacts with bivalent calcium and forms an insoluble gel in the water and thus hiding the taste is achieved. [13,16]

14. Formation of salt and derivative

Reducing the solubility of a tree by its salty structure makes the tree less palatable as it does not melt in the saliva so much that it is less sensitive to secretions. Prepared into N, N- di benzyl ethylenediamine diacetate salts or N, N bis (deyhdroabiety) ethylene diamine salts tasteless. [11] Adding alkaline metal bicarbonate-like sodiumbicarbonate mask to the unpleasant taste of water - the dissolving ibuprofen salt in the aqueous solution. [24] Aspirin tablets can be made to taste less by making magnesium salts aspirin. D-chlorpheniramine maleate is a secreted salt of chlorpheniramine. [19] Sodium salts such as sodium chloride, sodium acetate, sodium gluconate have been shown to be potentially short-acting compounds of the bitter mixture. How it is not known, however, studies show that sodium action at the peripheral taste level rather than the cognitive effect. [16]

15. Use of Amino Acids and Protein Hydrolysates

By combining amino acids or their salts with bitter drugs, it is possible to significantly reduce irritability. [14] Other popular amino acids include sarcosine, alanine, taurine, glutamic acid, and glycine. [19] The taste of ampicillin improved significantly by adjusting its granules and glycine and mixing them with additional amounts of glycine, sugars, flavors and finally squeezing them into tablets. [11,16]

16. Miscellaneous.

a) By effervescent agents

Active agents have been shown to be useful and beneficial in oral administration of the drug and are also used for flavoring agents in undigested dose forms in water prior to administration. The composition of the bitter gum is designed to provide the drug in the oral cavity for local use or buccal absorption. It includes a chewing gum base, an oral contraceptive, a carbon dioxide disposal generator, and a composition that eliminates the taste of tastebud (e.g., oral anesthetics such as benzocaine and spilanthol) and other inactive substances, such as sweeteners, flavor. components, and fillers. [24]

Recently, the active fentanyl and prochlorperazine tablets have been developed to provide these drugs in the oral cavity to absorb buccal, sublingual, and gingival. The formulation contains the drug in combination with an effervescent agent to promote its absorption into the oral cavity and to eliminate its bitter taste. An additional pH adjustment element is incorporated into the fentanyl structure to improve continued absorption.. [13]

b) Rheological modification

Increasing viscosity with a rheological modifier such as gums or carbohydrates can reduce the spread of bitter substances from saliva to taste buds. [14] This provides for the preparation of flavored secreted liquids to be used in greater quantities compared to the undesirable flavors. The composition of this composition includes a taste masking liquid base with high viscosity caused by thickening agents such as polyethylene glycol and sodium carboxy methylcellulose. [16,19] Acetaminophen suspension can be performed with xanthan gum (0.1-0.2%) and microcrystalline cellulose (0.6-1%) to reduce the bitter taste. [24] The antidepressant mirtazapine is formulated as an aqueous suspension using methonine (stabilizer) and maltitol (thickening agent). Maltitol is stable in acidic pH range of 2 to 3 and in addition to masking the unpleasant taste of the drug, it also inhibits its local anti-inflammatory effect. [13] cough syrupups, terbutaline given in doses of 4mg / 5ml can be effectively controlled by increasing the viscosity of the formulation. [11]

c) Continuous multipurpose melt (CMT) technology

The CMT method is designed for continuous gradient and therapeutic properties. It was concluded that this method could be used effectively to mask the taste of bitter drugs. [13,24]

d) Wet Spherical Agglomeration (WSA)

The novel Microencapsulation process combined with the wet spherical agglomeration (WSA) method was used to mask the bitter taste of enoxacin. [24]

IV. Preparation of drug resin complex (DRC)

The DRC was prepared by the collection process, using a composite design in the middle of the prepared resin ratio and pH. The resin is allowed to swell in water 20 ml under magnetic resuscitation for 25-60 minutes at room temperature. Azithromycin was added to the swollen resin slurry with a high-dose drug: resin concentration under magnetic motion and the resulting mixtures were stirred for 0-7 hours. The drug-resin complex was separated by filtration and the residues were washed with 5 ml of distilled water to remove any impurities, and finally dried at room temperature. The complex was kept in a glass vial holding air.

Optimization of process parameters

Statistically designed tests using a Medium-compact design (Design-Expert 8, version 8.0.7.1) were performed to study the effect of two key factors - inflammatory time (X1) and stimulus time (X2) on the combined drug percentage and drug release percentage (% CDR). The central composite design uses orthogonal arrays from the construction of experimental theory to study a large number of variables with a small number of experiments. In addition, this design has the added advantage of determining the location of the quadratic response, which is not achieved using factorial design at two levels. [29] Two-dimensional studies at three levels (-1, 0, +1) using a medium-compound design lead to twelve drug and resin problems (ARC1-ARC12).

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