WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 17, 318-338. Review Article ISSN 2277– 7105

AN OVERVIEW ON: APPROACHES FOR TASTE MASKING

Raj Dake, Bhagyashri Shelar*, Tejaswini Kande, Snehal Choudhary, Snehal Bichukale, Naziya Sayyad and Kiran Ghule

India.

Article Received on
25 October 2022,

Revised on 15 Nov. 2022,
Accepted on 05 Dec. 2022

DOI: 10.20959/wjpr202217-26475

***Corresponding Author**
Prof. Bhagyashri Shelar
India.

ABSTRACT

One of the most common ways to give medications is through oral administration. Many medications taken by mouth have a bitter taste. The likelihood that the recipients will consume the medications depends heavily on how tasty they are. Patients' inability or unwillingness to ingest dosage forms like pills is a persistent issue during treatment. syrups, particularly for old people and children. These dose forms enable the active medicinal ingredient to be detectably exposed to the taste receptor. As a result, a key component in the formulation of these medications is hiding the disagreeable taste qualities of the drug. It used to be believed that the worse the medication tasted, the better the outcome of the treatment.

KEYWORDS:- Taste bud, Evaluation of taste masking, Anatomy of the tongue, Taste masking techniques, Taste masking.

INTRODUCTION[1,4,6,12]

An unpleasant taste is one of the significant formulation issues that are present with some medications. A major concern for healthcare professionals is the oral delivery of bitter medications with an acceptable level of palatability, particularly for paediatric patients. There are bitter-tasting ingredients in many oral medications, food and beverage products, and bulking agents. Therefore, any pharmaceutical formulation with a tasty product would unquestionably be favoured over a rival's offering, resulting in higher patient compliance and therapeutic benefit as well as increased sales and profits for the manufacturer. Numerous formulations with increased performance and acceptance have been created as a result of consumer demand for these products improved palatability.

Taste can be separated into five primary taste qualities - sweet, sour, salty, Bitter and Umami or savoury.

- **Salty taste (Edge, upper portion)**

The salty taste is one of the four taste receptors of the tongue. They are found on the tongue's border and upper front region. The salty flavour is mostly caused by the cations in salts, particularly sodium cations, with some contribution from anions.

- **Sweet taste (tip)**

One of the four taste receptors on the tongue is responsible for the sweet flavour. They are located at the tongue's tip. A single class of chemicals does not exclusively account for sweet taste. Organic compounds with hydroxyl groups tend to get sweeter as the number of -OH groups rises.

- **Sour taste (Along sides in black)**

One of the four taste receptors on the tongue is also responsible for sour taste. They are located on the sides of the tongue and are mostly triggered by acids.

- **Bitter taste (back)**

The last and one of the four taste receptors on the tongue is for bitter flavours. That is situated near the tongue's back. A wide range of chemical compounds, the majority of which are organic, long-chain alkaloids, stimulate it. However, some inorganic compounds, like magnesium and calcium, also cause bitter sensations.

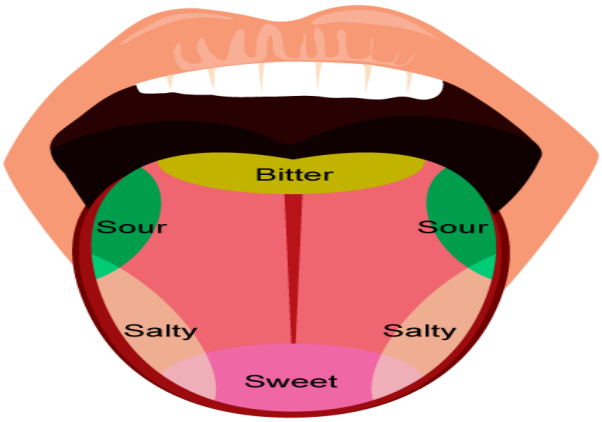

Fig. 1: Taste points in tongue.

Anatomy of tongue

Two types of special structures are seen on the tongue, the papillae and taste buds.[2,5,12,15]

1) **Taste bud -** The taste sense organ is the taste buds. 10,000 taste buds are present in humans when they are just three months old. 50–100 taste cells make up each taste bud. The "gatekeeper to the body" is the ability to respond to dissolved molecules and ions through taste. Taste receptor cells, which are grouped in onion-shaped organs called "Taste buds," are used by humans to detect flavour. Each taste bud has a channel that extends to the tongue's surface, allowing chemicals and ions swallowed to enter the mouth and enter the receptor cells there. 10,000 taste buds are present in humans, and they first develop in the foetus at roughly three months. 50–100 taste cells make up each taste bud. These transmembrane proteins bind to the ions and chemicals that cause the taste sensation.

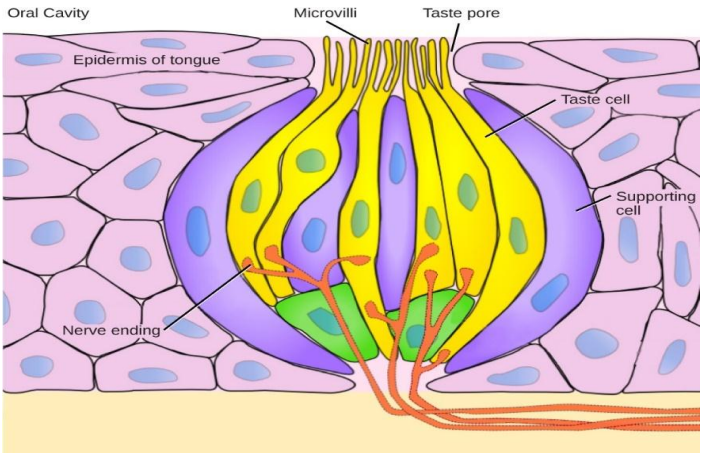

Fig. 2: Taste buds.

2) **Papillae**- The tongue is made up of many papillae structures. There are various kinds of papillae, including fungiform papillae and circumvallate papillae, both of which have multiple taste buds. Even though they are more numerous, filiform papillae do not possess taste buds.

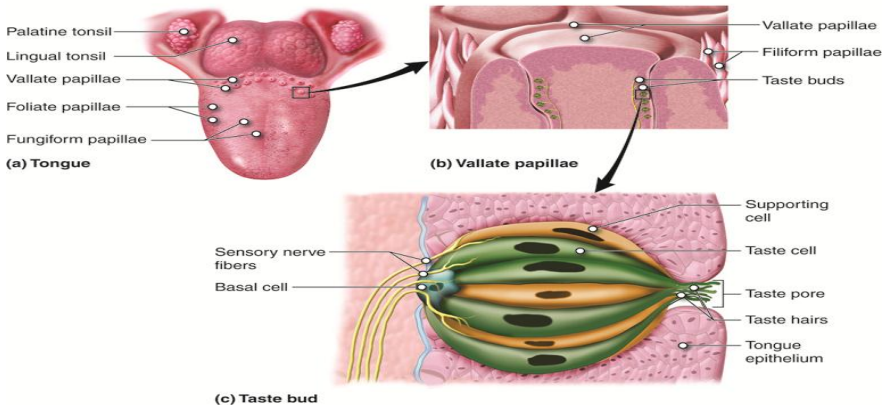

Fig. 3: Structure of papillae.

Physiology of taste

To combat the drug's poor taste, two methods are frequently used. The first involves lowering medication solubility in saliva, where it is important to strike a balance between lowered solubility and bioavailability. Altering the drug's capacity to interact with taste receptors is an alternative strategy.

Taste signaling pathways

Taste transduction begins with the interaction of a tastant (eg. medicine or food) with taste receptor cells in the taste buds. The tastant binds with G-Protein coupled receptors (GPCRS) in the cells triggering the release of G-Protein called Gustducin.

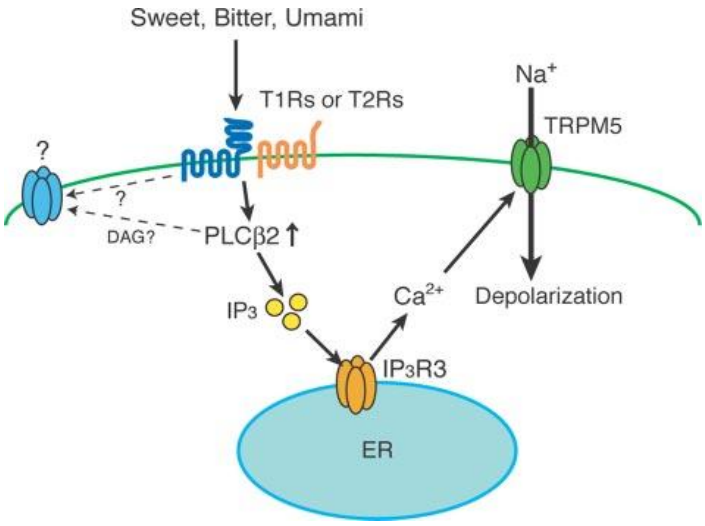

Fig. 4: Taste signaling pathways.

The process of taste sensation begins when Gustducin activates the effector enzymes phosphodiesterase IA (PDE) or phospholipase C beta-2(PLC). The effector enzyme then changes 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 ion channels including the calcium channel inside the cell and sodium, potassium and calcium channel on the extracellular membrane. This ionization depolarizes the cell causing the release of neurotransmitters that send nerve impulses to the brain that carries the signal of bitter taste and taste blockers work by interfering with taste transduction.[5,6]

An Ideal Taste Masking Process and Formulation should have the following properties-[11,9,13]

1) Involve the least number of equipment and processing steps.
2) Require a minimum number of excipients for an optimum formulation.

3) No adverse effect on drug bioavailability.
4) Require excipients that are economical and easily available.
5) Least manufacturing cost.
6) Can be carried out at room temperature.
7) Require excipients that have a high margin of safety.
8) Rapid and easy to prepare.

Factors affecting the selection of taste masking technology-[1,5,7,9,11]

1. Dose of active pharmaceuticals

The dosage of medicine may determine which formulation approach is best for achieving flavour masking. The dose in paediatric formulations is low enough to permit the use of flavourings to cover the taste of the medication. By adding sweeteners, for instance, low dose palatable paediatric aspirin oral formulation was created. However, due to the high dose of acetaminophen, the same strategy failed to address the issue. In these circumstances, the coating is preferred in conjunction with sweeteners to ensure flavour masking and a suitable final dosage form size.

2. Extent of bitter taste

Even a small amount of exposure is enough to detect the foul taste in medications with an aggressively unpleasant flavour. For instance, due to the dominant flavour of ibuprofen's oral formulation, sweets were unable to hide their taste. Even though coating defects, if present, limit the technique's effectiveness, the coating is a more effective approach for bitterly aggressive medications. Similar to this, liquid oral solutions cannot have the taste of strong, bitter active drugs like azithromycin sufficiently covered by microencapsulation. Viscosity boosters can supplement the effectiveness of flavour masking. Viscosity enhancers in oral suspensions can mask the unpleasant taste that results from drug leakage from coated medications or microcapsules. The drug transport from the polymer-coated oxazolidinone particles was similarly constrained using this method.

3. Drug particle Shape and Size distribution

The effectiveness of the taste-masking technique would depend on the drug's particle properties. Small particle sizes and irregularly shaped core materials result in inconsistent coating breakdown and poor flavour masking effectiveness. The taste mask coating may become degraded as a result of fines, abrasion, and varying coating thickness. Such coating flaws can be minimised or eliminated by using a multilayer coating with an inner spacing

layer to separate the medicine from the taste-masking layer. Gatifloxacin and dextromethorphan taste-masked granules were created using a multilayer coating that included an inner spacing layer and an outside taste-mapping layer.

4. Drug solubility

The drug's physicochemical characteristics are crucial when choosing a taste-mapping technology. Ondansetron, for instance, has a relatively lower water solubility at higher pH levels. Based on this fact, an alkalizing agent (sodium bicarbonate) was added to an ondansetron formulation to reduce the water solubility and the resulting taste perception. Different methods for disguising the taste of ranitidine base and its salts with various solubility profiles were described by Douglas and Evans (1994). The lipid coating of the medication may successfully disguise the bitter taste associated with a poorly soluble type of ranitidine. However, the degree of taste masking provided by the drug substance's simple lipid coating may not be sufficient for ranitidine's water-soluble forms (such as ranitidine hydrochloride), especially if the product is to be prepared in an aqueous medium. To effectively mask the taste, ranitidine hydrochloride was first added to the inner core of a polymeric binder, a lipid, or wax that has a higher melting point than the coating.

5. Ionic characteristics of the drug

The choice of ion exchange resin polymers and the acceptability of the drug candidate for this technique are determined by the Ionic properties of pharmaceuticals. For instance, cationic polymers are a suitable choice of excipients for anionic pharmaceuticals like sildenafil while anionic polymers are ideal choices for cationic drugs like donepezil hydrochloride (e.g., alginic acid).

6. Dosage forms

It is estimated that 50% of the population has problems swallowing tablets, especially the pediatric and geriatric populations. Chewable tablets and liquid oral dosage forms have been used to address these problems. However, it is difficult to formulate some drugs in these dosage forms due to their poor palatability. For formulations which are swallowed in unchewed capsules, coated tablets and slowly disintegrating hard tablets have been used as preferred taste masking technologies. Chewable tablets and liquid oral formulations are preferable in the case of large-dose drugs for ease of intake. Taste masking technologies such as sweeteners, particulate coating, microencapsulation and granulation can be employed for chewable tablets and supported with technologies such as viscosity enhancers and pH

modifiers to achieve taste masking in liquid oral formulations. Microencapsulation of the unpleasant-tasting active agent with ethyl cellulose or a mixture of ethyl cellulose and hydroxypropyl cellulose or other cellulose derivatives has been used to provide chewable dosage forms. However, this approach suffers from the disadvantage that the polymer coating inconsistently releases the active agent and may not provide an immediate release. Moreover, the coating is more suitable when the formulation is stored in a dry form. Viscosity enhancers or pH modifiers can be used in the suspending medium to achieve taste masking of suspended coated particles, especially for extremely bitter drugs like erythromycin and its derivatives during the shelf life of a reconstituted suspension.

Taste masking techniques[1,3,8,12,14,20]

To achieve the goal of taste abatement of the bitter or unpleasant taste of the drug, various techniques are reported.

These are as follows:

1) Addition of flavouring and sweetening agents.
2) Microencapsulation.
3) Ion exchange.
4) Inclusion complex formation.
5) Granulation.
6) Taste masking by adsorption.
7) Prodrug approach.
8) Bitterness inhibitor.
9) Multiple emulsion technique.
10) Gel formation.
11) Miscellaneous.

1) Addition of Flavouring and Sweetening agents[1,4,12,13,21]

Sweeteners and other flavourants can be used as taste-enhancing additions to cover up or mask the taste of an unpleasant active ingredient. Unfortunately, the most popular method of taste masking involves combining sugars and flavours to disguise an unpleasant flavour. For a variety of reasons, this overly straightforward approach is problematic. Sweet excipients do not offer the optimal stimulation for bitterness-tuned receptors and thus are not entirely successful at masking the taste of particularly bitter (especially extremely water-soluble) actives on their own. However, they may work better at masking a sour flavour. Sweeteners

and other taste-improving additives can be quite effective when combined with another main tactic for disguising tastes. Sweeteners are frequently highly soluble and quickly wash away from taste receptors. Adding extended-release granules, which might keep delivering sweetness to taste receptors for the length of bitterness (10 to 60 seconds), together with granules or a solubility retardant, could be one strategy to compete at an appropriate time scale. Both natural and artificial sources can be used to create flavourings and fragrances. Fruit juices, aromatic oils like lemon and peppermint, herbs, spices, and their distilled fractions are examples of natural products.

Table 1: Addition of Flavouring and Sweetening agents.

Author	Drug	Flavouring / Sweetener	Result
Havlir et. al	Cetirizine Dihydrochloride	Grape, Vanilla	Taste masking of the drug achieved.
Mishra R. et. al	Cetirizine Hydrochloride	Aspartame, sucralose, Lemon flavour and citric acid	Optimized taste masked rapid dissolving films were obtained
Francesco C et.al	Nicotine Hydro Tartrate	Milk-mint	Combination of milk bitter taste of nicotine, but this formulation is perceived as an irritant in the mouth (fast-dissolving films).

2) Microencapsulation[1,2,6,9,15]

Microencapsulation is a process in which the active moiety (solid or liquid droplets) is coated with a polymeric material or film.

Types of microencapsulation include-

- Air suspension coating
- Co-acervation phase separation
- Spray drying and Spray congealing
- Solvent evaporation
- Pan coating
- Interfacial polymerization

Of these processes, the first four are mostly used techniques for achieving taste masking

Table 2: Microencapsulation.

Author	Drug	Polymer	Result
Omran et.al	Diclofenac Sodium	Ethylcellulose	Diclofenac sodium microcapsules were prepared using ethyl cellulose-toluene-petroleum ether, with a solvent: nonsolvent ratio of 1:2
Maccariet.al	Flucloxacillin	17% Ethyl cellulose	Flucloxacillin microencapsulation for taste abatements is available from the tablet as the raw unprocessed antibiotic
Sugar H et.al	Indeloxazine (fluidized bed with side spray method)	Hydrogenated oil and surfactant	Taste masking of the drug without loss of bioavailability by heat treatment of wax-coated microparticles.
Ozer AY et.al	Beclamide (simple coacervation)	Gelatine, anhydrous sodium sulfate-Coacervating agent	Core: wall ratio 1:1, microencapsulation to mask the bitter taste.

Table 3: Spray congealing.

Author	Drug	Polymer	Result
Yajimaet. al	Clarithromycin	Amino Alkyl Methacrylate Polymer E (AMCE)	Taste masking is prevented by drug release in the mouth while ensuring rapid release in GIT.

Table 4: Solvent evaporation technique.

Author	Drug	Polymer	Result
Srikanth. al	Drotaverine Hydrochloride	Polymethlyacrylic Polymer	Polymethylacrylic polymer improves the unpleasant taste of orodispersible Drotaverine hydrochloride tablet.
V. Anand et. Al	Prednisolone	Eudragit E 100	Drug polymer 1:10 microspheres of Prednisolone are tasteless and further

			used for formulation into ODT.

3) Ion exchange resins[1,3,7,10,17,18,19]

Ion exchange resins are artificial, inert organic polymers with ionisable groups attached to a hydrocarbon network. They can exchange their labile ions for ions in the solution they are in contact with. Styrene and divinylbenzene copolymer is the most widely utilised polymeric network (DVB). In addition, various polymers have been employed as ion exchange drug carriers, such as those made of acrylic and methacrylic acid that have been crosslinked with divinyl benzene and contain the proper functional groups.

Types of resins

Ion exchange resins contain positively or negatively charged functional groups and are thus Classified as either anionic or cationic exchangers. Within each category, they are classified as strong or weak, depending on their affinity for capable counter ions.

Table 5: Common ion exchange resins.

Type	Functional Group	Polymer Backbone	Commercial resins
Strong Anion	-N+R3	Polystyrene-DVB	Amberlite IR 400, Dowex 1
Weak Anion	-N+R2	Polystyrene-DVB	Amberlite IR 4B, Dowex 2
Strong Cation	-SO3H	Polystyrene-DVB	Amberlite IR 120, Dowex 50
Weak Cation	-COOH	Methacrylic acid-DVB	Amberlite IRC 50, Indian 204,234, Tulsion 335,339

These insoluble ion exchange resins can be supplied as sodium, potassium, or ammonium salts for cation exchangers and typically as chloride for anion exchangers. The entire transformation of a resin from one ionic state to another is frequently required. The two methods of column loading and batch loading are typically used to load charged medicines onto ion exchange resins.

Column method

In this method, a highly concentrated drug solution is passed through a column of resin particles. Since the reaction is an equilibrium phenomenon, maximum potency and efficiency are best obtained by the column method.

Batch method

In this method, the drug solution is agitated with several resin particles until equilibrium is established.

The reaction involved during the complexation of the drug with resin may be indicated as follows-

$Re\text{-}COO\text{-}H^{+} + Basic\ drug^{+} \rightarrow Re\text{-}COO\text{-}\ Drug^{+} + H^{+}$

$Re\text{-}N(CH3)+CL^{-}+Acidic\ drug \rightarrow Re\text{-}N(CH3)+3Drug+Cl^{-}$

Upon ingestion, drugs are most likely eluted from cation exchange resins by H^{+}, Na^{+} or K^{+} ions and from anion exchange resins by CI^{-}, as these ions are most plentiful and available in gastrointestinal secretions.

Typical reactions involved in the gastrointestinal fluids may be investigated as follows:

In the stomach:

$Re\text{-}COO\text{-}Drug^{+} + HC = Re\text{-}COOH + Drug\ Hydrochloride$

$Re\text{-}N(CH3)+3\ Drug^{-} + FCI\text{-}* Re\text{-}N(CH3)_3Cl^{-} + Acidic\ drug$

In the intestine:

$Re\text{-}COO\text{-}Drug^{+} + NaCl \rightarrow Re\text{-}COONa + Drug\ Hydrochloride$

$Re\text{-}N(CH3) + 3\ Drug^{-} + NaCl \rightarrow Re\text{-}N(CH3)_3CI + Sodium\ salt\ of\ drug$

Exchange capacity

The number of ionic sites per unit weight or volume (meq/gram or meq/mL) is the exchange capacity of an ion exchange resin. Due to the bulkier ionic substituents in sulfonic acid resin and polystyrene matrix, the exchange capacities of sulfonic acid resin and polystyrene matrix are less than those of carboxylic acid resin formed from an acrylic acid polymer, which has a capacity of roughly 10 meq/gm.

Since weak acid cation exchange resins have a pKa value of about 6, their exchange capacity tends to rise at pH 4 or higher. Only in alkaline solution, or in their salt form, does weak acid cation exchange resin ionise to a significant degree. Their exchange capacity is said to be very poor below pH 7 and somewhat steady values at pH levels higher than around 9. The permeability of the solvent and solute via the pores of the resin, whose number and size are affected by the degree of crosslinking, affects the rate of ion exchange. Of course, the size of the resin particle has an impact on the diffusion route length as well.

Applications

To stabilise the sensitive components, maintain medication release, and conceal taste, Ion exchange resins are utilised in the manufacture of pharmaceuticals. According to research on how amine medications interact with polycarboxylic acid ion exchange resin, taste resins could be very helpful for flavour covering. According to these studies, saliva's typical pH is 6.7 and its cation concentration is 40meq/1, which means that only a small amount of medicine would be eluted from adsorbate by saliva. However, as soon as the adsorbates are exposed to the stomach's low pH, fast elution will start to take place. Another strategy for covering up the flavour is to use polycarboxylic acid ion exchange resin adsorbates to coat the particles. This is advantageous since the uncoated adsorbate can cover a wide range of tastes.

Table 6: Ion exchange resin.

Author	Drug	Polymer	Result
Patel et.al	Topiramate	Kyron T-114, Kyron T-134, Doshion T-542	Kyron-114 with drug - the resin of 1:3 was found to offer the best taste masking.
Jena et.al	Ondansterone Hyrochloride	Indion 294	Indion 294 provides improved taste masking of Ondansetron Hydrochloride.
Saikat Das et.al	Ciprofloxacin	Indion 234	Indion 234 was used to mask the bitter taste of the drug.
Patel K. et .al	Fexofenadine HCL	Indion 234	Use of Indion 234and Eudragit E100 offers taste masking with good flow properties and drug release.

4) Inclusion complex formulation[1,2,4,13,20]

When an inclusion complex is formed, the drug molecule fits within the host molecule, which functions as a complexing agent, to create a stable complex. By either reducing the drug's oral solubility upon administration or limiting the number of drug particles exposed to taste buds, the complexing agent can disguise the taste of the drug's bitterness and lessen the bitterness perception. Inclusion complexes mostly involve van der Waals forces.

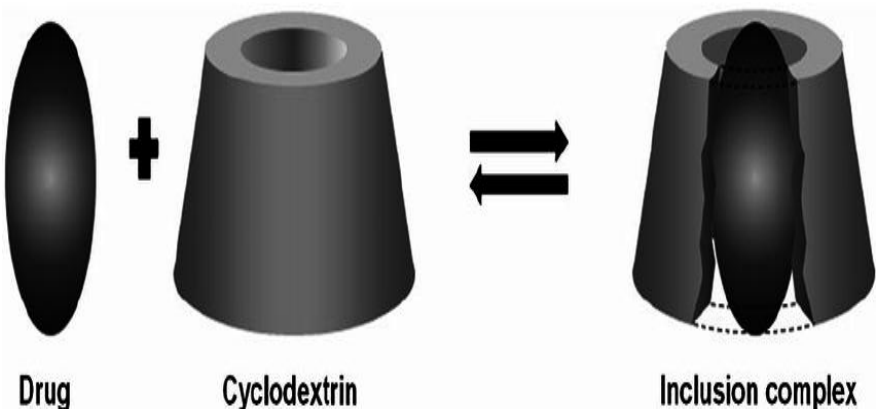

Fig. 5: Inclusion complex formation.

Cyclodextrins are frequently utilised as complexing agents for the production of inclusion complexes. Cyclodextrins are cyclic macromolecules produced when glycosyltransferases break down starch. Different cyclodextrins—each containing six (alpha-cyclodextrin), seven (beta-cyclodextrin), and eight (gamma-cyclodextrin) glucose units—are produced depending on the unique characteristics of the corresponding transferases. The most used complexing agent for inclusion-type complexes is beta-cyclodextrin. It is a cyclic oligosaccharide made from starch that is delicious and non-toxic. Alpha, gamma, and beta-cyclodextrin were used in increasing amounts to reduce the bitter flavour.

Table 7: Inclusion complex formation.

Author	Drug	Polymer	Result
Shah P. et. al	Primaquine phosphate	Beta - cyclodextrin	Cachets are prepared using a physical mixture of drug and beta-cyclodextrin in a ratio of 1:25 showed complete bitter taste masking & easy dispersibility.
Soloman M. et. al	Ibuprofen Aqueous solution	Hydroxypropyl Beta-Cyclodextrin	Taste masking was achieved by weight ratio of Ibuprofen: hydroxypropyl-beta cyclodextrin 1:11 to 1:15.
Patel et. al	Famotidine	HPMC	Taste masking due to complex formation with HPMC.

5) Granulation[1,3,9,14]

Granulation is a process that can hide the bitter taste of medication. Granulation is a significant and frequent step in the manufacture of tablets. In this method, the binding agents employed to make the tablets are saliva-insoluble polymers. Because these polymers are insoluble in saliva, the drug's harsh taste can be covered up. EUDRAGIT® E polymers aid to seal sensitive actives and promote patient compliance by disguising tastes and odours in the taste-masked granules as well as chewable and fast-disintegrating tablets.

Table 8: Granulation.

Author	Drug	Technique	Result
Sona P.S et . al	Diclofenac Sodium	Wet Granulation	Taste-masked diclofenac sodium fast-disintegrating tablets using veegum as a taste-masking agent (1:1.5) and sodium starch glycolate and croscarmellose sodium (5%) as super disintegrants were successfully prepared.
Shakeel et.al	Norfloxacin Tinidazole	Ethyl Cellulose, HPMC	More acceptability than plain film-coated tablets. Improved performance and acceptability.
Kawano Y et. al	Furosemide	Wet Granulation	Taste masking was achieved with yoghurt powder when mixed in the ratio of furosemide: yoghurt (1:1).

6) Taste masking by adsorption[9,16]

Adsorbates of bitter-tasting medications can be thought of as less saliva-soluble variations of these medications. To adsorb a substance, one must first prepare a solution of the substance, combine it with an insoluble powder that will adsorb the substance, drain the solvent from the resulting powder, and then dry the resulting powder. The dried adsorbates are then used to create the final dosage form. For the creation of bitter drug adsorbates, a variety of substrates including veegum, bentonite, silica gel, and silicates can be employed. To create a bitter

taste-masked solution of these medications, loperamide and phenyl propanolamine have been adsorbed on magnesium aluminium silicates, also known as Veegum F.

7) Prodrug formaton[1,7,13]

Prodrugs are inert drug precursors that have undergone chemical modification; when they undergo biotransformation, the pharmacologically active parent drug is released. Many of these compounds have a bitter taste, making it challenging to administer them by that route. For instance, 3-hydroxymorphinans are well absorbed from the buccal cavity. The current invention relates to prodrugs of 3-hydroxymorphinans that have no taste and are therefore more suited for delivery via the buccal, sublingual, or nasal routes. By choosing prodrugs with the proper solubility and hydrolysis rates, one can accomplish quick absorption, a fall in plasma drug concentrations, or sustained plasma concentrations of the active drug. These can be made into lozenges, patches, gels, pastes, tablets, or gel capsules.

Table 9: Prodrug formation.

Author	Drug	Prodrug with improved taste
Taylor E.T et. Al	Chloramphenicol	Palmitate ester
Hussain Met. Al	NalbuphineHC1, Naltrexone, Naloxone, Oxymorphone HCL, Levallorphan	Esters of Nalbuphine, Naltrexone, Naloxone, Oxymorphone, and Levallorphan.

8) Bitterness inhibitors[3,12]

In the domains of taste physiology and pharmaceutical sciences, the creation of a particular universal inhibitor for bitter taste has been highly desired but has not yet been made available. The fact that compounds that block the bitterness of one class of compounds do not affect the bitterness of another chemical searches for a universal bitter taste inhibitor challenging. It has been demonstrated that sodium salts including sodium chloride, sodium acetate, and sodium gluconate are powerful inhibitors of some bitter chemicals. Although the mechanism is unknown, research indicates that sodium has a taste-related effect rather than a cognitive one.

Since bitter chemicals are frequently hydrophobic, lipoprotein (PA-LG) made of phosphatidic acid and B-lactoglobulin can cover up the taste receptor membrane's target sites for bitter substances without altering reactions to salts, acids, sugars, or sweet amino acids.

Lipoprotein has been shown to inhibit the bitter taste of berberine, brucine, chloride, caffeine, denatonium benzoate, glycyl L-leucine, L-phenylalanine, naringin, propranolol hydrochloride, quinine hydrochloride, strychnine nitrate, and theophylline. It has been documented that phospholipids such as phosphatidic acid, phosphatidylinositol, and soy lecithin selectively decrease the bitter taste of certain medicines. By fractionating soy lecithin to obtain BMI 60, the bitter taste of trimethoprim-sulfamethoxazole and polymixin B sulphate has been covered up.

9) Multiple emulsions technique[5,9,13]

By dissolving the drug moiety in the inner aqueous phase of an o/w/o emulsion with good shelf life stability, a novel technique for taste masking of pharmaceuticals utilising multiple emulsions have been accomplished. O/W/O emulsions are a type of multiple emulsion in which the oil acts as a divider between the mixture's internal and external aqueous phases, while O/W/O emulsions are the opposite. Phase inversion or membrane emulsification techniques are used to prepare it. In the presence of gastrointestinal fluid, the formulation is intended to release the medication through the oil phase. It's also a good idea to use many emulsions to hide the taste of harsh medications.

10) Gel formation[8,14]

For taste masking, water-insoluble gelation can be applied on the surface of tablets containing bitter medications. When bivalent metal ions are present, sodium alginate can lead to water-insoluble gelation. The taste of tablets containing amiprolose hydrochloride has been concealed by coating them with calcium gluconate on top and sodium alginate underneath. When saliva is present, sodium alginate combines with bivalent calcium to generate a gel that is insoluble in water, so disguising the flavour.

11) Miscellaneous[1,2,4,7,8,13,17]

11.1. Use of effervescent agents

Effervescent substances have been used as taste-masking substances for dosage forms that are not dissolved in water before administration and have been demonstrated to be favourable and useful for oral drug delivery. A bitter medicine chewing gum composition was created to deliver the medicine to the mouth cavity for local administration or buccal absorption. It consists of a chewing foundation, an oral medication, carbon dioxide to mask the taste, and, optionally, a taste bud desensitising substance (such as an oral anaesthetic like benzocaine) as well as additional inert ingredients including sweeteners, flavourings, and fillers. Fentanyl

and prochlorperazine effervescent tablets were recently created to deliver these medications to the mouth cavity for buccal, sublingual, and gingival absorption. To increase oral absorption and cover up their bitter taste, the medications are combined with an effervescent ingredient in the formulations. The formulation of fentanyl also had an extra pH-adjusting ingredient to help absorption even further.

11.2 Rheological modification

Gums and carbohydrates, which are rheological modifiers that increase viscosity, can reduce the transport of bitter compounds from the saliva to the taste buds. To lessen the harsh taste of the acetaminophen solution, xanthan gum (0.1-0.2%) and microcrystalline cellulose (0.6-1%) were added to the formulation. Methionine (a stabiliser) and maltitol are used in the preparation of the antidepressant medication mirtazapine to create an aqueous solution (thickening agent). In addition to masking the bad taste of the medicine, maltitol is stable in the acidic pH range of 2 to 3. Inhibiting the drug's undesired local anaesthetic action is another benefit.

11.3 pH Modifiers

Many medications become less soluble at pH levels other than the mouth's 5.9 pH level. If the equilibrium concentration is below the taste threshold, drugs may not be sufficiently solubilized to be detectable by taste. The bitter taste of the medicine was successfully covered up by a sweetener alone when a solubilization inhibitor, such as sodium carbonate, sodium bicarbonate, sodium hydroxide, or calcium carbonate, was added to elevate the pH when granules including sildenafil dissolved in an aqueous medium. For taste masking, a variety of natural and synthetic polymers, resins, and waxes have been used alone or in combination. Eudragit L and other enteric polymers are used to mask the taste, however, because saliva has a pH close to 5.8 and these polymers solubilize at pH levels above 5.5, there is a chance that some medications may be partially leached. Therefore, a taste-masking polymer that completely covers the bitter taste at the pH of saliva in the mouth and the reconstitution medium, as in the case of liquid orals, as well as one that can shield the drug from moisture in the dosage form while releasing the drug quickly in the stomach without affecting its absorption and bioavailability, is needed.

11.4 Salt formation

The multi-particulate salting-out taste-masking system consists of a drug core, a salting-out layer with salts and water-soluble polymers, and a water penetration control layer with water-

insoluble components. The technique creates a lengthy lag time (the time when the amount of drug released is less than 1%), followed by a rapid drug release for high bioavailability. In this study, the system was optimised to minimise particle size and contain pharmaceuticals with high water solubility to contain the system and medications that cause numbness in oral disintegrating tablets. The location of the components, the coating solvent, and the amount of coating on the layers were all optimised.[1,2,4,7,8,13,17]

Evaluation of taste masking[2,6,12,15,16]

Evaluation of taste masking is tedious work as the taste sensation varies from person to person and the release of the drug from the taste-masked complex and asses in vivo and in vitro.

In vivo evaluation

A trained taste panel of healthy participants with an organoleptic sense conducted an in-person taste evaluation with their previous agreement. Bitterness was measured against pure medication after 60 seconds of oral administration using a numerical scale. The numerical scale can include values of 0 being pleasant, 1 being tasteless, 2 being no bitterness at all, 3 being bitterness that comes right away, 4 being slightly bitter, and 5 being highly bitter. Large panel A and complex analyses are frequently needed for in vivo assessment, which also creates scheduling and safety concerns and can be time- and money-consuming.

In vitro evaluation

This issue is solved by the development of "E-Tongue" electronic sensor array technology, a tool for artificially assessing taste and flavour as well as for recognition and quantitative multicomponent analysis. It distinguishes between three levels of biological taste, including perceptual level, circuit level, and receptor level (human taste buds, E-tongue probe membranes, and brain transmission in humans) (cognition in the thalamus humans, computer and statistical analysis in the E-Tongue). The probes are made of a silicon transistor with specialised organic coatings that control their sensitivity and selectivity and use potentiometric measurement. Each probe is cross-selective to cover the entire flavour profile, and statistical software converts the sensor data into taste patterns. Solid samples need to be first dissolved before measurement while liquid samples can be analysed right away without any prior preparation. The sensors and the reference electrode are submerged in the test fluid for 120 seconds in a beaker. The E-Tongue programme detected and evaluated the potentiometric variance between each sensor and a reference electrode. During the creation of

the manufacturing process, clinical use, stability studies, validation, commercial manufacture, and batch release, sensory analysis is used to assess and manage the quality of the taste and flavour. These facts serve as the raw material for effective mathematical processing. In the early stages of drug development, the E- Tongue makes it possible to precisely analyse taste without the use of human participants. The E-Tongue also won't get sick, become tired, or lose its sense of taste even after extended testing.

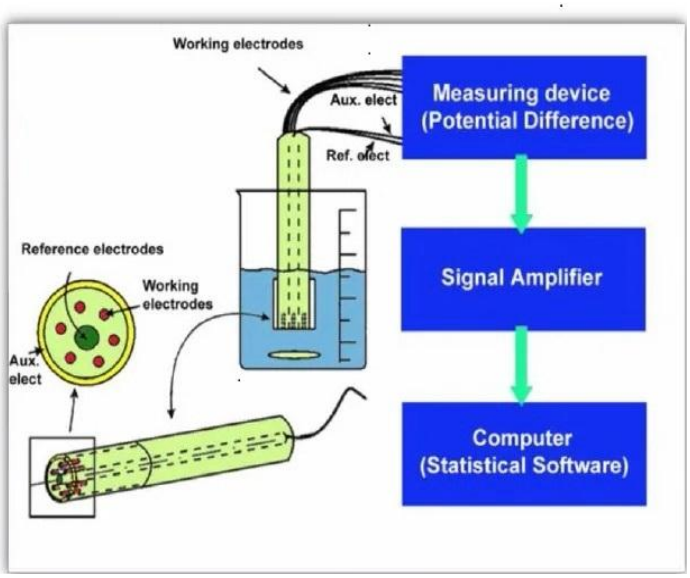

Fig. 6: Evaluation of taste using e-tongue.

Spectrophotometric method

By rotating the 10 ml syringe five times end to end in 30 seconds, a known amount of the taste-masked formulation is combined with 10 ml of distilled water. A membrane filter is used to filter the test medium, and the concentration of the drug in the filtrate is then determined using spectrophotometry. The bitter taste might be covered up in vivo if this concentration is lower than the threshold concentration. The taste-masked sparfloxacin granules have been evaluated using this method, with a 100 g/ml threshold concentration.

Measurement of frog taste nerve response

With this technique, adult bullfrogs are intraperitoneally anaesthetized before the glossopharyngeal nerve is located, separated from the surrounding tissue, and cut proximally. The nerve impulse is amplified and integrated using an A.C. amplifier and an electronic integrator. The magnitude of the response is then determined by the integrated response's peak height. This method has reportedly been used to test quinine sulphate formulations with taste-masking PA-LG (phosphatidic acid-lactoglobulin) combinations.

SUMMARY

Although there are numerous taste masking strategies for effectively concealing the unappealing taste of medications, their administration takes competence so as not to impair the drug's bioavailability. Applying these strategies and accurately assessing how taste masking effects influence patients can increase patient compliance with a product to a greater extent. Scientists have a significant hurdle in disguising the taste of bitter medications. However, we have attempted to outline several appropriate strategies for disguising offensive medications' taste. These methods described in this review are also applicable at the bench scale and pilot scale. This evaluation also mentions numerous novel technologies for efficient flavour masking in addition to the patented taste-masking methods now in use. One can significantly increase product preference by using these strategies. In addition to oral drug administration, research on taste-masked drug delivery is becoming more significant for quality. The care is given to patients, particularly young and old. The development of pleasant dose forms with good patient compliance without impeding medication release is generally acknowledged, as indicated by the number of patients and technological advancements.

REFERENCES

1. Shet N., Vaidya I., "Taste Masking: A Pathfinder for Bitter Drugs", International Journal of Pharmaceutical Sciences Review and Research'", 2013; 18(2): 1-12.
2. Patil V., Tambe V., "Modern Taste Concealing Techniques In Pharmaceuticals: A Review", World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(8): 293-316.
3. Sharma S., Lewis S., "Taste Masking Technologies: A Review", International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(2): 6-13.
4. Patel C., Tyagi S., Gupta A., "Pharmaceutical Taste Masking Technologies of Bitter Drugs: A Concise Review", Journal of Drug Discovery and Therapeutics, 2013; 1(5): 39-46.
5. Sonawane V., Saiffee M., Shinde N. "An update of taste masking methods and evaluation technique", 2010; 2(6): 1-15.
6. Gupta A., Madaan S., Dalal M. "Practical Approaches for Taste Masking of Bitter Drugs: A Review, International Journal of Drug Delivery Technology, 2010; 2(2): 56-61.
7. Kumar K., Bhowmik D., Deb L. "RECENT TRENDS IN TASTE MASKING OF BITTER DRUGS, Journal of Drug Delivery Research, 2012; 1-11.

8. Kalaskar R., Singh R., "TASTE MASKING: A NOVEL TECHNIQUE FOR ORAL DRUG DELIVERY SYSTEM', Asian Journal of Pharmaceutical Research Development, 2014; 2(3): 1-14.
9. Patil S., Ghatge G., "REVIEW ON TASTE ABATEMENT TECHNIQUES", International Journal of Institutional Pharmacy and Life Sciences, 2013; 3(5): 43-67.
10. Ahire S., Bankar V., Pawar S., "A REVIEW: TASTE MASKING TECHNIQUES IN PHARMACEUTICALS, An International Journal of Pharmaceutical Sciences, 2012; 3(3): 68-82.
11. Jain M., Pareek A., Bagdi G., "Taste masking methods for bitter drug- A review", International Journal of Pharmacy and Life Sciences, 2006; 1(6): 336-339.
12. Vummaneni V., Nagpal D. "Taste Masking Technologies: An Overview and Recent Updates", International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012; 3(2): 510-521.
13. Pandey S., Kumar S., Prajapati S., "AN OVERVIEW ON TASTE PHYSIOLOGY AND MASKING OF BITTER DRUGS", International Journal of Pharma and Bio Sciences, 2010; 1(3): 1-11.
14. Jha S., Sharma R., "TASTE MASKING IN PHARMACEUTICALS: AN UPDATE", Journal of Pharmacy Research, 2008; 1(2): 126-130.
15. Gupta R., Sharma P., "ION EXCHANGE RESIN AS A POTENTIAL TECHNOLOGY ON FOR TASTE MASKING: A REVIEW", International Journal of Pharmacy, 2014; 4(4): 220-225.
16. Bansal A., "Trends in Pharmaceutical Taste Masking Technologies: A Patent Review", Recent Patents on Drug Delivery and Formulation, 2009; 3(1): 26-39.
17. Jena A., Kumar M., "Formulation and Evaluation of Taste Masked Orally Disintegrating Ondansetron Hydrochloride Tablet", International Journal of Research and Pharmaceutical Sciences, 2010; 1(3): 328-332.
18. Das S., Saha S., "Taste Masking of Ciprofloxacin by Ion Exchange Resin", International Journal of Preclinical and Pharmaceutical Research, 2010; 1(1): 7-13.
19. Patel K., "Comparative Evaluation of Taste Masking Methods for Fexofenadine Hydrochloride ", ThePharma Review, 2007; 5(30): 176-178.
20. Mundada A., "Taste Masking Approaches -A Review: Part 1 and 2, American Pharmaceutical Review, 2008; 11(2): 74-82.
21. Rossi D., "A Spoonful of Sugar: Taste Masking Strategies in Pharmaceutical Product Development- Part 1 and 2, American Pharmaceutical Review, 2008; 11(1): 91-102.