INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com ISSN 2230 – 8407

Review Article

TASTE MASKING IN PHARMACEUTICAL: AN UPDATE

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Article Received on: 12/04/12 Revised on: 20/05/12 Approved for publication: 06/07/12

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ABSTRACT

Taste is an important factor in the development of dosage form. Nevertheless it is that arena of product development that has been overlooked and undermined for its importance. The problem of bitter and obnoxious taste of is a challenge to the pharmacist in the present scenario. Taste is an important parameter governing compliance. Several oral pharmaceuticals and bulking agents have unpleasant, bitter-tasting components. In numerous cases, the bitter taste modality is an undesirable trait of the product or formulations and can considerably affect its acceptability by consumers. Bitter characteristics found in such systems have been eliminated or minimized by various known processes, but no universally applicable technology for bitterness inhibition has ever been recognized. The desire of improved palatability in these products has prompted the development of numerous formulations with improved performance and acceptability Taste masking technologies offer a great scope for invention and patents. Several approaches like adding flavors and sweeteners, use of coating polymers for inhibiting bitterness, microencapsulation, prodrug formation, formation of inclusion and molecular complexes, solid dispersion system, addition of effervescent agents and application of ion exchange resins have been tried by the formulators to mask the unpleasant taste of the bitter drugs. The present review attempts to give a brief account of different technologies of taste masking with respect to dosage form and novel methods of evaluation of taste masking effect.

Key words: Taste masking, microencapsulation, effervescent agent, solid dispersion, prodrug, unpleasant taste etc.

INTRODUCTION

Taste drives appetite and protects us from poisons. So, we like the taste of sugar because we have an absolute requirement for carbohydrates (sugars etc.). We get cravings for salt because we must have sodium chloride (common salt) in our diet. Bitter and sour cause aversive, avoidance reactions because most poisons are bitter (most bitter substances are bad for you - certainly in excess) and off food goes sour (acidic)[1]. Taste is an important parameter in administering drugs orally. Undesirable taste is one of the important formulation problems that are encountered with many drugs. Administration of bitter drugs orally with acceptable level of palatability is a key issue for health care providers. Proven methods for bitterness reduction and inhibition have resulted in improved palatability of oral pharmaceuticals[2].

Taste masking of the drugs which are bitter in taste has been proved to be accepted for pediatric and geriatric patients. The bitterness of pharmaceutical medicines plays a critical role in patient compliance, as the oral administration of bitter drugs is often hampered by their unpleasant taste which leads to non-compliance and further worsening of diseased condition. Unwillingness to swallow solid dosage form such as tablets is a general problem for all age groups, especially elderly and pediatrics mainly due to the physiological changes. Forty five per cent of stroke survivors, thirty three per cent of nursing home residents and sixty three per cent of cancer patients undergoing palliative care in the community or hospital report dysphagia[3].

The methods most commonly involved for achieving taste masking include various chemical and physical methods that prevent the drug substance from interaction with taste buds. The simplest method involves use of flavor enhancers. Where these methods fail more complex methodologies are adopted. Various techniques have been identified for taste masking which include polymer coating, inclusion complex formation with cyclodextrin, use of ion exchange resins, solubility limiting methods, liposome, multiple emulsions, use of anesthetic agents, etc. The present review attempts to give a brief account of different technologies of taste masking with respect to dosage form along with novel methods of evaluation of taste masking effect. Two approaches are commonly utilized to overcome bad taste of the drug. The first includes reduction of drug solubility in saliva, where a balance between reduced solubility and bioavailability must be achieved. Another approach is to alter the ability of the drug to interact with taste receptor. An ideal taste masking process and formulation should have the following properties[4].

1) Involve least number of equipments and processing steps.
2) Require 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 high margin of safety.
8) Rapid and easy to prepare.

PHYSIOLOGY OF TASTE

Physiologically, taste is a sensory response resulting from a chemical stimulation of taste buds on the tongue. The sense of taste is conducted to the brain by a process called taste transduction. This process begins with the interaction of tastant (i.e., food or medicine) with taste receptor cells in the taste buds. The tastant binds with G-protein coupled receptors in the cells, triggering the release of a G-protein called gustducin. Taste sensation begins when gustducin activates the effector enzymes phosphodiesterase 1A or phospholipase C ı-2. The effector enzymes then change the intracellular levels of second messengers such as cyclic adenosine monophosphate (cAMP), inositol 1,4,5-tri phosphate(IP3), and idacylglycerol (DAG). The second messengers activate ion channels, including calcium channels inside the cell, and

sodium, potassium and calcium channels on the extracellular membrane. This ionization depolarizes the cell, causing the release of neurotransmitters that send a nerve impulse to the brain that carries the signal of taste.

Taste constitutes four primary effects, viz., sweet, sour, bitter and salty. Correspondingly, there are four different kinds of taste buds. Sweet sensations are most easily detected at the tip, where as bitterness at the back of the tongue, but salty sensations are usually detected at the tip and the sides of the tongue. During ingestion, taste buds react to soluble substances. The resulting sensations are transmitted to the brain by the ninth cranial nerve and tastes are detected. The sensitivity of the tongue to different sensations varies widely among individuals[5].

TASTE BUDS AND TASTE PAPILLAE

Taste buds[6,8] (figure 1) are situated on the taste papillae (middle section). At the base of the taste bud, afferent taste nerve axons invade the bud and ramify extensively, each fibre typically synapsing with multiple receptor cells within the taste bud[9].Taste buds are small sense organ in most vertebrates, helps in the detection of taste. Hence a group of cells, found especially on the tongue Taste buds have been identified on the soft palate, pharynx, epiglottis, which allows different types of taste to be recognized[6]:-

Salty taste (edge, upper portion)

The salty taste is one among the four taste receptors of tongue. They are located on the edge and upper front portion of the tongue.

Sweet taste (tip)

The sweet taste is one among the four taste receptors in the tongue. They are found on the tip of the tongue.

Sour taste (along sides in back)

The sour taste is also one of the four taste receptors of the tongue. They occur at sides of the tongue and are stimulated mainly by acids.

Bitter taste (back)

The bitter taste is the last and one of the four taste receptors in the tongue. That is located toward the back of the tongue. It is stimulated by a variety of chemical substances, most of which are organic compounds, although some inorganic compounds such as magnesium and calcium also produce bitter sensations.

WORKING OF TASTE BUDS

Taste buds works by transmitting information about different kind of taste to brain via nerve fibers. Taste buds for all four type of tastei.e. sweet, sour, salty and bitter shows distinct distribution patterns on the surface of human tongue Taste buds have been identified on the soft palate, pharynx, epiglottis e. The tongue, soft palate and epiglottis consists of taste buds, that allow human to recognize different tastes in food they eat. The taste buds are chemo receptor, meaning that they transmit chemical signals in food into electrical signals. These signals travel to the brain via nervous system to experience sensation of taste[6].

Taste papillae can be seen on the tongue as little red dots, or raised bumps, particularly at the front of the tongue. These ones are actually called "fungiform" papillae, because they look like little button mushrooms. There are three other kinds of papillae, foliate, circumvallate and the nongustatory filiform. You can see that the taste buds are collections of cells situated on top of, or on the sides of, the different papillae. **Figure 1** shows the taste **papillae** (on the left) - there are fungiform, foliate and circumvallate papillae[7].

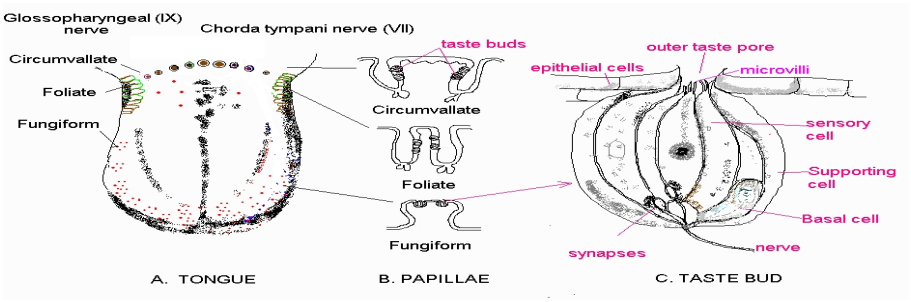

Figure 1. Papillae and taste buds

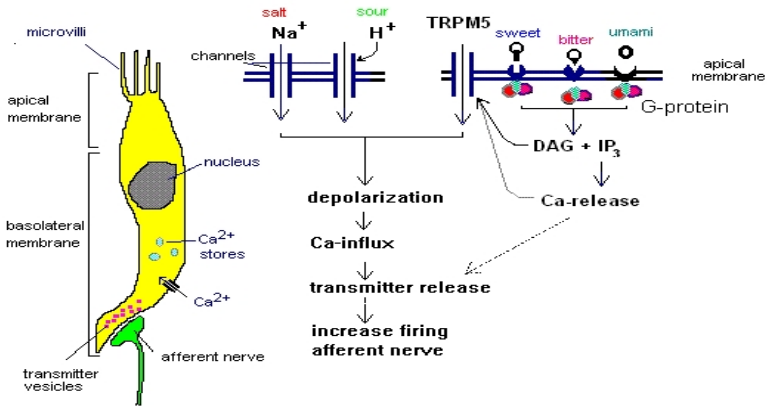

Figure 2. A taste receptor cell[8]

TABLE 1: TASTE MASKING BY ADDITION OF FLAVOURS AND SWEETNERS

S.No.	Basic Taste	Masking Agent
1.	Sweet	Vanilla, Grapefruit, Bubblegum
2.	Acid	Lemon, Orange, Cherry, Lime
3.	Metallic	Grape, Gurana, Mellow, Berriesmint
4.	Bitter	Liquorice, Raspberry, Chocolate, Coffee etc

Taste transduction

There are five basic tastes: salt, sour, sweet, bitter and umami. The current (as of 2008) thinking is that sweet, amino acid (umami), and bitter taste converge on a common transduction channel, the transient receptor potential channel TRPM5, via phospholipase C (PLC) (Figure 3). TRPM5 is a newly discovered TRP related to other channels in sensory signalling systems. It has been shown that PLC, a major signaling effector of G-protein coupled receptors (GPCRs), and TRPM5 are coexpressed with T1Rs and T2Rs and are vital for sweet, amino acid, and bitter taste transduction. Activation of T1R or T2R receptors by their respective taste molecules would stimulate G proteins, and in turn PLC (PLC-ß2). The activation of PLC generates two intracellular messengers - IP3 and diacylglycerol (DAG) - from the hydrolysis of phosphatidylinositol-4,5-bisphosphate (PIP2) and opens the TRPM5 channel, resulting in the generation of a depolarizing receptor potential. Other additional pathways may modulate sweet, amino acid, or bitter taste reception but would not, themselves, trigger a taste response. It is not at present known how PLC activates TRPM5 or whether DAG is involved. Future experiments should help reveal the G proteins for the various taste modalities and the mechanism of TRPM5 gating.

Salt taste: Salt is sodium chloride (Na+ Cl-). Na+ ions enter the receptor cells via Na-channels. These are amiloride-sensitive Na+ channel (as distinguished from TTX-sensitive Na+ channels of nerve and muscle). The entry of Na+ causes a depolarization, Ca2+ enters through voltagesensitive Ca2+ channels, transmitter release occurs and results in increased firing in the primary afferent nerve.

Sour taste: Sour taste is acid and acid is protons (H+). There is exciting new evidence that there is an acid-sensing channel - the PKD2L1 channel1.This channel is a member of the transient receptor potential channel (TRP) family and is a non-selective cation channel. The activity of PKD2L1 is gated by pH (H+ ion concentration). This new discovery displaces the previous ideas that H+ ions block K+ channels causing a depolarization, or that H+ ions enter the cell through ENaC channels. These mechanisms may exist but do not lead directly to sour perception.

Sweet taste: There are receptors T1R2 + T1R3) in the apical membrane that bind glucose (sucrose - a combination of glucose and fructose – and other carbohydrates). Binding to the receptor activates a G-protein which in turn activates phospholipase C (PLC-ß2). PLC generates IP3 and diacyl glycerol (DAG). These intracellular messengers, directly or indirectly, activate the TRPM5 channel and depolarization occurs. Ca2+ enters the cell through depolarization-activated Ca2+ channels, transmitter is released increasing firing in the primary afferent nerve.

Bitter taste: Bitter substances bind to the T2R receptors activating the G-protein and causing activation of PLC. The second messengers DAG and IP3 are produced (by hydrolysis of phosphatidylinositol-4,5-bisphosphate) activating TRPM5 and mediating release of Ca2+ from internal stores. The elevated Ca2+ causes transmitter release and this increases the firing of the primary afferent nerve.

Umami taste: Umami is the taste of certain amino acids (e.g. glutamate, aspartate and related compounds). It was first identified by Kikunae Ikeda at the Imperial University of Tokyo in 1909. It was originally that the metabotropic glutamate receptor (mGluR4) mediated umami taste. Binding to the receptor activates a G-protein and this elevates intracellular Ca2+. More recently it has been found that the T1R1 + T1R3 receptors mediate umami taste .

TASTE MASKING TECHNOLOGIES

Taste masking by addition of flavouring & sweetning agents

Generally natural products and their extracts are used in the taste masking of bitter drugs. Flavouring and perfuming agents can be obtained from either natural or synthetic sources. Some natural products include aromatic oil (eg. Peppermint oil, lemon oil etc.), fruit juices, herb spices and distilled fraction of these substances. An additional composition includes phosphorylated amino acids such as phosphoserine, phosphothreonine, phosphotyrosine etc. Sweetning agents have been classified on the basis of taste that is masked. Some of them are given below[9],

Taste masking by polymer coating of drugs

Coating is one of the most efficient and commonly used taste masking technologies. Here, it is classified based on the type of coating material, coating solvent system, and the number of coating layers. Hydrophobic polymers, lipids, sweeteners and hydrophilic polymers can be used as coating materials, either alone or in combination, as a single or multi-layer coat, to achieve the taste masking by aqueous or organic based coating process[10]. One of the most important factors to be considered in taste masking by coating is selection of coating polymers. By Coating one avoid the contact of bitter drug by preventing release of bitter drug in oral cavity. Proper selection of coating material will ask taste of bitter drug completely without affecting drug release profile. These coating agents simply provide a physical barrier over the drug particles. Various inert coating agents are shown in (Table 3) like starch; povidone, gelatin, methylcellulose, ethyl cellulose etc. are used for coating drug particles. Any nontoxic polymer that is insoluble at pH 7.4 and soluble at acidic pH, would be an acceptable alternative for taste masking. Taste masking of ibuprofen has been successfully achieved by using the air suspension coating technique to form microcapsules, which comprises a pharmaceutical core of a crystalline ibuprofen and methacrylic acid copolymer coating that provides chewable taste masked characteristics. One of the most efficient method of drug particle coating is the fluidized bed processor. In this approach powder's as fine as 50µm, are fluidized in 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 spray through nozzle. The coated granules are dried with warm air[11].

Formation of inclusion complexes

In this process, the drug molecule fits into the cavity of a complexing agent forming a stable complex. The complexing agent is capable of masking the bitter taste of a drug by either decreasing its oral solubility on ingestion, or decreasing the amount of drug particles exposed to taste buds, thereby reducing the perception of bitter taste. The inclusion complexes with cyclodextrin owe their existence to van der Waals forces between the host and guest[12]. The most notable feature of cyclodextrins is their ability to form solid inclusion complexes (host–guest complexes) with a very wide range of solid, liquid and gaseous compounds by a molecular complexation. In these complexes **Figure 3**, a guest molecule is held within the cavity of the cyclodextrin host molecule. Complex formation is a dimensional fit between host cavity and guest molecule. The lipophilic cavity of cyclodextrin molecules provides a microenvironment into which

appropriately sized non-polar moieties can enter to form inclusion complexes[13] .

TABLE 2: TASTE MASKING BY POLYMER COATING

S. No.	Drugs	Techniques	Polymer Used
1	Pinaverium bromide	coating	Cellulose or shellac
2	Propantheline Bromide	Coating	L-HPC,EC
3	Ibuprofen	Air-suspension coating	Methacrylic acid copolymer (Eudragit)
4	Triprolidine HCL	Dispersion coating	HPMC
5	Dimenhydrinate	-	Eudragit or CMC
6	Cefeanel daloxate HCL	Granulation and coating	PVP,EC,HPMC
7	Enoxacin	-	HPMC,HPC,EC
8	Sparfloxacin	-	HPMC,HPC,EC, L-HPC
9	Aspirin	Rotagranulation and coating	Cellulose acetate latex and Triacetine
10	Famotidine	-	HEC,HPMC
11	Amoxicillin trihydrate	Granulation	MCC,L-HPC

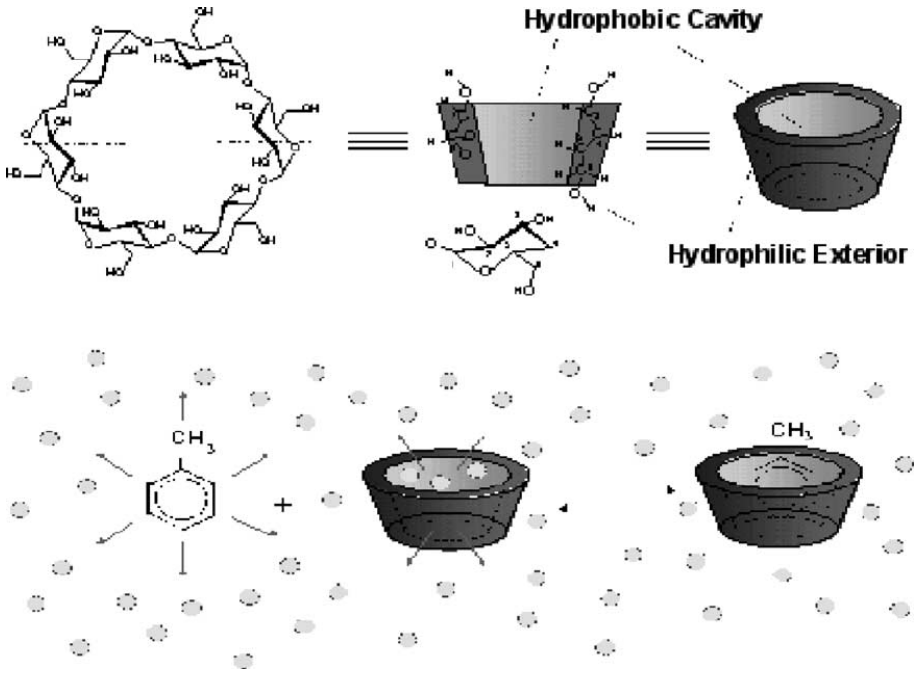

Figure 3. Cyclodextrins structure and inclusion complex formation.

Mechanism of inclusion complex formation

The consideration for complexation is the thermodynamic interactions between the different components of the cyclodextrin and the drug active. For a complex to form to form energetic driving forcethat pulls the drug active into the cyclodextrin. The most stable three dimensional structure of cyclodextrine is a toroid with larger and smaller openings presenting hydroxyl groups to the external environments and mostly hydrophobic functionality lining the interior of the cavity. The unique configuration gives cyclodextrine their interesting properties and creates the thermodynamic driving force needed to form drug active cyclodextrin complexes with apolar molecules and functional groups[14].

There are four energetically favourable interactions that helps shift the equilibrium towards complex formation:

1. The displacement of polar water molecules forms the apolar cyclodextrins cavity.
2. The increase number of hydrogen bonds formed as the displaced water returns to the larger pool.
3. The reduction of the repulsive interaction between the hyphobic guest and the aqueous environment.
4. An increase in the hydrophobic interactions as the guest inerts itself into the apolar cyclodextrine cavity.

Taste-masking by viscosity modifications

Increasing the viscosity with thickening agents such as gums or carbohydrates can lower the diffusion of bitter substances from the saliva to the taste buds. This provides a taste masked liquid preparation for administration of a relatively large amount of unpleasant tasting medicines. The composition of such a formulation comprises a tastemasking liquid base with a high viscosity induced by thickening agents such as polyethylene glycol and sodium carboxy methylcellulose. Surprisingly, it has been observed that the high viscosity liquid excipient base provides taste-masking benefits to such an extent that extra strength compositions can be prepared with high concentrations of bitter tasting ingredients. For example, guaifenesin, which is normally administered in doses of not more than 100 mg in 5 ml of liquid, may be administered in doses of 200mg/5 ml, without the feel of bitter taste[15].

Taste masking by microencapsulation

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. Coating is an extremely useful technique for a number of applications in pharmaceutical field. Although it is used primarily for production of sustained release, Gastro-intestinal dosage forms, it also has major applications in masking the unpleasant taste. 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[16].

The goal of Microencapsulation may be accomplished by any of the following techniques:

- Air suspension coating
- Coacervation - phase separation
- Spray drying and spray congealing
- Solvent evaporation
- Multiorifice - centrifugal process
- Pan coating
- Interfacial polymerization

Taste masking by ion exchange resin

Ion exchange resins are insoluble polymers that contain acidic or basic functional groups and have the ability to exchange counter-ions within aqueous solutions surrounding them. An ion exchange resin is an insoluble matrix (or support structure) normally in the form of small (1-2 mm diameter) beads, usually white or yellowish, fabricated from an organic polymer substrate backbone. The material has a highly developed structure of pores on the surfaces from where the ions are trapped or released. The trapping of ions takes place only with simultaneous release of other ions; thus, the process is called ion exchange[17].

Classification of Ion exchange resins

IERs contain positively or negatively charged sites and are accordingly classified as either cation or anion exchanger. The functional group in cation exchanger and anion exchanger undergoes reaction with the cations and anions of the surrounding solution respectively. The strong cation exchanger contains sulphuric acid sites whereas weak cation exchangers are based on carboxylic acid moieties. The strong anion exchange resins have quaternary amine ionic sites attached to the matrix, whereas weak anion exchanger has predominantly tertiary amine substituents[18]. Detail of IERs are available which are summarized in Table 3.

TABLE 3: EXAMPLES OF IER – DRUG COMPLEX

Resin			Medicament
Name	Functionality	Polymer backbone	
Amberlite™ IRP64	Weak acid COO^-	Crosslinked Polyacrylic	Dextromethorphan, Dimenhydrinate
Amberlite™ IRP69	Strong acid SO^{3-}	Styrene-Divinyl Benzene	Ranitidine
Amberlite™ IRP88	Weak acid COO^-	Crosslinked Polyacrylic	Talampacillin-HCl, Paroxetine
Indion 204	Weak acid COO^-	Crosslinked Polyacrylic	Norfloxacin, Ofloxacin
Indion 214	Weak acid COO^-	Crosslinked Polyacrylic	Azithromycin
Indion 234	Weak acid COO^-	Crosslinked Polyacrylic	Ciprofloxacin, Chloroquin phosphate
Kyron T-104	Weak acid COO^-	Crosslinked Polyacrylic	Cefpodoxime proxetil
Kyron T-114	Weak acid COO^-	Crosslinked Polyacrylic	Ofloxacin
Kyron T-134	Weak acid COO^-	Crosslinked Polyacrylic	Metronidazole

Taste masking by solid dispersion

Solid dispersions using insoluble matrices or bland matrices may be used to mask the bitter taste of drugs. Also using them as absorbates on various carriers may increase the stability of certain drugs. They are dispersions of one or more active ingredient in an inert carrier or matrix in solid state, and insoluble or bland matrices may be used to mask the taste of bitter drugs.

Carriers used in solid dispersion syste povidone, polyethylene glycols of various molecular weights, hydroxypropyl methylcellulose, mannitol and ethylcellulose. Various approaches for preparation of solid dispersion are described below[19].

Melting method

In this method, the drug or d are melted together by heating. The melted mixture is cooled and solidified rapidly in an ice bath with vigorous stirring. The final solid mass is crushed and pulverized.

Solvent method

In this method, the active drug and carri in a common solvent, followed by solvent evaporation and recovery of the solid dispersion.

Melting-solvent method

In this method the drug in solution is incorporated into a molten mass of polyethylene glycol at a temperature below 70^0C.

Taste masking by prodrug approach

Chemical modification, including prodrug design is an effective method for reducing solubility, and thereby improving taste. A prodrug is chemically modified inert drug precursor which upon biotransformation liberates the pharmaceutically active parent compound. Bitterness of a molecule may be due to the efficiency of the taste receptor substrate adsorption reaction, which is related to the molecular geometry of the substrate. If alteration of the parent molecule occurs by derivative formation, the geometry is altered, affecting the adsorption constant. Thus the magnitude of a bitter taste response or taste receptor-substrate adsorption constant may be modified by changing the molecular configuration of the parent molecule. The extremely bitter antibiotics have been the focus of much work in reversible drug modification. Taste masking of drug by Prodrug approach is given in table 4[20].

Table 4. Taste masking of drug by Prodrug approach

Parent Drug	Pro-drug with improved taste
Clindamycin	Alkyl ester
Chloramphenicol	Palmitate or phosphate ester
Erythromycin	Alkyl ester
Lincomycin	Phosphate or alkyl ester
Tetracyclin	3,4,5-Trimethoxy benzoate salts

Taste masking by formation of salts or derivatives

In this approach, an attempt is made to modify the chemical composition of the drug substance itself, so as to render it less soluble in saliva and thus make it less sensitive to the taste buds. Aspirin tablets can be rendered tasteless by making magnesium salt of aspirin. D-chlorpheniramine maleate is a taste-masked salt of chlorpheniramine. The alkyloxy alkyl carbonates of clarithromycin have remarkably alleviated bitterness and improved bioavailability when administered orally[21].

Use of amino acids and protein hydrolysates

By combining amino acids or their salts with bitter drugs, it is possible to substantially reduce the bitterness. Some of the preferred amino acids include sarcosine, alanine, taurine, glutamic acid, and glycine. The taste of ampicillin improved markedly by preparing its granules with glycine and mixing them with additional quantity of glycine, sweeteners, flavors and finally compressing them into tablets.

Taste masking by by effervescent agent

Effervescent agents have been shown to be useful and advantageous for oral administration of drugs and have also been employed for use as taste-masking agents for dosage

forms that are not dissolved in water prior to administration. A chewing gum composition of bitter medicament(s) was formulated to supply the medicament(s) to the oral cavity for local application or for buccal absorption. It comprises a chewing gum base, an orally administrable medicament, a taste masking generator of carbon dioxide, and optionally a taste bud desensitizing composition (e.g., oral anesthetics such as benzocaine and spilanthol) and other nonactive materials, such as sweeteners, flavoring components, and fillers. Recently, effervescent tablets of fentanyl and prochlorperazine were developed to supply these drugs to the oral cavity for buccal, sublingual, and gingival absorption. The formulations contain the drugs in combination with effervescent agent(s) to promote their absorption in the oral cavity and to mask their bitter taste. An additional pH adjusting substance was also included in fentanyl formulation for further promotion of absorption[22].

REFERENCES:

1. Pandey S, Kumar S, Prajapati SK and Mahadev NVS., An overview on taste physiology and masking of bitter drugs, Int J Pharm Bio Sci. 3(1): 2010; 1.
2. Das S, Srikanth L and Saha S., Taste masking of Ciprofloxacin by Ion exchange resin, Int J Preclinical Phar Res. 1(1): 2010; 7.
3. Wadhwa J and Puri S., Taste masking: a novel approach for obnoxious drugs, Int J Bio Pharm Toxicological Res. 1(1): 2011; 47.
4. Jha SK, Sharma UR and Surendra V., Tsate masking in pharmaceuticals: an update, J Pharm Res. 2(1): 2008; 126- 127.
5. Das S, Srikanth L and Saha S., Taste masking of Ciprofloxacin by Ion exchange resin, Int J Preclinical Phar Res. 1(1): 2010; 7-8.
6. Sharma V and Chopra H., Role of taste and taste masking of bitter drugs in pharmaceutical industries – an overview, Int J Pharm Pharm Sci. 2(4): 2010; 14.
7. Sharma S and Lewis S., Taste masking technologies: a review, Int J Pharm Pharm Sci. 2(2): 2010; 6.
8. Pandey S, Kumar S, Prajapati SK and Mahadev NVS., An overview on taste physiology and masking of bitter drugs, Int J Pharm Bio Sci. 3(1): 2010; 2.
9. Sikandar MK, Malviya R and Sharma PK., Taste masking: an important pharmaceutical technique for the improvement of organoleptic properties of pharmaceutical active agents, Eur J Bio Sci. 3(3): 2011; 68.
10. Ayenew Z, Puri V, Kumar L and Bansal AK., Trend in pharmaceutical taste masking technologies: a patent review, Recent Patents Drug Delivery Formulations 3(1): 2009; 27.
11. Ahire SB, Bankar VH, Gayakward PP and Pawar SP., A review: taste masking techniques in pharmaceuticals, Pharm Sci Monitor: 2011; 1648.
12. Agrawal VA, Chiddarwar AP, Mahale AM and Wakade RB., Taste abatement techniques to improve palatability of oral pharmaceuticals: a review, Int J Pharm Res Dev. 2(7): 2010; 3.
13. Valle EMMD., Cyclodextrines and their uses: a review, Elsevier: 2003; 3.
14. www.online1.ispcorp.com/brochures/pharma/cavamaxbulltn.pdf., "Cyclodextrins forming and analyzing drug inclusion complexes", 4.
15. Wagh VD and Ghadlinge SV., Taste masking methods and techniques in oral pharmaceuticals: current perspectives, J Pharm Res. 2(6): 2009; 1052.
16. Priya YD, Chowdary YA, Murthy TEGK and Seshagiri B., Approaches for taste masking of bitter drugs: a review, J Advances Drug Res. 1(2): 2011; 16.
17. Singh I, Rehni AK, Kalra R, Joshi G, Kumar M and Aboul-Enein HY., Ion exchange resin: drug delivery and therapeutic applications, FABAD J Pharm Sci. 32: 2007; 91.
18. Suthar AM and Patel MM., Ion exchange resinas an imposing method for taste masking: a review, Pharm Sci Monitor Int J Pharm Sci. 1(2): 2010; 8-9.
19. Gandhi CK, Patel MR, Patel KR and Patel NM., A review: taste masking in pharmaceuticals, Int J Pharm Res Dev. 3(3): 2011; 23.
20. Tripathi A, Parmar D, Patel U, Patel G, Daslaniya D and Bhimani B., Taste masking: a novel approach for bitter and obnoxious drugs, J Pharm Sci Bio Sci. 1(3): 2011; 139.
21. Gowthamarajan K, Kulkarni GT and Kumar MN., Pop the pills without bitterness taste masking technologies for bitter drugs, Resonance J Sci Edu.: 2004; 32.
22. Sohi H, Sultana Y and Khar RK., Taste masking technologies in oral pharmaceuticals: recent development and approaches, Drug Dev Ind Pharm. 30(5): 2004; 429-48.