Review Article

Taste Masking Technologies: An Overview and Recent Updates

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ABSTRACT

Taste, smell and texture are the important factors in development of oral dosage forms. Taste is now a factor influencing the patient compliance and product quality. "The worser the taste of the medication, the better the cure" an older attitude which now totally changed. Taste masking of obnoxious drugs has gained the importance as the most of them are administered orally. This reason is an initiative for the development of various taste masking technologies by which the characteristics of the dosage form is improved and good patient compliance is achieved. The main objective of this review is to explore various methodologies for masking the taste of obnoxious drugs, applications, evaluation and also the recent trends in taste masking technologies.

Key Words: Taste masking, Bitter, Patient compliance, Drug product, Dosage form.

INTRODUCTION

Taste is the ability to detect the flavour of substances like food, drugs etc. Taste is now became an important factor governing the patient compliance. It gained importance as the most of the drugs are administered through oral route. Administration of unpalatable drugs is hampered by their unpleasant taste particularly in case of paediatric and geriatrics. Various methods like coating, inclusion complexes, microencapsulation, granulation, adsorption, prodrug approach, addition of flavours and sweeteners, ion exchange resins are used for masking the taste of obnoxious drugs. However, there is no universal method for taste masking. Each method offers specific advantages and applications. One method is not suitable for taste masking all the obnoxious drugs. Several parameters like extent of bitter taste, dose, dosage form and type of the patient influence the method to be used for masking the taste of the bitter drugs. Evaluation of taste masking by electronic tongue is a recent innovation. Advatab, Microcaps, Liquitard, Kleptose, Formulplex and Formulcoat are the new taste masking technologies which are found to be better than existing ODT technologies like Zydis, Orasolv and Quicksolv etc. In addition to oral drug delivery, the taste masked drug delivery research is gaining importance for improving the quality of the treatment for paediatrics and geriatrics.

TYPES AND MECHANISM OF TASTE

Taste is one of the traditional five senses and is the ability to detect the flavour of substances such as food, certain minerals, and poisons, etc. It determines the selection of food, its palatability and stimulation of reflexes for secretion of saliva, gastric juices and pancreatic juices. The sensation of taste can be categorized into[1,3]:

a) Sweet (sugars, glycerol)
b) Saltish (sodium)
c) Sour (acidic substances)
d) Bitter (quinine, nicotine)
e) Umami

Humans receive tastes through sensory organs, taste buds, (also known as gustatory calyculi) concentrated on the upper surface of the tongue.

Taste buds

Taste buds are the structures present primarily on the surface of tongue which contains receptors that mediate the sense of taste.

Distribution[2]

Taste buds are also present on palate, pharynx, epiglottis and larynx. Tongue consists of numerous structures called papillae. There exists different types of papillae, of which fungiform papillae contain single taste bud on the tip and circumvallate papillae contains several taste buds. However, filiform papillae donot contain taste buds even their number is more. Different types of tastes have different threshold concentration based on the distribution of taste buds on surface of the tongue, enlisted in table no:1

Structure

Taste bud is oval in shape and opens into epithelial surface through a small opening called taste pore(Fig.no: 1). Microvilli protrudes from the taste pore arising from the individual taste cells. Each taste bud has 50-100 receptors and support cells. Based on the electron microscopy, receptors are classified into basal, dark, intermediate and light.

The receptors are connected through synapse (ATP releasing) to sensory neuron, leading back to the brain. The sensation of taste thus resides in the brain. However, a single sensory neuron can be connected to several taste cells[1-3].

Interpretation of Taste

The receptor cells are of two types functionally. One is ion channel type receptor(Fig. no: 2), is a trans membrane protein which allows the ions that give rise to sensation of salt and sour. These ionic interactions causes electrical change within taste cells that trigger neurons to send chemical signals (that translate into neuro transmission) to the brain. These cells have a net negative charge in normal state. Tastants alter this state by using various means to increase positive ion concentration with in the taste cell. This depolarization causes the cell to release neuro transmitters, there by relaying the electrical messages to brain[2,3].

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(Fig. no: 3). Further leads to the splitting of G-Protein subunits and activation of the nearby enzyme present, finally resulting the release of secondary messengers. The secondary messengers intiate the 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[3,4].

TASTE MASKING TECHNIQUES

Various techniques reported in the literature are as follows[5-6,8-11]

- Addition of flavours and sweeteners
- Coating
- Microencapsulation
- Ion exchange resin
- Inclusion complexes
- Granulation
- Adsorption
- Prodrug approach
- Bitterness inhibitors
- Multiple emulsion
- Gel formation

Factors that are taken into consideration during the taste-masking formulation include[5-10]

- Extent of the bitter taste of the API
- Required dose load
- Drug particulate shape and size distribution
- Drug solubility and ionic characteristics
- Required disintegration and dissolution rate of the finished product
- Desired bioavailability
- Desired release profile
- Required dosage form

Taste masking by coating[5-8]

Coating is one of the commonly used and efficient method used in taste masking technologies. The coating material is classified into lipids, polymers and sugars. These materials can either be used alone or in combinations, as a single layer or multiple layer coat to achieve taste masking of the bitter drugs as reported in table no:3.

Hydrophobic polymers have been popularly used for coating of bitter drugs than hydrophilic polymers to achieve taste masking. Sweeteners can also be incorporated in the coating solution of better taste masking.

Multilayer coating has been done to overcome the coating imperfections otherwise leads to decrease in taste masking performance, especially for aggressively bitter drugs.

Of the several types of materials existing for coating, polymers are widely used for coating. Polymers are further classified into water soluble, water insoluble and their mixtures (Fig. 4). Examples of each type of polymer are listed in table no:2.

Acidic compounds like citric acid and malic acid are used for creating acidic micro environment to promote the release of drug in the upper intestine from the drug particles coated with reverse enteric polymers[6].

Water soluble organic acids and their salts such as tartaric acid can be used with hydrophilic polymers for achieving taste masking. These acids promote salivation to facilitate the formation of thick, viscous and a mouldable particle paste, which increases the swallowing of that drug.

Multi layer coating with addition of first spacing layer reduces the coating imperfections, drug excipient incompatabilities there by improving the taste masking efficiency.

Ion exchange resins

Ion exchange resins are synthetic organic polymers inert in nature, consists of a hydrocarbon chain to which insoluble groups are attached and they have ability to exchange their labile ions for ions present in the solution with which they are in contact.

Types[5,9,10]

Based on the charge of the functional groups present, ion exchange resins are classified into cation exchange resins and anion exchange resins. With in each category, they are classified into strong and weak depending on their affinity for counter ions.

Cation exchange resins are exchangers of sodium, potassium or aluminium salts and anionic resins are for chloride ions. The drugs are loaded on to the resins by column method and batch method[5,8-11].

Reactions involved in complexation of drug with resins

Acidic drug

$Re\text{-}N(CH_3)^+{}_3\ Cl^- + Drug^- \rightarrow Re\text{-}N(CH_3)^+{}_3\ Drug^- + Cl^-$

Basic drug

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

Typical reactions involved in gastrointenstinal fluids

Acidic drug

In stomach

$Re\text{-}N(CH_3)^+{}_3\ Drug^- + HCl \rightarrow Re\text{-}N(CH_3)_3\ Cl + Drug$ (Free form)

In intestine

$Re\text{-}N(CH_3)^+{}_3\ Drug^- + NaCl \rightarrow Re\text{-}N(CH_3)^+{}_3\ Cl^- + Drug$ (Sodium salt)

Basic drug

In stomach

$Re\text{-}COO^-\ Drug^+ + HCl \rightarrow Re\text{-}COOH + Drug\text{-}HCl$

In intestine

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

In taste masking by ion exchange resins, the resin-drug complexes formed will elute only a limited % of drug in the saliva P^H. Thus the taste of the drug is masked without interrupting the drug release profile (as shown in above reactions).

Table no: 4 is a literature report of various ion exchange resins employed in taste masking of drugs. Examples of drugs listed in table no: 5 are those by which the taste of the drug is masked by ion exchange resins.

Flavours and sweeteners

Sweeteners are commonly used in taste masking of drugs. These are commonly used in combination with other taste masking technologies. These can be mixed with bitter drugs so as to improve the taste of the core material. Sweeteners are classified into natural and synthetic, based on the origin. Synthetic sweeteners such as sucralose, aspartame, saccharin are showing their prominence in taste masking than the natural ones. These sweeteners are used in combination with sugar alcohols like lactitol, maltitol and sorbitol to decrease their after-taste perception. Sucralose can be used with acids (citric acid) to increase the taste masking efficiency of the sweetener[11,12]. Each sweetener will have their own significance in taste masking and different value of sweetness when compared to standard (Sucrose), examples listed in table no:6.

There is often a correlation between the chemical structure of a compound and its taste. Low molecular weight salts tend to taste salty where higher molecular weight salts tend toward bitterness. Nitrogen containing compounds, such as the alkaloids, tend to be quite bitter.

Flavours are also commonly used in taste masking of drugs in solids and liquid dosage forms. Flavours are classified into natural and artificial(table no:7). Selection of suitable flavouring agent to be added depends on the original sensation of drug substance (table no:8). The cooling effect of some flavours aids in reducing after-taste perception. Eucalyptus oil is a major constituent of many mouth washes and cough syrup formulations. Examples of various classes of drugs of which the taste masking is achieved by the use of sweeteners and flavouring agents are listed in table no:9.

Column method

Highly concentrated drug solution is passed through the column containing resins. Maximum efficiency is best obtained by the column method.

Batch method

In this method the drug solution is agitated with a quantity of resin until equilibrium is attained.

Formation of inclusion complexes

Inclusion complex is a 'host-guest' relationship in which the host is complexing agent and guest is the active moiety. The complexing agent is capable of masking bitter taste either by decreasing its oral solubility or decreasing the availability of drug to taste buds. Vanderwaal forces are mainly involved in inclusion complexes[4-11].

β- cyclodextrin is widely used complexing for taste masking of drugs due to its sweet taste and is non toxic in nature.

Table no:10 is a literature report of various complexing agents used for taste masking of bitter drugs.

Prodrug approach

Prodrugs are therapeutic agents that are initially inactive but on biotransformation liberate active metabolite by which the therapeutic efficacy is obtained.

Molecular geometry of the substrate is important for the taste receptor adsorption reaction i.e., mechanism of taste. Hence if any alteration is done in molecular geometry, it lowers the adsorption rate constant. Thus taste masking can be achieved

through prodrug approach. Other advantages of prodrugs include change in aqueous solubility, increase lipophilicity, improved absorption, less side effects and change in membrane permeability etc[10,11]. Table no: 11gives a list of active moieties and their prodrug approaches done in recent years.

Microencapsulation

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[5,6,11]:

- Air suspension coating
- Coacervation phase separation
- Spray drying
- Spray congealing
- Solvent evaporation
- Pan coating
- Interfacial polymerization etc.

Of these processes, first four are mostly used techniques for achieving taste masking. Microencapsulation by coacervation phase separation consists of three steps carried out under continuous agitation, such as: formation of three immiscible phases, deposition of coating and rigidization of coating.

Polymers and their selection selection of coating polymer is an important factor to be considered for taste masking by coating.

Ideal characteristics of a coating polymer

- Should not allow the release of drug in oral cavity, but should allow the release of the drug at the expected site (intestine or stomach).
- Should be insoluble in salivary P^H (6.8) but Should be soluble in gastric P^H (1.2)

Choosing one of the polymers is not a simple selection. Before making the decision on coating material, the following factors of drug are to be considered[5,6,10,11]

- Particle size
- Flow properties
- Moisture sensitivity
- Long term stability
- Effect of temperature on processing
- Form of Drug delivery etc.

Once the type of coating and polymer is decided, then the level of coating has to be optimized. Thick coating may cause problems both in terms of size and cost. However, by coordinating the right type of coating material it is possible to mask the bitter taste of the drug completely while at the same time not affecting the intended drug release. Table no.:12 gives a literature report on various coating materials used for taste masking the drugs.

Granulation

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[6-8]. The taste masked granules can also be formulated as chewable tablet and rapidly disintegrating tablets. Table no.13 gives the literature report on the list of drugs whose taste is masked by granulation techniques by using saliva insoluble polymers.

Adsorption

Adsorbate of bitter tasting drug can be considered as less saliva soluble version of that drug. In this technique, adsorbates of the bitter drugs are prepared by adsorption process. This process involves the adsorption of the drug solution using insoluble materials like silica gel, bentonite , veegum etc. The adsorbate (resultant powder) is dried and used for the formulation of final dosage forms[10].

Taste suppressants and potentiators

Most of Linguagen's bitter blockers (adenosine mono phosphate) compete with bitter substances to bind with GPCR sites. In general, hydrophobic nature of these bitter substances have good binding affinity to the receptor sites. Lipoproteins are universal bitter taste blockers. Neohesperidine phospholipids have bitter taste suppression characteristics by chemically interacting with the taste receptors. Cooling and warming agents suppress unpleasant taste of medicament by subjecting taste receptors to extreme sensations to overcome/ overpower the bitter taste so as to confuse the brain. Eucalyptol (Cooling agent) and Methyl salicylate (Warming agent) mixture was used for suppression of the bitter taste of Thymol[3,5-7].

Potentiators increase the perception of the taste of sweeteners and mask the unpleasant taste. Various potentiators include thaumatine, neohesperidine dihydro chalcone (NHDC) and glycyrrhizin increase the perception of sodium or calcium saccharinates, saccharin, acesulfame, cyclamates etc. Thaumatine along with sugar alcohols to achieve taste masking of bromhexine[5,8].Table no:14 enlists various taste suppressants and potentiators used for taste masking.

Liposomes and multiple emulsions[5,6]

Liposomes are carrier molecules comprising several layers of lipids, in which the bitter drug is entrapped within the lipid molecule. Oils, surfactants, polyalcohols and lipids effectively increase the viscosity in the mouth due to which the time of contact between the bitter drug and taste

receptors is decreases, thus improving the overall taste masking efficiency.

Inhibition of bitterness of drugs by phospholipids such as phosphatidic acid, phosphatidylinositol, soya lecithin etc has been reported. The bitterness of Chloroquine phosphate in HEPES buffer (P^H 7.2) is masked by incorporating into a liposomal formulation prepared with egg phosphatidyl choline.

Multiple emulsions is also a good approach for taste masking of bitter drugs. This is achieved by dissolving the drug moiety in the inner aqueous phase of w/o/w emulsion with good self life stability. o/w/o emulsion is a type of multiple emulsion in which water globules themselves containing dispersed oil globules, conversely w/o/w emulsions are those in which internal and external aqueous phases are separated by the oil. Both types of multiple emulsions are prepared for Chloroquine sulphate and reported to be partially effective in masking the bitterness of the drug. Examples of drug listed in table no: 15 indicates the use of liposomes and multiple emulsions technique in taste masking.

EVALUATION OF TASTE MASKING EFFECT

All the medicines are not always compatible. So, there is a necessity of incorporating an agent for taste masking of the drug and provides the patient with a pleasant product experience. Next step is to determine what additional functional excipients are required for the final product. These excipients include sweeteners, flavours and super disintegrants. Before incorporation of these materials all the preformultion parameters have to satisfy and they should be physically, chemically and therapeutically compatible with the drug and should be optimized.

The evaluation is classified into two types[8,10,11]. They are Subjective methods and Objective methods(table no: 16).

Evaluation of solid and liquid dosage forms (except microspheres)

Soutakagi., et al. discovered a multi channel taste sensor (E- tongue) which is almost similar to the human tongue. This sensor consists of transducer, which is composed of several kinds of polymer/ lipid membrane with different characteristics. Taste information is transformed into electrical signals of membrane potential of the receptor. It was previously reported to record the bitterness of quinine and acesulfame K, as a bitterness inhibitor[10,11].

E-tongue provides a fast and simple assessment of oral formulations like chewable tablets, liquids, rapid dissolving tablets, films and lozenges etc.

Evaluation of microspheres

This can be done by determining the rate of release of the drug from microspheres. The reason is that the drug release rate can serve as an index of the degree of taste masking achieved.

Recent innovations

Taste analyzing system by Alpha MOS is now commercially available. It consists of a taste sensor comprised of silicon transistors with an inorganic coating that governs the sensitivity and selectivity of each individual sensor. The life of the sensor lasts for about 1 year.

RECENT TRENDS[13,14,15]

AdvaTab ODT Technology

Advatab ODT Technology is developed by APTALIS Pharmaceutical technologies. Various advantages offered by this technology includes high physical stability, stability during package and transport, pleasant taste (with Microcaps technology) and good patient compliance.

Microcaps ODT Technology

Microcaps ODT technology is developed by APTALIS Pharmaceutical technologies. This technology uses coating method for taste masking. The polymeric membrane eliminates the unpleasant taste and / or odour. Offers advantages like precise taste masking, good release profiles and patient compliance.

Liquitard ODT Technology

This sophisticated Liquitard technology is developed by APTALIS Pharmaceutical technologies with an aim to provide an effective, convenient, ready-to-use, taste-masked powder formulation in single dose sachets that can be administered as a suspension or sprinkle on easy to swallow foods. This is developed with a wide variety of flavours and is compatible with customized release profiles.

Formulplex and Formulcoat

Pierre Fabre developed a new taste masking technologies in which, coating of micro or nano-sized particles at room temperature with non organic solvent.

KLEPTOSE® Linecaps

Roquette offers a new taste-masking technology: KLEPTOSE® Linecaps, uses a pea maltodextrin for masking the bitter taste of drugs by decreasing the overall amount of drug particles exposed to the taste buds.

CONCLUSION

Taste masking of bitter drugs is a big challenge to scientist. However we have made an attempt to describe various methods, techniques suitable for taste masking of obnoxious drugs. These

techniques mentioned in this review can be used for bench scale and pilot scale also.In addition to the existing patented taste masking technologies, several new technologies for effective taste masking are also mentioned in this review. With application of these techniques one can improve product preference to a large extent.In addition to oral drug delivery, the taste masked drug delivery research is gaining importance for the quality of the treatment provided to patients, especially children and old. As evidenced by number of patients and technology developments, an attempt of ideal taste masking is widely accepted in the development of palatable dosage forms having good patient compliance without interfering the drug release.

Table 1: List of Threshold Concentrations for Primary Taste Sensations on Specific Areas of Tongue[5,7]

Taste	Threshold concentration	Area of tongue
Sweet	0.5%	Tip of tongue
Salt	0.25%	Tip and sides of tongue
Sour	0.007%	Sides of tongue
Bitter	0.00005%	Back of tongue

Table 2: List of different types of polymers with examples[6,8,10,11]

Type of polymer	Examples
Water soluble polymers	Cellulose acetate butyrate, polyvinyl pyrrolidone, hydroxyl ethyl cellulose
Water insoluble polymers	Ethyl cellulose, polyvinyl avetate, crospovidone, cros caramellose
pH dependent Water insoluble polymers	Polycarbophil, polyacrylic acid
pH independent Water insoluble polymers	Cellulose ethers, cellulose ester, polyvinyl acetate
Reverse enteric polymers	Eudragit E 100, Eudragit EPO, methyl methacrylate, hydroxyl ethyl methacrylate, vinyl pyridine
Enteric polymers	Phthalate, hydroxyl phthalates, acrylic acid esters
Spacing layer polymers	Ethyl cellulose : PVP

Table 3: Literature report on taste masking by coating[16-28]

Drug	Category	Coating material used
Acetaminophen	NSAIDs	Cellulose acetate(CA) or cellulose acetate butyrate(CAB) and polyvinyl pyrrolidone(PVP)
Cefpodoxime Proxetil	Penicillin antibiotics	1.Eudragit RD 100 in combination with Sodium CMC 2. Kollicoat IR
Desloratadine	Anti allergic	ethylcellulose(EC) and Eudragit EPO
Dextromethorphan	Anti tussive	EC:PVP and Eudragit E 100
Diphenhydramine Hydrochloride	Anti histamines	polyvinyl acetate and aminoalkyl methacrylate copolymer
Ibuprofen	NSAID	EC and hydroxyethylcellulose(HEC) in Vaseline or silicon oil
Vitamins and Minerals	Diet Supplement	Hydrophilic additives and poly vinyl acetate
Adipic acid and ascorbic acid	Diet Supplement	Reverse enteric polymer and acidic compound
Macrolide antibiotics	Antibiotics	Enteric coating polymer and osmotically active substance
NSAIDS	NSAIDS	Methacrylate ester co polymer
Cefuroxime axetil	Penicillin antibiotics	Acid soluble or swellable polymers, enteric polymer
Amobarbital	Sedatives	First water swelling gel forming layer and second water swelling gel forming layer and adhesive layer
Ciprofloxacin hydrochloride	Fluoro Quinolone antibiotics	Nonionic and ionic polymers
Sildenafil citrate	Vaso dilator	HPMC, EC (first coating layer), methyl or ethyl acrylate esters (second coating layer), sucrose (third coating layer)

Table 4: List of commonly used ion exchange resins[5,8,10]

Type of resin	Functional group	Functional backbone	Commercial resins
Strong anion	$-N^+R_3$	Polystyrene –DVB	Amberlite IR 400, Dowex 1, Indion 454, Duolite AP 143
Weak anion	$-N^+R_2$	Polystyrene –DVB	Amberlite IR 4B, Dowex 2
Strong cation	$-SO_3H$	Polystyrene- DVB	Amberlite IR 120, Dowex 50, Indion 244, Purolite C 100 HMR, Kyron –T-154
Strong cation	$-SO_3Na$	Polystyrene- DVB	Amberlite IRP 69, Indion 254, Tulsion-T-344
Weak cation	-COOH	Methacrylic acid- DVB	Amberlite IRC 50, Indion 204-234, Tulsion 335, 339, Purolite C 102DR, Kyron-T-104, Tulsion T 335, Doshion P544 (R)
Weak cation	-COOK	Methacrylic acid- DVB	Amberlite IRP 88, Indion 234, Tulsion T 339, Kyron-T-134

Table 5: Literature report on taste masking by Ion exchange resins[8,10,29-41]

Drug	Category	Dosage form	Commercial Resin used
Chloroquine phosphate	Anti malarial		Indion cation exchange resin
Ciprofloxacin	Fluoro quinalones		Lewatit CNP
Dextromethorphan hydrobromide	Anti tussisive	Dry/ Liquid Suspension	Carbomer 934
Ephedrine hydrochloride	Sympathomimetic drug		Indion CRP 244/254
Erythromycin	Macrolide antibiotic	Liquid suspension	Carbomer 934
Clarithromycin	Macrolide antibiotic	Liquid suspension	Carbomer 934
Orbifloxacin	Fluoro quinalones Antibiotic	Dry / Liquid suspension	Amberlite IRP 64/69
Paroxetin hydrochloride	Anti depressant	Liquid suspension	Amberlite IRP 88
Ranitidine hydrochloride	Anti histamines	Chewable tablet	Amberlite IRP 69/88
Remacemide hydrochloride	Anti parkinson's drug	Dry / Liquid suspension	Amberlite IRP 64
Erythromycin sterate	Macrolide antibiotic		Amberlite IR 120, Dowex 50, Indion 244
Dicyclomine hydrochloride	Anti spasmodic		Amberlite IR 120, Dowex 50, Indion 244, kyron-T-154, Purolite C 100 HMR
Spiramycin, dimenhydrinate, roxithromycin, Levocetrizine,Norfloxacin, Ofloxacin			Amberlite IRP 50, Indion 204, Purolite C 102 DR, Kyron-T-104, Doshin P 544(R)
Metronidazole, Azithromycin, Quinine sulphate, Paracetamol, Erdosteine			Amberlite IR 4B, Dowex 2
Buflomedil	Vasoactive agent		Amberlite IRP 69
Chlorpheniramine maleate	Anti histamines		Indion CRP 244, Indion CRP 254
Clopidogrel sulphate	Anti platelet drug		Water soluble cation exchange resin with sulfonic acid groups
Donepezil chloride	Indirect Para sympathomimetic agent		Anionic polymer and PVP
Sildenafil citrate	Vaso dilator		Anionic polymers (Carragenan, xanthan gum, dextran sulphate)

Table 6: List of commonly used sweeteners and their relative sweetness[42]

Sweetening agent	Relative sweetness	Significance
Aspartame	200	Less stable in solution
Acesulfame potassium	137-200	Bitter in higher concentration
Cyclamate	40	Banned
Glycerrhizin	50	Moderately expensive
Lactose	0.16	High amount is required
Mannitol	0.60	Negative heat of solution
Saccharin	450	Unpleasant after taste
Sucrose	1 (Standard)	Most commonly used
Sucralose	600	Synergestic sweetening effect

Table 7: Classification of flavouring agents[5,9]

Type	Example	Significance
Natural	Peppermint	Less stable
Artificial	Vanilla	Highly stable
Natural and artificial	Strawberry	Effective at low concentrations

Table 8: Selection of flavours based on sensation of taste[12]

Sensation	Flavour
Salt	Butterscotch, apple, apricot, peach, vanilla
Bitter	Wild cherry, walnut, chocolate, mint, passion fruit
Sweet	Fruit and berry, vanilla
Sour	Citrus flavours, liquorice, root bear, raspberry

Table 9: Literature report on taste masking by addition of flavours and sweeteners[43-58]

Drug	Category	Dosage form	Taste	Taste masking agent used
Eucalyptus oil	Freshener	Mouth wash	Bitter	Fenchone, Borneol
Ibuprofen	NSAID	Syrup, Suspension	Bitter	Saccharin sodium, sucrose, sorbitol
Thymol, triclosan	Dental caries	Oral rinses	Bitter	Citrus flavour, limonene
Zinc acetate dehydrate	Zinc supplement	Lozenges	Bitter	Saccharin sodium
Acetaminophen, Guaifenesin and Dextromethorphan hydrobromide				Sucralose , Citric acid
Aminoacids and proteins	Diet supplement			Sucralose
Dihydrocodeine phosphate, potassium guaiacol sulfonate				Aspartame, Saccharin sodium, Liquorice extract
Levofloxacin	Fluoroquinolone antibiotic			Aspartame, Sucralose, Saccharin sodium
Aspirin / Acetaminophen	NSAID			Menthol, Aspartame and or Sucralose
Iron compounds	Iron supplement			Sucralose, sorbitol, Xylitol, Maltitol or Erythritol
Mineral supplements	Diet supplement			Glycyrrhizin, Acesulfame potassium
Vegetable crude drug				Caramel
Vitamins	Diet supplement			Cacoa powder, Stevia extract, Aspartame etc.
Pseudoephedrine	Sympathomimietic drug			PEG with Sucralose

Table 10: Literature report on taste masking by inclusion complexation[59-67]

Drug	Category	Dosage form	Complexing agent used
Zinc acetate dehydrate	Recover zinc deficiency		Anethol -β- cyclodextrin complex and saccharin
Carbapentane citrate	Local anaesthetic	Oral liquid	Cyclodextrins
Ibuprofen	NSAID	Solution	Hydroxypropyl β- cyclodextrin
Gymnema sylvestre	Anti-diabetic	Oral liquid	β- cyclodextrin, Chitosan
Dioscin	CVS disorders		β- cyclodextrin
Benexate hydrochloride	Antiulcer	Granules	β- cyclodextrin
Metronidazole benzoate	Anti bacterial		γ- cyclodextrin
Hexitidine	Anti bacterial		β- cyclodextrin
Zipeprol	Anti tussive		β- cyclodextrin
Guaiacol	Anti diarrhetic		β- cyclodextrin
Levosulpiride	Anti psychotic		β- cyclodextrin
Chloroquine phosphate	Anti malarial	Syrup	Tannic acid
Dimenhydrinate	Anti emetic	Chewable tablet	Eudragit-S- 100

Table 11: Literature report on taste masking by prodrug approach[8,10,68-70]

Drug	Category	Modification done
Chloramphenicol	Broad spectrum Antibiotic	Palmitate or phosphate ester
Clindamycin	Lincosamide antibiotic	Alkyl ester
Erythromycin	Macrolide antibiotic	Alkyl ester
Lincomycin	Lincosamide antibiotic	Phosphate or alkyl ester
Tetracycline	Broad spectrum antibiotic	3,4,5- trimethoxy benzoate salts
Triamcinalone	Treatment of ulcerative colitis & skin disorders	Diacetate ester

Table 12: Literature report on taste masking by microencapsulation[71-88]

Drug	Category	Dosage form	Coating material used	Technique used
Acetaminophen	Anti pyretic	Dispersible tablet	Cross caramellose	Wurster fluid bed coating
Caffeine / Cimetidine	Diuretic / anti histamine	Chewable tablet	Eudragit RL 30D, RS 30D	Wurster fluid bed coating
Ciprofloxacin	Fluoroquinolone antibiotic	Oily suspension, sachets	Eudragit NE 30D / RL 30D, HPMC	Wurster fluid bed coating
Levofloxacin	Fluoroquinolone antibiotic	Suspension	Eudragit E 100, Cellulose acetate	Wurster fluid bed coating
Sildenafil citrate	Vaso dilator		Eudragit NE 30D, E 100	Top spray fluid bed coating
Chlorpheniramine maleate	Anti histamine	Mouth melt tablet	Ethyl cellulose	Top spray fluid bed coating
Dextromethorphan hydrobromide	Anti tussive		PVP-K30	Top spray fluid bed coating
Acetaminophen	Antipyretic	Chewable tablet	Eudragit E 100, Cellulose acetate	Tangential spray fluid bed coating
Theophylline	Diuretic	Dry suspension	Eudragit NE 30D, Guargum	Tangential spray fluid bed coating
Ampicillin trihydrate	Penicillins	Powders	Sodium CMC	Spray drying
Nizatidine	Anti histamine	Sprinkels	Eudragit E 100	Spray drying
Roxithromycin	Macrolides	Suspension	Eudragit RS 100/ RL 100	Spray drying
Clarithromycin	Macrolides	Powders	Glyceryl monostearate, Eudragit E 100	Spray congealing
Chloroquine di phosphate	Anti malarial	Powders	Eudragit RS 100	Coacervation phase separation
Metronidazole	Anti amoebic	Dry suspension	Eudragit E, Fattibase	Solvent evaporation
Ibuprofen, ketoprofen, aspirin and Fenamic acid	NSAIDS		Sodium alginate and calcium salt	Solvent evaporation
Prazequantel	Anti helmenthic		Alginic acid and its salts	Solvent evaporation
Isoprothiolane	Antifungal			Spray drying
Indeloxazine HCl	Neuroprotective			Fluidized bed drying

Table 13: Literature report on taste masking by granulation[89-102]

Drug	Category	Granulating agent used
Calcium compounds	Mineral supplement	Sugar alcohol
Erythromycin	Macrolide	Alginic acid
Dextromethorphan	Anti tussive	Cyclodextrin
Alprazolam	Anxiolytic	Eudragit E 100
Norfloxacin	Flouroquinolone antibiotic	Methacrylic acid ester
Macrolide antibiotic	Macrolides	Polycarbophil
Ondansetron	Anti nausent, antiemetic	Polacrillin potassium
Ibuprofen	Anti inflammatory	Micro Crystalline Cellulose(MCC)
Granisetron HCl	Anti nausent, antiemetic	Glycerol behenate or glycerol palmitostearate
Levofloxacin	Fluoroquinolone antbiotic	Castor oil, sugar alcohol
Clopidrogel sulphate	Anti platelet	Castor oil, sugar alcohol
Telithromycin and pristinamycin	Macrolides	Glyceryl stearate or bees wax
Vitamins	Diet supplement	Polyglycerol ester of poly valent fatty acids
Penicillins, Macrolides	Antibiotics	Hydrogel or Wax

Table 14: Literature report on taste masking by addition taste suppressants and or potentiators[103-108]

Drug	Category	Taste suppressant and / potentiator used
Bromhexine	Mucolytic	Thaumatin and sugar alcohol
Caffeine	Diuretic	Hydroxyflavones
Caffeine	Diuretic	Gamma-amino butyric acid
Paracetamol	Antipyretic	Potentiators: Glycyrrhizin, Thaumatin and neohesperidine dihydrochalcone (NHDC) Sweeteners: saccharin salts, acesulfame etc
Pioglitazone	Anti diabetic	Sodium chloride and coating with saccharides
Sugar alcohol	Nutritive agent	Aldehydes (citral dimethyl acetal) and flavours

Table 15: Literature report on taste masking by liposomes and multiple emulsions[5,8]

Drug	Category	Taste masking agent used
Isoprothiolane	Plant growth regulator	Hydrogenated oil and HPMC
Acetaminophen	NSAIDs	Molten stearyl stearate
Talampicillin HCl	Penicillin antibiotic	Magnesium alluminium silicate and soya bean lecithin
Clarithromycin	Macrolide antibiotic	Glyceryl monostearate and AMCE
Indeloxazine HCl	Cerebral activator	Hydrogenated oil and surfactants

Table 16: List of evaluation parameters[5,10]

Subjective Methods	Objective Methods
Preference test Paired testing Triangle testing Hedonic scale	Difference test Paired difference test Triangle difference test Duo trio test Ranking test Analytical test Flavour profile Time intensity test Single attribute test Dilution profile Statistical test

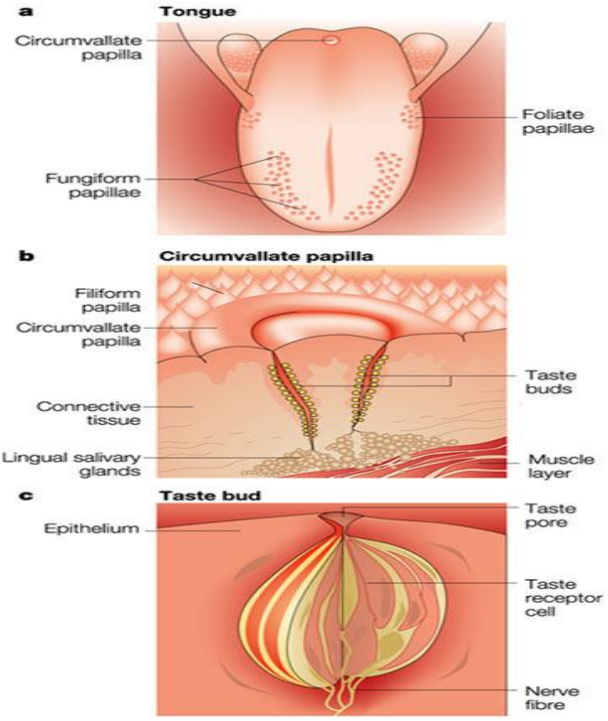

Fig. 1: Structure of taste bud

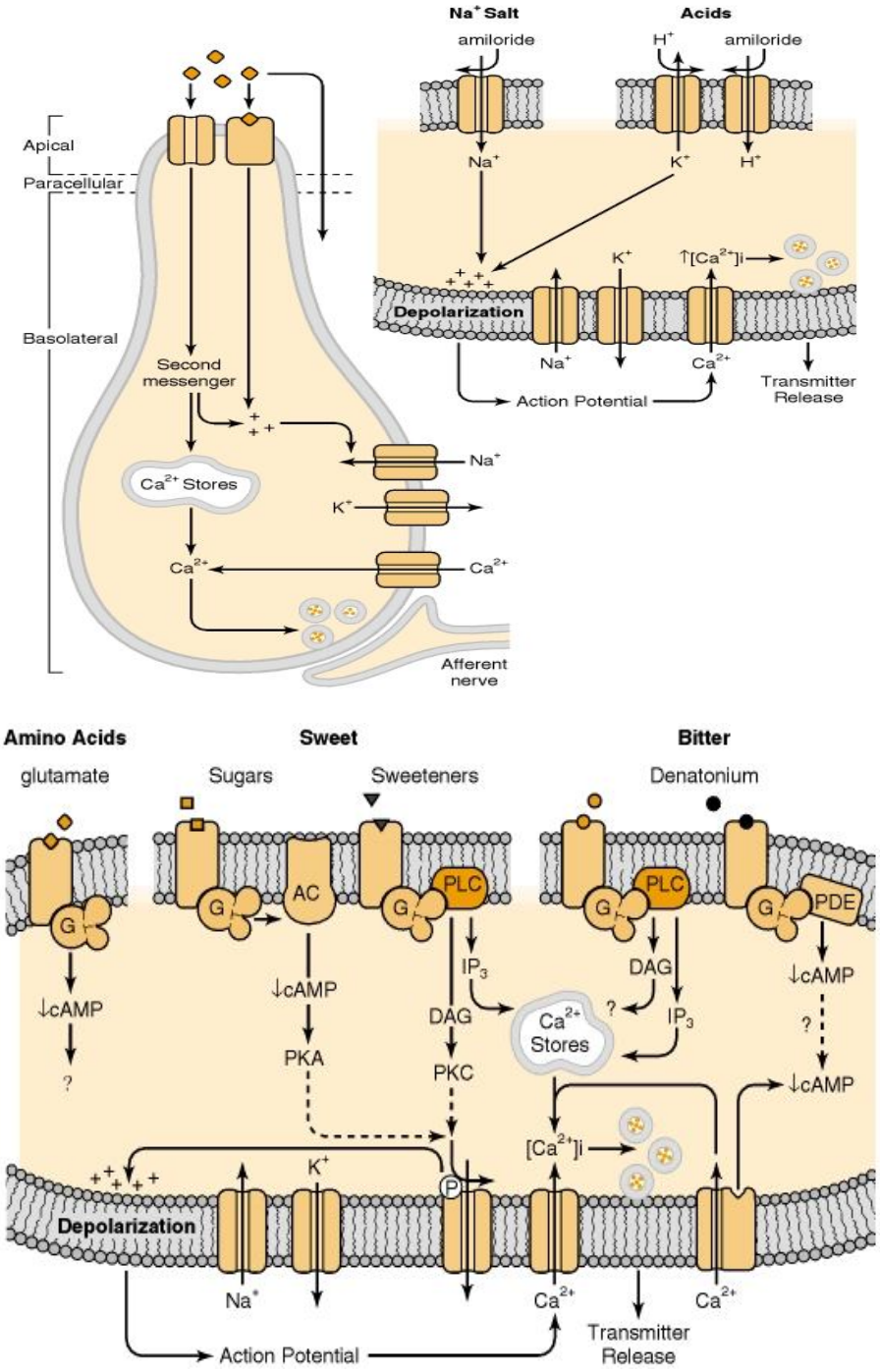

Fig 2, 3: Mechanism of taste perception

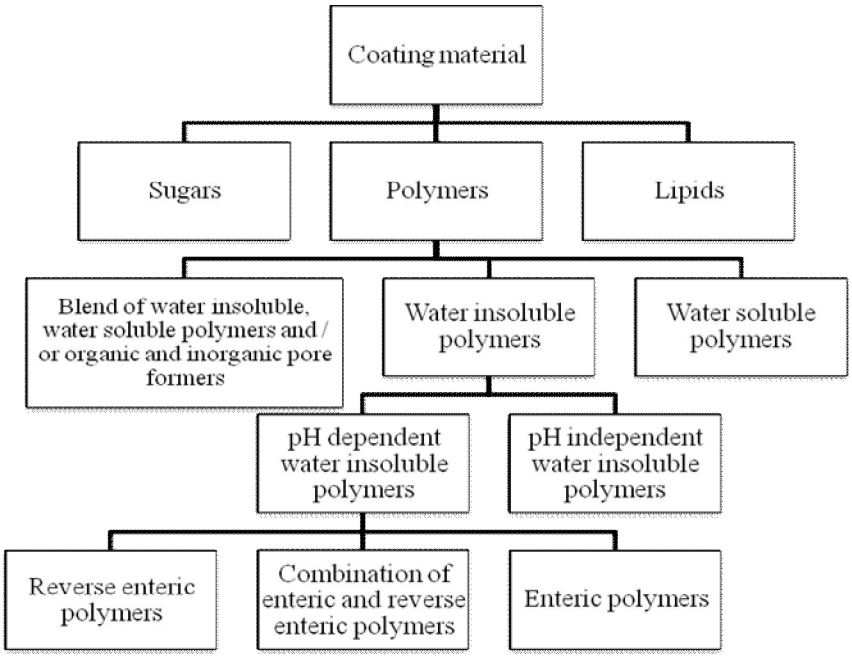

Fig. 4: Classification of Coating materials[6]

Fig. 5: Electronic tongue

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