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Open Access Review Article

Taste masking Technologies: A Boon for Oral Administration of Drugs

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ABSTRACT

Oral administration is widely used route of administration of drugs. The drug travels from the mouth, into the esophagus, then into the intestines. Sensing the taste is the major function of the tongue. In the formulation for pediatric & geriatric, bedridden & non-Cooperative patients, the main challenge to compounding pharmacist is to mask the taste of obnoxious and bitter drugs, result in patient non-compliance. Patients now expect and demand formulations that are pleasantly, or at least tolerable, flavored. This article reviews on taste-masking technologies and approaches for taste masking and bitterness reduction of dosage forms.

Keywords: Oral Administration, Drugs, Taste making, Taste bud

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INTRODUCTION:

Taste, gustatory perception, or gustation (Adjectival form: gustatory) is one of the five traditional senses that belongs to the gustatory system. Taste is the ability to respond to dissolved molecules and ions- "gatekeeper to the body".

Taste is the sensation produced or stimulated when a substance in the mouth reacts chemically with taste receptor cells located on taste buds in the oral cavity, mostly on the tongue. Taste, along with smell (olfaction) and trigeminal nerve stimulation (registering texture, pain, and temperature), determines flavors of food and/or other substances. Humans have taste receptors on taste buds (gustatory calyculi) and other areas including the upper surface of the tongue and the epiglottis. The gustatory cortex is responsible for the perception of taste. [1]

Taste buds are taste receptor cells that are clustered into onion-shaped organs. Pore opens out to the surface of the tongue enabling molecules and ions taken into the mouth to reach receptor cells inside. A single bud contains 50-100 taste cells. Human have around 10,000 taste buds, which appear in the fetus at about three months.

Five taste sensations are sweetness, salty, sour, bitterness, and umami are showed in Fig 1. Umami Scientific experiments have demonstrated that these five tastes exist and are distinct from one another.

Fig.1. Zones of taste sensations on the tongue.

A taste receptor is a type of receptor, which facilitates the sensation of taste. These receptors are of four types. When food or other substances enter the mouth, molecules interact with saliva and are bound to taste receptors in the oral cavity and other locations. [1]

There is often a correlation between the chemical structure of a compound and its taste. Low molecular weight compounds tend to taste salty whereas high molecular weight salts tend toward bitterness. Nitrogen-containing compounds, such as alkaloids, tend to be quite bitter. Organic compounds containing hydroxyl groups tend to become increasingly sweet as the number of OH group increase. [2]

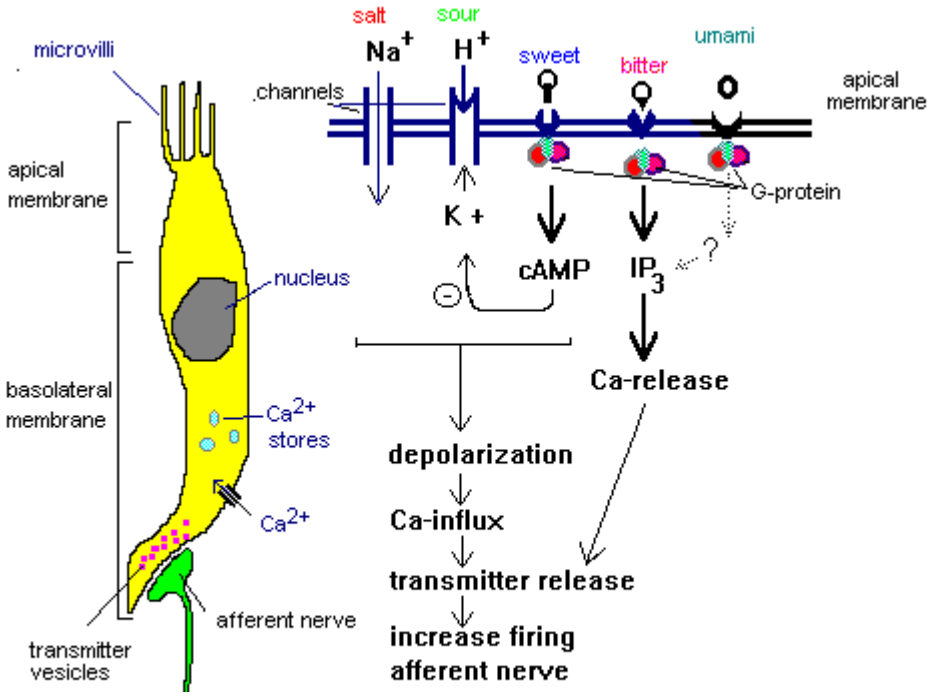

Fig.2. Taste receptor cell

Receptor mechanism involves initial depolarization of apical receptor site, which causes a local action potential in receptor cell. The structure of receptor cell is shown in Fig 2. This, in turn, causes synaptic activation of a primary sensory neuron.

TASTE THRESHOLD

The minimum concentration at which taste sensitivity to a particular substance or food can be perceived. [3]

Taste of the formulation, considered as one of the important factors in the administration of an oral dosage form. Pharmaceutical companies can save themselves much grief by addressing the taste factor early in product development. Primary taste sensations of specific areas of tongue and threshold concentrations are listed in Table 1.

Table.1.Primary Taste Sensations of Specific Areas of Tongue and Threshold Concentrations

Taste	Area of tongue	Threshold Concentration
Sweet (Sucrose)	Tip of Tongue	0.5%
Salt(NaCl)	Tip and sides of tongue	0.25%
Sour(HCl)	Sides of tongue	0.007%
Bitter(Quinine)	Back of tongue	0.00005%

TASTE MASKING TECHNOLOGIES:

Taste masking defined as the perceived reduction of an undesirable taste that would otherwise exist. Methods commonly used for taste masking involves physical and chemical method that prevent interaction of taste bud with drugs, Two approaches are commonly utilized to overcome the bad taste of the drug.

- By reducing the solubility of the drug in the pH of saliva (5-.6-6.8).
- By altering the affinity and nature of drug which will interact with the taste receptor.

Taste Masking Techniques:-

- Addition of Flavors and sweeteners.
- Polymer Coating of Drug.
- Micro Encapsulation.
- Ion Exchange.
- Inclusion Complexation.
- Granulation.
- Adsorption.
- Prodrug Approach.
- Multiple Emulsion Technique.
- Gel Formation.
- Miscellaneous.

[A]. Taste masking by addition of Flavors and Sweeteners:-

This is the simplest approach for taste masking. It is not successful for highly bitter drugs. Artificial sweeteners and flavors are generally being used along with other taste

masking techniques. Such recommendations are listed in table 2, 3.

– Flavors:- Two types of flavors

1. Natural Flavors: - Raspberry juices, Liqourices extract, Lemon and Orange Spirits, Ginger tinctures, Peppermint & Lemon Aromatic Oils.
2. Synthetic Flavors: - Alcoholic Solutions, Aqueous solutions, Powders.

The selection of flavors is based on taste sensation of drug as shown in Table 2.

– Sweeteners:-

1. Natural Sweeteners: - Sucrose, Glucose, Fructose, Sorbitol, Mannitol, Honey, Glycerol.
2. Artificial Sweeteners: - Saccharin, Saccharin Sodium, Aspartame.
3. Nutritive Sweeteners: - Sucrose, Glucose
4. Non-nutritive Sweeteners: - Aspartame, Neotame, Sucralose
5. Polyols: - Mannitol, Sorbitol, Xylitol, Malititol.
6. Novel Sweeteners: - Trehalose, Tagatose

The relative sweetness of commonly used sweetners are given in Table No 3.

Table.No.2 Flavor Selection Criteria:

Taste Sensation of Drug	Recommended Flavor
Salt	Butterscotch, Apple, Vanilla, Peach.
Bitter	Wild cherry, Walnut, Chocolate, Mint.
Sweet	Fruit & Berry, Vanilla.
Sour	Citrus flavor, Root Beer, Raspberry

Table.No.3 Relative sweetness of commonly used sweeteners: [4]

Sweetening agents	Relative sweetness	Comment
Aspartame	200	Not very stable in solution.
Acesulfame potassium	137-200	Bitter after taste if used in higher concentration.
Cyclamate	40	Banned.
Glycyrrhizin	50	Moderately Expensive.
Lactose	0.16	The large amount required.
Mannitol	0.60	Negative heat of solution
Saccharin	450	Unpleasant
Sucrose	1	Most commonly used.
Sucralose	600	Synergistic sweetening effect.

[B]. Taste masking by Polymer Coating of Drug:

This is the simplest and most feasible option to achieve taste masking. The coating acts as a physical barrier to the drug particles, thereby minimizing interaction between the drug and taste buds. In this approach, powders as fine as 50 mm are fluidized in an expansion chamber by means of heated, high-velocity air, and the drug particles are coated with a coating solution introduced usually from the top as a spray through a nozzle.

Agents used for coating

- Carbohydrates (Cellulose)
- Synthetic polymers (Eudragit etc.)
- Proteins, Gelatine, and Prolamines (Zein)
- Zeolites[5]

[C]. Taste masking by Micro Encapsulation:

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. 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. Various polymers and microencapsulation techniques are mentioned in table.4.

Table.No.4. Marketed taste-masked drugs by drug particle coating technique: [6]

Technique	Polymer	Taste Masked Drugs
Air Suspension Coating	Methacrylic acid copolymer	Ibuprofen
Phase Separation Coacervation	Eudragit E-100, Chitosan	Clarithromycin, Paracetamol
Fluidized Bed / Spray coating	Hydrogenated oil & Surfactant	Indeeloxazine
Solvent Evaporation Method	Eudragit E, PEG, Ethyl Cellulose	Pseudoephedrine, Ranitidine
Extrusion Coating	Eudragit E-100	Oxybutynin, Ofloxacin, Pirezepin.

[D]. Taste masking by Ion Exchange:

Ion exchange resins are water-insoluble cross-linked polymers containing a self-forming group at repeating positions on the polymer chain and have the ability to exchange counter-ions within aqueous solutions surrounding them. They are a synthetic organic polymeric network used in a copolymer of styrene and divinylbenzene (DVB) mentioned in table.no.5.

Table.No.5 Common ion exchange resins [6]

Type	Functional group	Polymer backbone	Commercial resins	Taste masked Drug
Strong anion	$-N^+R_3$	Polystyrene -DVB	Amberlite IR 400, Dowex1	NTM
Weak anion	$-N^+R_2$	Polystyrene -DVB	Amberlite IR 4B, Dowex2	NTM
Strong cation	$-SO_3H$	Polystyrene -DVB	Amberlite IR 120, Dowex50	Ciprofloxacin, Chloroquine
Weak Cation	-COOH	Methacrylic acid - DVB	Amberlite IRC 50, Indian 204,234, Tulsion335,339	Norfloxacin, Ofloxacin

NTM - Not used in taste masking

Ion exchange resins are used in drug formulation to stabilize the sensitive components, sustain release of the drug, and taste masking.

[E]. Taste masking by the formation of Inclusion Complexation:

In inclusion complex formation, the drug molecule fits into the cavity of a complexing agent, i.e. the host molecule, forming a stable complex, a low stability constant would lead to a rapid release of free drug in the oral cavity, resulting in inefficient taste masking. The complexing agent is capable of masking bitter taste of drug by either decreasing its oral solubility on ingestion or decreasing the number of drug particles exposed to taste buds, thereby reducing the perception of the bitter taste. Vander wall forces are mainly involved in inclusion complexes. [7] Various examples and complexing agents are listed in table.6.

Table.No.6 Taste masking of a bitter drug by complexation

Drug	Complexing Agent	Dosage form
Benxeate hydrochloride	Cyclodextrin	Granules
Carbetapentane citrate	Cyclodextrin	Oral liquid
Chloroquine Phosphate	Tannic Acid	Syrup
Dimenhydrinate	Eudragit 100 Chitosan	Chewable tablet
Gymnema Sylvester	Chitosan	Oral liquid
Ibuprofen	Hydroxy propyl-B-cyclodextrin	Solution

[F]. Taste masking by Granulation:

Granulation is a common processing step in the production of the tablet dosage form. This step can be exploited as a mean for taste masking of the slightly bitter-tasting drug. Some saliva insoluble polymers can also act as the 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 comes in contact with the tongue upon oral intake. But this reduction in surface area of the bitter substance may or may not be effective in masking the bad taste. [7]

[G]. Taste masking by Adsorption:

Adsorbate of the bitter-tasting drug can be considered as the less saliva soluble versions of these drugs. Adsorption involves preparing a solution of the drug and mixing it with an insoluble powder that will absorb the drug, removing the solvent, drying the resultant powder, and then using these dried adsorbates in the preparation of the final dosage form. Many substrates like veegum, bentonite, silica gel, and silicates can be used for the preparation of adsorbate of bitter drugs. Loperamide and phenyl propanol amine have been adsorbed on magnesium aluminum silicates also known as Veegum F to prepare a bitter taste-masked suspension of these drugs. [8]

[H]. Taste masking by Prodrug Approach:

A prodrug is chemically modified inert drug precursor, which upon biotransformation liberates the pharmacologically active parent compound. 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. Prodrugs can be used to increase or decrease the aqueous solubility, mask bitterness, increase lipophilicity, improve absorption, decrease local side effects, and alter membrane permeability of the parent molecule. Examples of prodrugs listed in table.no.7.

Table.No.7 Examples of Prodrugs with improved taste: [5]

Parent drug	Prodrug
Erythromycin	Erythromycin Propionate
Clindamycin	Clindamycin palmitate ester
Chloramphenicol	Chloramphenicol palmitate ester
Morphine	N-oxide derivatives of all Morphine
Triamcinolone	Triamcinolone diacetate ester
Gabapentin	Gabapentin XP_{13512}
Norfloxacin	Norfloxacin alkyl carbamates

The tasteless prodrug of nalbuphine HCL, naltrexone, naloxone, oxymorphone HCL, butorphanol, and levallorphan, were synthesized for buccal administration to improve bioavailability relative to that of oral dosing without the characteristic bitter taste.

[I] Taste masking by Multiple Emulsion Technique:

The w/o/w or o/w/o type multiple emulsion are vesicular systems in which active ingredients can be entrapped in the internal phase. The entrapped substances can be transferred from the internal phase to external phase through the membrane phase. This phase controls the release of drug from the system. If the system is stable enough for reasonable shelf life, the formulation could also mask the taste of the drug. Both w/o/w and o/w/o multiple emulsion of chloroquine phosphate has been prepared and reported to be partially effective in masking the bitter taste of the drug. [9]

[J] Taste Masking by Gelation:

Water-insoluble gelation on the surface of a tablet containing bitter drug can be used for taste masking. Sodium alginate can cause water-insoluble gelation in the presence of bivalent metal ions. Tablet of amiprolose hydrochloride has been taste masked by applying an undercoat of sodium alginate and overcoat of calcium gluconate. In the presence of saliva, sodium alginate reacts with bivalent calcium, form water-insoluble gel, and thus taste-masking achieved.

[K] Miscellaneous:

By effervescent agents:

Effervescent agents have been shown to be useful and advantageous for oral administration of drugs and have been employed for use as taste-masking agents for dosage forms that are not dissolved in water before administration. A chewing gum composition of bitter medicament was formulated to supply the medicament to the oral cavity for local application or for buccal absorption. It comprise a chewing base, an orally administrable medicament, a taste masking generator of carbon dioxide, and optionally a taste bud desensitizing composition (e.g., oral anesthetic such as benzocaine) and other non-active material such as sweeteners, flavoring components, and fillers.

Rheological modification

Increasing the viscosity with rheological modifier such as gums or carbohydrates can lower the diffusion of bitter substances from the saliva to the taste buds. Acetaminophen suspension can be formulated with xanthan gum (0.1-0.2%) and microcrystalline cellulose (0.61%) to reduce bitter taste. The antidepressant drug mirtazapine is formulated as an aqueous suspension using methionine (stabilizer) and Malititol (thickening agent). Malititol is stable in the acidic pH range of 2 to 3 and besides masking the unpleasant taste of the drug, it also inhibit its undesirable local anesthetic effect. [7]

Continuous multipurpose melt (CMT) Technology

The CMT method was developed for the continuous granulation and coating of pharmacologically active substances. It was concluded that this method could be successfully applied for taste masking of bitter drugs. [10]

Wet Spherical Agglomeration (WSA)

A Novel microencapsulation process combined with the wet spherical agglomeration (WSA) technique was used to mask the bitter taste of enoxacin. [11]

CONCLUSION:

After considering all the factors used for taste masking it is concluded that an ideal taste-masking formulation should have following characteristics:

- Involving least number of steps.
- Less expensive.
- No adverse effects.
- The stable taste-masking agent.
- Rapid and easy to prepare.
- Excipients that have a high margin of safety.

REFERENCES:

1. https://www.foodiesite.com/articles/2000-11/cheese.jsp
2. https://www.researchgate.net/publication/235956450_Review_On_Taste_masking_approaches_and_Evaluation_of_Taste_Masking
3. Shalini Sharma & Shaila Lewis, taste-masking technologies, International Journal of Pharmaceutical Sciences, 2010; 2(2): 6-13.
4. Gupta A.K., Practical Approaches for Taste Masking of Bitter Drug: A Review, International Journal of Drug Delivery Technology, 2010; 2(2): 56-61
5. Mackles, L., Chavkin, L., Tasteless forms of basic drugs prepared by absorption in situ. International journal of pharmaceutical innovations, 2014, 2(8), 1896-1918
6. Vijay A. Agrawal, taste abatement techniques to improve palatability of oral pharmaceuticals: A review, International journal of Pharma research and development,2008; 2(2): 22-30.
7. S. B. Ahire, A Review: Taste masking techniques in Pharmaceuticals, International journal of pharmaceutical sciences, 2015; 4(2): 1645-1656.
8. Jijo Abraham, Flowerlet Mathew: Taste masking of pediatric formulation: A review on technologies and recent trends and regulatory aspects 2014; 6(1): 12-18.
9. Vinod sonawane, Maria saiffee, Nitin Y. Shinde: An update of taste masking methods and evaluation techniques, Scholars research library 2010; 2(6): 1-12.
10. K.P. Sampath, Debjit Bhowmik, and Lokesh Deb, Recent trends in taste masking of bitter drugs: Review article, Journal of drug delivery research 2012; 1(1):1-9.
11. Lieberman H.A., Lachman L. (Eds.2). Chewable Tablets. In Pharmaceutical Dosage Forms, Vol-1(Tablet). New York: Marcel Dekker Inc.; 1981. p. 387-391.