WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 14, 1085-1103. Review Article ISSN 2277–7105

REVIEW ON TASTE MASKING

Anuja A. Malgunde[1]*, Sayali S. Thorbole[2] and Apeksha V. Masal[3]

[1]Shivnagar Vidhya Prasarak Mandal, Malegaon (BK), Baramati-413115, Maharashtra, India.

[2]Jaywantrao Sawant College of Pharmacy Hadpsar-028 Dist. Pune, Maharashtra, India.

[3]Agriculture Development Trust's Shardabai Pawar Institute of Pharmaceutical Science And Research, Shardanagar, Baramati-413115, Maharashtra, India.

Article Received on
01 June 2024,

Revised on 22 June 2024,
Accepted on 12 July 2024

DOI: 10.20959/wjpr202414-25466

***Corresponding Author**
Anuja A. Malgunde
Shivnagar Vidhya Prasarak Mandal, Malegaon (BK), Baramati-413115, Maharashtra, India.

ABSTRACT

Taste is an important parameter in case of drugs administering orally and is a critical factor to be considered while formulating or dispersible, melt in mouth, buccal tablet and other formulations which comes in contact with taste buds. Bitter and unpalatable taste is a major problem of certain drugs in formulations. Masking the bitter taste of drugs is a potential tool for the improvement of patient compliance which in turn decides the Taste refers to a perception arising from the stimulation of taste buds present on the surface of the tongue. Human's commercial success of the product. According to the year 2003 survey of paediatricians by the American Association of Paediatrics, unpleasant taste was the biggest barrier for completing treatment in paediatrics. The field of taste masking of active pharmaceutical ingredients (API) has been continuously evolving with varied technologies and new excipients. Two approaches are commonly utilized to overcome the bad taste of the drug. The first includes reduction of drug solubility in the saliva and second approach is to alter the ability of the drug to interact with taste receptor. Various methods are available to mask the undesirable taste of the drugs. Some of them are coating of drug particles, by formation of inclusion complexes, molecular complexes of drugs with other chemicals, solid dispersions, melting method, micro encapsulation, prodrugs, mass extrusion methods and ion exchange resins.

KEYWORDS: Taste, taste masking, formulations of taste masking.

INTRODUCTION

The sense of taste

Taste is the ability to respond to dissolved molecules and ions- "gatekeeper to the body". Human detects taste with taste receptor cells that are clustered in to onion-shaped organs called taste buds. Each taste bud has a pore that opens out to surface of the tongue enabling molecules and ions taken into the mouth to reach the receptor cells inside. Human have around 10,000 taste buds which appear in fetus at about three months. A single taste bud contain 50-100 taste cells. Each taste cells receptors on its apical surface. These are Transmembrane proteins which bind to the molecules and ions that give rise to the four primary taste sensations namely - salty, sour, sweet and bitter. Recently, a fifth basic taste umami has been discovered. The umami is the taste of certain amino acids (e.g., monosodium glutamate). There is often correlation between the chemical structure of a compound and its taste. Low molecular weight salts tend to taste salty where as 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 number of OH group increase1. Receptor mechanism involves initial depolarization at apical receptor site, which causes local action potential in receptor cell. This in turn causes synaptic activation of the primary sensory neuron. Four basic tastes are confirmed to specific regions of tongue (Table1). But some workers deny the presence of specific regions of the tongue for a particular taste and consider it as a misconception.2 Threshold for taste is a minimum concentration of a substance that evokes perception of a taste. The following table 1 gives the threshold concentration of four primary taste sensations. It can be seen that tongue is 10,000 times more sensitive to the bitterness of quinine than to sweetness of sugar. Saccharine, on this scale would rate about 0.001%. Pharmaceutical companies can save themselves much grief by addressing the taste factor early in the product development. In so doing, they can get their medications to market more quickly, ensure patient compliance, gain market leadership and reap generous economic rewards. They can also stay in compliance with FDA's final rule, which went into effect December 2000.5 So major taste masking efforts are required before bitter drugs are acceptable for market trials. Major taste masking technologies are based on the reduction of solubility of the drug in the saliva so the drug concentration in saliva will remain below taste threshold value. The desire for improved palatability of formulations has prompted the development of various new technologies for taste abatement.

Many of these technologies have been successfully commercialized. But, the ideal solution of taste masking would be the discovery of universal inhibitor of bitter taste of all drug.

Interpretation of Taste

The receptor cells are of two types functionally. One is ion channel type receptor, is a trans membrane protein which allows the ions that give rise to sensation of salt and sour. These ionic interactions cause electrical change within taste cells that trigger neurons to send chemical signals (that translate into neuro transmission) to the brain.

The other is a surface protein receptor, allows binding of tastants (molecules having sense of taste) which give the sensation of sweet, bitter and umami. In case of bitter taste, stimuli acts by binding to G-Protein coupled receptors.

A. 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.

B. 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.

C. 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.

D. 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 sensations1, 4-6.release of Ca+2 ions from endo plasmic reticulum of the taste cell. The increased concentration of calcium ions in the cell leads to depolarization and release of neuro transmitters. This message is sent to the brain through sensory neuron and interpreted as “bitter” taste.

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

1) Bitter:
2) Drug:

3) Drug particulate shape and size distribution
4) Ionic characteristics of the drug
5) Formulation

Taste masking techniques

The drug has to be made palatable in order to enhance patient adherence to reach the at par standard therapeutic efficacy. Hence forth aggressively bitter tasting drugs like the fluoroquinolone antibiotics, penicillins, macrolide antibiotics, and non-steroidal anti-inflammatory drugs are candidates for taste masking. Without changing its safety and efficacy, a drugs taste has to be masked and techniques are being adapted to meet this need, especially for the paediatric and juveniles patients. In present days techniques such as microencapsulation, coating, granulation, ion exchange resins, solid dispersion, complexing agents, suppressants, potentiators, viscosity enhancers, adsorbates, pH modifiers, and have been used in combination with the sweeteners & flavors to mask.

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

1. Addition of flavouring and sweetening agents.
2. Microencapsulation
3. Ion-exchange.
4. Inclusion complexation
5. Granulation
6. Adsorption
7. Prodrug approach
8. Bitterness inhibitor
9. Gel formation
10. Miscellaneous
11. pH modifier
12. Viscosity enhancers

1. Addition of flavouring and sweetening agent

A combination of flavouring agents is usually employed. Flavour adjuvants like menthol and chloroform are considered as a desensitizing agents because addition to their own odour and flavour they also have mild anaesthetic effect on taste receptors. Aspirin medicated floss

contains sodium phenolate as an anaesthetizing agent in addition to chocolate flavour to mask the Bitter taste of aspirin.

A survey of the taste preferences of human race, as a whole, indicates that sweet taste is very agreeable to our species. Hence for controlling the taste qualities effort are directed to make the preparations sweet to different degrees. Sweeteners are commonly used for this purpose. Table 4 presents a compilation of the most common artificial and natural sweeteners used in pharmaceutical products, their relative sweetness levels, and pertinent comments.

Aspartame is used as prominent sweetener in providing bitterness reduction. A very small concentration (0.8%) is effective in reducing bitterness of 25% acetaminophen. Cyclamates have been banned by the USFDA since 1970 due to its carcinogenic effect. The neohesperidine dihydrochalone is an artificial bitterness suppressor and flavor modifier. It is a pen chain analogue of neohesperidine, a bitter flavone that occurs in Seville oranges (citrus aurantium). Taste masking properties of the neohesperidine dihydrochalone have been reviewed by Cano et al. It is a bitterness suppressor and flavour modifier that also elicits a very intense lingering sweet taste. Due to its lingering sweet taste the taste of bitter substance appears later in time and taste could be masked.

Table 1: Taste masking of drug by flavours and sweeteners.

Drugs	Taste	Taste masking Agents	Dosage Form
Eucalyptus oil	Bitter	Fenchone, Borneol	Mouth washes
Ibuprofen	Bitter	Saccharine Sodium, Sucrose, Sorbitol solution	Syrup, Suspension
Thymol, Tricoslan	Bitter	Citrus Flaour, lemolene	Oral resins
Zinc acetate dehydrate	Bitter	Saccharin sodium	lozenges

2. Microencapsulation

Microencapsulation is a modified form of film coating differencing only in the size of the particle to be coated and the methods by which coating is achieved. The bitter drug particle is held in the polymer matrix or polymer film and thus taste of drug can be successfully masked. A number of polymers have been successfully used in microencapsulation technique includes gelatine, polyvinyl alcohol, ethyl cellulose, cellulose acetate phthalate and styrene maleic anhydride. Microencapsulation can be achieved by phase coacervation, polymerisation, solvent evaporation and ionisation. Bitter taste of Enoxin was masked by using novel microencapsulation process. The microencapsulation was achieved by wet spherical agglomeration along with modified phase separation coacervation method. The

bitter taste of chloroquine diphosphate was masked by microencapsulation technique, in which coating materials were obtained from Vinyl pyridine compounds and microencapsulated products formulated in suspension and found to have acceptable taste. Microencapsulation using phase coacervation was used for model bitter drug Beclamide. Conventional chewable and effervescent tablets were prepared from microencapsulated drug using gelatine as a polymer. Incubation of unmodified corn-starch in aqueous solution of drug and converting them into microencapsulated particles could also mask the taste of bitter drug. Diphenhydramine (DPH) was incubated with starch at different temperatures (35 to 550C) for different time periods (1 to 4 hours). DPH-loaded starch particles were then dried and results revealed taste masking of parent drug. Taste masking can be achieved by combination of encapsulation and CO2 based techniques. Acetaminophen and pseudoephedrine hydrochloride (PE) were used as model bitter drug and different Eudragits, ethyl cellulose (EC), cellulose acetate (CA) with different plasticizers and emulsifying agents as excipients for encapsulation. Coated particles were mixed with super critical carbon dioxide (at 35-65°C and 100bar) and composite polymeric particles (50–300mm) showed sustained release and some taste masking.

A new reverse enteric polymer, which collapses above pH 4 unlike Eudragit E, which is permeable above pH 5, was conceptualized and synthesized. Taste masking of cefuroxime axetil was evaluated by polymeric encapsulation. Polymers inhibited polymorphic transformation of cefuroxime axetil, which led to the coclusion that the new reverse enteric polymer provides new technology platform for formulating taste masked and immediate release products such as granules, film coated / ODT and chewable tablet.

Nanoparticle is a submicroscopic solid particle with a size ranging from 10 nm-1 µm. Polymers that can be used for preparation of nanoparticles includes albumin, ethyl cellulose, casein, gelatin, polyesters, polyanhydrides and polyalkyl cyanoacrylates. As the drug particles are individually coated they prevent drug contact with taste bud and thus mask bitter taste of drug. Those nanoparticles can also be delivered in form of nanosuspension or nanoemulsion for pediatric and geriatric patients. Nonotechnology can be used for taste masking of fish oils, salts, alkaloids, clofibrate and sulfa drugs.

Lipid nano particles containing omega –3 fatty acids as an alternative of fish oil capsules were developed. Lipids like Dynasan 118 and adipic acid were used with sodium dodecyl sulfate (SDS), TPGS and polyvinylpyrrolidon (PVP) are used as stabilizers. Lipid

nanoparticles were prepared by high-pressure homogenization using a Micron LAB 40 (APV Homogenizers, Unna, Germany). Further addition of citrus food flavour covered taste and odour, which further represents an easy swallowable formulation with taste masking effect.

Neural technique can also be used for taste masking. In this technique heat-sensitive model drug with strong bitter taste was selected. Injecting the suspensions containing drug substance and different levels of cellulose type polymers with plastizers into spray dryer developed fine particles. That fine particles resulted in to taste masked formulation.

3. Ion exchange

Ion exchange resin are synthetic inert organic polymers consisting of a hydrocarbon network to which ionisable groups are attached and they have the ability to exchange their labile ions for ions present in the solution with which they are in contact.

The most frequently employed polymeric network used is a copolymer of styrene and divinylbenzene (DVB). Apart from this other polymers such as those of acrylic and methacrylic acid cross-linked with divinyl benzene and containing appropriate functional groups, have been used as ion exchange drug carriers.

Recent years have seen a tremendous progress in the **technique of masking the unacceptable taste** of an orally administered pharmaceuticals, such as filling in capsules, coating with water in soluble polymers or pH dependent water soluble polymer, adsorption on **ion-exchange resin**, micro encapsulation with various polymers complexing with cyclo dextrin, chemical modification such as use of insoluble pro drugs, effervescent systems, salt formation, and use of excipient like flavors, sweeteners, gelatin, gelatinized starch and surfactants.

Physiological approaches consist of inhibiting or modifying an API-mediated biternes response by in corporating agents into a pharmaceutical formulation. Agents like sodium chloride, phosphatidic acid and peppermint flavor are known to inhibit bitterness by selected API molecules via a mechanism that takes place at the bitterness receptors in the taste buds.

Drug release from ion exchange resin depends upon two factors.

1. The ionic environment (i.e. pH and electrolyte concentration) with in the gastrointestinal tract.
2. The properties of resin.D

4. Inclusion complexes

In inclusion complex formation, the drug molecule fits into the cavity of a complexing agent i.e., the host molecule forming a stable complex. The complexing agent is capable of masking the bitter taste of the 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**.**

Inclusion complexs are 'host-guest' relationship in whichcomplexing agent act as host and provide cavities in which foreign guest molece may fit. Cyclodextrin form inclusion types of complexes with organic molecules both in solid state and in solution.

The complexing agent is capable of masking bitter taste of drug by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste buds, thereby reducing the preception of bitter taste. Vanderwall forces are mainly involved in inclusion complexes. B-cyclodextrin is most widely used complexing agent for inclusion type complexes. It is sweet, non-toxic, cyclic oligosaccharide obtained from starch.

Carbepentane citrate can be formulated in palatable liquid formulation with 50% reduced bitterness by forming 1:1 complex with cyclodextrin. Similarly a 1:11 to 1:15 inclusion complex of ibuprofen and hydroxy propyl-β-cyclodextrin can be formulated as palatable solution.

Bitter amine drugs such as chloroquine phosphate can be treated with tannic ad for taste abatement purpose.58 Bitter taste of dimenhydrinate can be masked by forming a porous drug-polymer smatrix with an copolymer hanving a plurality of carboxylic acid and ester groups, eg., Eudragit.

Benefits after complexation

Drugs having limited oral bioavailability due to poor dissolution rate and solubility can be complexed with cyclodextrins to improve their absorption. Complexation reduces active recrystallization of drugs, which may help to increase their aqueous solubility. Drugs, which are irritant to mucus membrane of GIT and skin, are complexed with cyclodextrins to minimize the irritation. Cyclodextrins can prevent the deterioration of active pharmaceutical ingredients due to light, temperature and atmospheric oxidation.

5. Granulation

Granulation is a common processing step in the production of tablet dosage form. This step can be exploited as a mean for taste masking of slightly bitter tasting drug. Some saliva insoluble polymers can also act as binding agent, granules prepared from these polymers show less solubility in saliva and thus taste could be masked. Granulation lower the effective surface area of the bitter substance that come in contact with the tongue upon oral intake. But this reduction in surface area of bitter substance may or may not be effective in masking the bad taste. Taste masked granules, prepared from saliva insoluble polymer, can be formulated in various type of tablet dosage form eg. Rapidly disintegrating tablet and chewable tablet.

Taste masked granules of bitter tasting drug pirenzepine and oxybutynin have been prepared by the extrusion using amino alkyl methacrylate copolymer. (EudragitE-100).

Taste masking of a bitter taste drug can be masked by granulation process. Granulation is major and a common process in tablet production. In this approach, saliva insoluble polymers are used as binding agents in the tablet preparation. As these polymers are insoluble in saliva, thus the bitter taste of the drug can be masked. The taste masked granules can also be formulated as chewable tablet and rapidly disintegrating tablets. The literature report on the list of drugs whose taste is masked by granulation techniques by using saliva insoluble polymers.

6. Adsorption

Adsorbate of 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 adsorb the drug, removing the solvent, drying the resultant powder, and then using this dried adsorbates in the preparation of the final dosage form. Many substrates like vee gum, bentonite, silica gel and silicates can be used for the preparation of adsorbate of bitter drugs. Loperamide and phenyl propanolamine have been adsorbed on magnesium aluminium silicates also known as Vee gum F to prepare bitter taste masked suspension of these drugs.

7. Prodrug approach

A prodrug is chemically modified inert drug precursor which upon biotransformation liberates the pharmaceutically active parent compound. A combination of factors is perhaps operative in the demonstration of a taste response molecular geometry is one of them, for eg,

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. This effect, in turn, may or may not be due to lack of aqueous solubility of the derivative to eliminate the bitter taste response. 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.

8. Bitterness inhibitors

The development of a specific universal inhibitor for bitter taste has been widely required in the fields of taste physiology and pharmaceutical sciences, but no such inhibitors has been available. One difficulty in discovering of universal inhibitor for bitter taste is that substances that inhibits bitterness of one compound will not influence the bitterness of a second because many different classes of compound impart bitterness. Sodium salts such as sodium chloride, sodium acetate, sodium gluconate have been shown to be potent inhibitors of some bitter compounds. The mechanism is not known, however, research shows that sodium act at peripheral taste level rather than a cognitive effect. Bitter substances are commonly hydrophobic in nature hence lipoprotein (PA-LG) composed of phophatidic acid and β-lactoglobulin can mask the target sites for bitter substances on the taste receptor membrane without affecting responses to salts, acids, sugars or sweet amino acids. Bitter taste of brucine, berberine, chloride, caffeine, denatonium benzoate, glycyl L-leucine, L-phenylalanine, naringin, propranolol hydrochloride, quinine hydrochloride, strychnine nitrate and theophylline 69-71 have been suppressed by lipoprotein.

Selective inhibition of bitter taste of various drugs by phospholipids such as phosphatidic acid, phosphatidylinositol, soy lecithin, have been reported.72 Bitter taste of polymixin B sulfate and trimethoprim-sulfamethoxazole have been masked by BMI 60 obtained by fractionating soy lecithin. The w/o/w or o/w/o type multiple emulsions are vesicular systems in which active ingredients can be entrapped in internal phase. The entrapped substances can be transferred from internal phase to external phase through the ‘membrane phase’. This phase controls the release of drug from system. These system could be used for controlled-release delivery of pharmaceuticals. If the system is stable enough for a reasonable shelf life, the formulation could also mask the taste of drug. Both w/o/w and o/w/o multiple

emulsions of chloroquine phosphate have been prepared and reported to be partially effective in masking the bitter taste of drug.

9. Gel Formation

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

10. Miscellaneous

i) 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 prior to administration. A chewing gum composition of bitter medicament was formulated to supply the medicament to 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 anaesthetic such as benzocaine) and other non-active material such as sweeteners, flavouring 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 formulation contain the drug in combination with effervescent agent 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 for absorption.

ii) 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 (0.6-1%) to reduce bitter taste79. The antidepressant drug mirtazapine is formulated as an aqueous suspension using methonine (stabilizer) and maltitol (thickening agent). Maltitol 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 anaesthetic effect.

iii) 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.

11. Viscosity enhancers

Usage of viscosity enhancers in these cases would retard the migration of dissolved medicament from the surface of the solid particle to the suspending medium. Additionally, they can also decrease the contact between the bitter medicament and the taste receptors, thus improving the overall taste masking efficiency. Hypromellose was used as a viscosity modifier in taste masked azelastine suspension consisting of sucralose as the sweetening agent.

12. pH Modifiers

pH Modifying agents are capable of generating a specific pH microenvironment in aqueous media that can facilitate in situ precipitation of the bitter drug substance in saliva thereby reducing the overall taste sensation for liquid dosage forms like suspension. Wyley described an application of pH modifying as L-Arginine for taste masking of bitter medicament. L-arginine maintains alkaline pH of the suspending vehicle to promote in situ precipitation of des-quinolone in saliva.

Evaluation

Evaluation of taste masking is tedious work as the taste sensation varies person to person and involves taste masking efficiency as quality control parameter and determining the rate of release of drug from taste-masked complex and asses by *in vivo* and *in vitro*.

***In vivo* Evaluation**

In vivo taste evaluation carried out on a trained taste panel of healthy volunteers with organoleptic sense, with their prior consent. On placing the dosage form in mouth for 60 seconds, bitterness recorded against pure drug using a numerical scale. The numerical scale may bears values as 0 = pleasant, 1 = Tasteless, 2 = No bitter but after taste give bitterness, 3= immediately gives bitterness, 4 = slightly Bitter, 5 = extremely bitter. *In vivo* assessment usually demands large panels and elaborates analysis, raises safety and scheduling issues and can be time consuming and expensive.

In vitro Evaluation

Invention of "E-Tongue" electronic sensor array technology overcomes this problem, which is a device for recognition, quantitative multicomponent analysis and artificial assessment of taste and flavour. It recognizes three levels of biological taste including receptor level (Taste buds in humans, probe membranes in E-Tongue), circuit level (neural transmission in humans, transducer in E-Tongue), and perceptual level (cognition in the thalamus humans, computer and statistical analysis in the Tongue). The probes consist a silicon transistor with proprietary organic coatings, which govern the probe's sensitivity and selectivity, and measurement done potentiometrically. Each probe is cross selective to allow coverage of full taste profile and statistical software interprets the sensor data into taste patterns. Liquid samples directly analysed without any preparation, whereas solids require a preliminary dissolution before measurement. Reference electrode and sensors are dipped in a beaker containing a test solution for 120 seconds. A potentiometric difference between each sensor and a reference electrode measured and analysed by the Tongue software. Sensory analysis employs to measure and control taste and flavour quality during manufacturing process development, clinical use, stability studies, validation, and commercial man.

EVALUATION TECHNIQUES

Sensory evaluation

Taste, to think of, is a very subjective perception. Depending on individuals, the perceived taste may vary to different degrees. If we have well controlled experimental set up, it is possible to accurately and reproducibly measure taste thresholds. To quantitatively evaluate taste sensation, following methods have been reported in literature.

- Panel testing (human subjects)
- Measurement of frog taste nerve responses.
- Multichannel taste sensor/ magic tongue
- Spectrophotometric evaluation/ D30's value

i) Panel Testing

The panel testing is a psychophysical rating of the gustatory stimuli. In this method, a group of about 5-10 human volunteers is trained for taste evaluation by using reference solutions ranging in taste from tasteless to very bitter. Numerical values are then assigned to these levels of bitterness (eg. 0-5). Subsequently, test solution is tasted and rated on the same scale to assess its bitterness. Literature reports panel testing in invariably all the taste-masked drugs

being evaluated. The ease of the method combined with the accuracy of human perception of taste against any other gustatory evaluation technique makes panel testing the most commonly used technique.

ii) Measurement of Frog Taste Nerve Responses

In this method, adult bull frogs are anaesthetized intraperitoneally and the glossopharyngeal nerve is then located and dissected from the surrounding tissue and cut proximally. An ace-amplifier and an electronic integrator are used to respectively amplify and integrate the nerve impulses. The peak height of the integrated response is then taken as the magnitude of response.

Quinine sulphate formulations, taste masked by PA-LG (phosphatidic acid-lacto globulin) combination have been reported to be evaluated by this technique.

iii) Multichannel Taste Sensor / Magic tongue

This is an automated taste sensing device to detect the magnitude of bitterness of a drug substance. The device has a transducer which is composed of several kinds of lipid/polymer membranes with different characteristics that can detect taste in a manner similar to human gustatory sensation. Taste response is transferred into a pattern composed of electric signals of membrane potentials of the receptor part. Different response electric potential pattern are obtained for substance producing different taste qualities.

Recently, the technique has been applied, for the quantitative evaluation of the bitterness of some commercially available medicines. Quinine hydrochloride was taken as the standard for bitterness. Basic drug with amino groups in the molecule such as quinine, show a comparatively good correlation between the relative response electric potential (mV) of channels 1 or 2 of the taste sensor, which contain negatively charged membranes, and the bitterness as determined by human gustatory sensations tests. Secondly, for anionic drugs, such as diclofenac sodium or salicylic acid, the positively charged membrane in channel 5 or 6 seemed to the useful even though they are being sour rather than bitter. For drugs with both an amino (cationic) groups and a carboxylic acid (anionic) group in the molecule, such as theophylline, caffeine and metronidazole, the electric potential (mV) of channel 1 or 2 did not increase, even though bitterness was observed in human gustatory sensation test. Therefore, different types of membrane component will be needed for a complete evaluation of the bitterness of medicines.83

iv) Spectrophotometric Method

A known quantity of the taste-masked formulation is mixed with 10 ml of distilled water in 10ml syringe by revolving the syringe, end to end, five times in 30 seconds. The test medium is then filtered through a membrane filter, followed by spectrophotometric determination of the concentration of the drug in the filtrate. If this concentration is below the threshold concentration, it may be concluded that the bitter taste would be masked *in vivo*. This technique has been applied to evaluate the taste masked granules of sparfloxacin, with threshold concentration being 100µg/ml.

FACTORS AFFECTING SELECTION OF TASTE MASKING TECHNOLOGY

1. Dose of Active Pharmaceuticals

Dose of a drug may dictate whether a particular formulation strategy would be suitable to achieve taste masking. In paediatric formulations, the dose is small enough so as to allow the usage of flavouring agents to mask the taste of the medicine. For example, low dose palatable paediatric aspirin oral formulation was developed by adding sweeteners, but the same approach failed to address the problem of drugs like acetaminophen because of its high dose. In such cases, coating is preferred to achieve taste masking along with sweeteners to attain an acceptable final dosage form size.

2. Extent of Bitter Taste

With aggressively bad tasting medicaments even a little example, sweeteners could not achieve taste masking of oral formulation of ibuprofen due to its dominating taste. Coating is more efficient technology for aggressively bitter drugs even though coating imperfections, if present, reduce the efficiency of the technique. Similarly, microencapsulation of potent bitter active agents such as azithromycin is insufficient to provide taste masking of liquid oral suspensions. Viscosity enhancer's can complement the taste masking efficiency. Oral suspension containing viscosity enhancers can masquerade the objectionable taste, which arises from the leakage of drug from the coated medicaments or microcapsules. This approach was also used for the microencapsulated oxazolidinone particles to limit the transport of drug from the polymer coated drug particles to the vehicle. Conventional taste masking techniques such as the use of sweeteners, amino acids and flavouring agents alone are often inadequate in masking the taste of highly bitter drugs such as quinine, celecoxib, etoricoxib, antibiotics like levofloxacin, ofloxacin, sparfloxacin, ciprofloxacin, cefuroxime axetil, erythromycin and clarithromycin3, 8.3. Drug Particle Shape and Size Distribution

Particle characteristics of the drug would affect the taste masking process efficiency. Core materials with irregular shapes and small particle size lead to poor taste masking efficiency and varying dissolution of coated particles.[108] Fines, abrasion and variable coating thickness can lead to situations wherein the taste mask coating is compromised. Multilayer coating using inner spacing layer to sequester the drug from taste masking layer helps to reduce or eliminate such coating imperfections. Taste masked granules of gatifloxacin and dextromethorphan were formulated by multilayer coating consisting of inner spacing layer followed by outer taste masking layer. Drug Solubility Physicochemical properties of the drug play an important role in the selection of taste masking technology. For example, ondansetron has a relatively lower water solubility at higher pH, based on which a rapidly disintegrating taste masked composition of ondansetron was formulated by adding an alkalizing agent(sodium bicarbonate) to reduce the water solubility and the consequent taste perception. Douglas and Evans (1994) described different approaches to achieve the taste masking of ranitidine base and its salts having different solubility profiles. The bitter taste associated with a poorly soluble form of ranitidine may be satisfactorily masked by lipid coating of the drug substance. However, for water-soluble forms of ranitidine (e.g. ranitidine hydrochloride), the degree of taste masking achieved by simple lipid coating of the drug substance may not be entirely satisfactory, particularly if the product is to be formulated in an aqueous medium. Thus ranitidine hydrochloride was first incorporated into the inner core of a polymeric binder, or a lipid or wax having a melting point higher than that of the outer lipid coating to achieve an efficient tastemasking3, 8.5. Ionic Characteristics of the Drug Ionic characteristics of drugs govern the selection of ion exchange resin polymers and the suitability of the drug candidate for this technology. For example, anionic polymers (e.g. alginic acid) are good candidates for cationic drugs like donepezil hydrochloride, and the cationic polymers are choice of excipients for anionic drugs like sildenafil. Dosage Forms It is estimated that 50% of the population have problem of swallowing tablets, especially the paediatric and geriatric population. 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 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 case of large dose drugs for an 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 taste masked dosage forms. However, this approach suffers from the disadvantage that the polymer coating releases the active agent in an inconsistent fashion and may not provide an immediate release. Moreover, coating is more suitable when the formulation is stored in a dry form. Viscosity enhancers or pH modification 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 are constituted suspension.

Advantages of taste masking

1. Masking the taste of bitter drugs.
2. It improves the patient's compliance.
3. It also improves the therapeutic efficacy and bioavailability of certain drugs.
4. It prevents the degradation of hygroscopic drugs from atmospheric moisture thus improves stability of drugs.
5. It improves the organoleptic characteristics of drugs.

CONCLUSION

Now a day's most of the potent drugs that may be cardiac, analgesics, anti-inflammatory, anti-tubercular, Anthelmintic, antibacterial, anticoagulants, anti-epileptics, antimalarial, anti-neoplastic, anti-thyroids, antiprotozoal, diuretics, histamine receptor antagonists, agents, opioids analgesics, oral vaccines and sex hormones, most of them are bitter in taste. So it becomes necessary to develop such a dosage for that must be acceptable in taste to patient especially in case of children or geriatrics. Taste masked drug delivery research is gaining importance and commercial success for the quality of treatment nutritional provided to suffering patients, especially children. As evidenced by the number of patents and technological developments we made an attempt that an ideal taste masking is widely accepted in the development of more palatable and acceptable dosage forms which not only lead to better patient compliance but with an ultimate clinical output.

After considering all these factors it is concluded that an ideal taste masking formulation should have following properties.

• Involve least number of equipment's and processing steps.
• Require minimum number of excipients for an optimum formulation.

• No adverse effect on drug bioavailability.
• Require excipients that are economical and easily available.
• Least manufacturing cost.
• Can be carried out at room temperature.
• Require excipients that have high margin of safety.
• Rapid and easy to prepare.

REFERANCES

1. Sharma. S, Lewies.S, Taste Masking Technologies: a review, Manipal college of Pharmaceutical Sciences, Manipal University, Karnataka, Jan 2010; 1-5.
2. Jyothi. N, Prasanna. A, Microencapsulation techniques, factors influencing encapsulation efficiency, Hindu College of pharmacy, Guntur, Andhra Pradesh, 2010; 27(3): 187–197.
3. Sharma. S, Lewies.S, Taste Masking Technologies: a review, Manipal college of Pharmaceutical Sciences, Manipal University, Karnataka, Jan 2010; 3.
4. Margret. R, Chandir. D**,** Resent Aspects of ion exchange resin used as a taste masking agent, Vinayaka missions University Salem, Tamilnadu, India.
5. Vishnumurthy. V, Dheeraj. N, Taste Masking Technologies: An Overview and Recent Updates Amity Institute of Pharmacy, Amity University, Sector-125, Noida, Uttar Pradesh, India.
6. Sharma, Kumar. D, Taste Masking Technologies: An Approch for the Improvement of organoleptic property of Pharmaceutical active substrate, CT Institute of Pharmaceutical Science Shahpur, Jalandhar 144020, Punjab, India.6 April 2012.
7. Patel C.Anil G. Dhruv M. Pharmaceutical Taste Masking Technologies of bitter drugs: A concise review, 2012.
8. Swati C.Vaibhav U.Rajaram C.Formulation and in vitro evaluation of taste-masked oro-dispersible dosage form of diltiazem hydrochloride, MAEER's Maharashtra Institute of Pharmacy, Maharashtra, India, 2013.
9. Mohammed J. Boateng Z.A review on the taste masking of bitter APIs: School of Science, University of Greenwich (Medway Campus), Central Avenue, Chatham Maritime, Chatham, Kent, UK.
10. Hussein M.M., Barcelon S.A. Flavor enhancing and medicinal taste masking agent. U.S.Pat. No. 4, 983, 394 to Warner-Lambert Co., 1991.
11. Chase G.D, Gennaro AR., Gibson M.R. Pharmaceutical Necessities. In Remington's Pharmaceutical sciences. 16th ed. Pennsylvania: Mackpublishing Company, 1980.

12. Lachman L, Lieberman H.A., kanig J.L. Liquids. In Tand Practice of Industrial Pharmacy Febiger, 1987; 470.
13. Munira M., Sudha R., Swapna K. Taste masking techniques for bitter drugs-An overview IJPT, July 2012; 4(2): 2100-2118.
14. World Journal of Pharmacy and Pharmaceutical Sciences, 2014.
15. International Journal of Molecular Sciences ISSN 1422-0067.
16. Https: /www.taste masking.
17. www.mdpi.com/journal/sensors.