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Approaches in Technologies of Taste Masking of Oral Dosage Forms

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ABSTRACT

Many oral dosage forms, bulking agents and beverage products have unpleasant taste. The bitter taste is an undesirable trait of the product or formulations and can considerably affects its acceptability by consumer. So, they should be formulated in a palatable form. Bitter taste in such systems can be reduced or eliminated by various methods, but no universally applicable technologies are yet recognized. This article is about the discussion of recent approaches for minimizing the unpleasant taste for oral pharmaceuticals.

Key words: Taste masking, Eudragit.

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INTRODUCTION:

More than 50% of pharmaceutical products are orally administered for several reasons, undesirable taste is one of the important formulation problems that are encountered in certain drugs. Organoleptic properties of the products are more essential particularly in pediatrics and geriatric patients.[1] Minimizing or eliminating the unpleasant taste has become a potential tool to improve patient compliance, therapeutic benefits and thereby commercial success in market during the last decades.[2] Considerable amount of progress has been achieved in the development of taste masked formulations in recent years. Taste masking technologies prevent the interaction among the drug molecule and the oral mucosal surface. It acts with the mechanism of creating a physical barrier around each particle, by which the drug substance is being prevented from going into solution and interacting directly with taste receptors.[3]

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.[4] Various methodologies are identified and developed to improve the taste of the formulations by using polymeric coating strategies, complexation with cyclodextrin, complexation with ion exchange resins, salt formation, micro encapsulation technique, use of viscosity modifiers, emulsions and liposomes, use of excipients like flavors and sweeteners.[5,6] The present article is an attempt to review strategies and methodologies for taste masking of bitter oral formulations for adapting the technologies.

METHODOLOGIES

Polymer coating:

The selection of the coating polymers is based on the fact that the polymer should prevent rapid release of drug in the saliva, but allows it in the gastric cavity or in the duodenal region where the drug is expected to be absorbed.

Eudragit E, a FDA approved cationic co-polymer on dimethyl amino ethyl methacrylate and neutral methacrylic acid esters dissolves in gastric juice. The coating materials may be applied using a variety of methods including spray coating and pan coating.[7] In case of suspensions, the coating material will maintain its integrity to mask disagreeable taste in a liquid medium with a pH greater than 5.5 stored at refrigerated temperature.[8]

Another approach of coating for taste masking oral medications includes a combination of a polymer and a triglyceride. The triglyceride mixture melts at body temperature and the

copolymer causes the coating to dissolve upon reaching the acidic environment of the stomach. Triglyceride when mixed together melts at body temperature leaving the polymer, which is insoluble at pH 7.4 but soluble in stomach.[7]

Practically when the patient places the medication in his mouth, the triglyceride portion of the coating begins to melt as it is now at body temperature. The coating remains intact, because the polymer portion will dissolve only when it reaches a pH of 5.5, which is much more acidic than the pH of the mouth. The medication then travels down the esophagus and enters the stomach. Once in the acidic environment of the stomach, the dissolution of such dosage form occurs and the medication is then available for absorption.[1]

Complexation with cyclodextrin:

Cyclodextrin are cyclic oligomers of glucose. They form inclusion complex with any drug whose molecules can fit to the lipophile seeking cavities of the cyclodextrin molecules. The resulting complexes can markedly improve the coating with suitable lipids, such as palmitic or stearic acid, glyceryl tripalmitate, glyceryl tristearate or a mixed acid ester triglyceride and a stearyl alcohol.[9]

Strong bitter taste of carbentane citrate syrup was reduced to approximately 50% by preparing a 1:1 complex with cyclodextrin.[10] palatable ibuprofen solutions are prepared by forming a 1:11 to 1:15 inclusion complex with ibuprofen and hydroxy propyl ß-cyclodextrin, respectively. The complex masked the bitter component but creates a sore taste that is masked by sweeteners.[11]

Complexation with ion exchange resin:

Most of the bitter drugs have the functional groups like nitrogen atom and amine, which is the main cause of their bitter taste. If the nitrogen atom and the functional groups are blocked by complex formation the bitterness of the drug reduces drastically.[12]

Cation exchange resin and anion exchange resins are polyacrylic acid derivatives were used to absorb ester drugs for both taste masking of bitter taste and also for achieving sustained release action.[13] Drugs can be bound to the resin by either repeated exposure of the resin to the drug in a chromatographic column or by prolonged contact of resin with the drug solution. The resin from insoluble adsorbents or resinate through weak ionic bonding with oppositely charged drugs. Drug release from the resin depends on 2 factors

1. **The ionic environment** (i.e., pH and electrolyte concentration) with the GIT.
2. **The properties of the resin.**

Drug molecules attached to the resin are released by exchanging approximately charged ions in the gastrointestinal tract, followed by diffusion of free drug molecule out of the resins. The

process can be depicted by the following equation 1 and 2 for anion exchange and cation exchange respectively. Where x and y are ions in the gastro intestinal tract.

$Resin^{+}$ ——— $Drug^{-} + X^{-}$ ⟶ $Resin^{+}$ ---- $X^{-} + Drug^{-}$ ---------- (1)

$Resin^{-}$ ——— $Drug^{+} + Y^{+}$ ⟶ $Resin^{-}$ ---- $Y^{+} + Drug^{+}$ ---------- (2)

Resins involve ion exchange as the reversible inter change of ions between a solid and a liquid phase in which there is no permanent change in the structure of solid. The solid is the ion exchange material while the ion could be a drug. When used as a drug carrier, ion exchange materials provide a means for binding drugs onto an insoluble polymeric matrix and can effectively mask the problems of taste and odor.[14]

Bitter cationic drugs can get absorbed onto the weak cation exchange resins of carboxylic acid functionality to form the complex which is non bitter. E.g. Rodec decongestant tablet containing pseudoephedrine.[15] The complex of cationic drugs and weak cationic exchange resin does not break at pH 6-7 of saliva with cation concentration of 40meq/lit. But at high cation concentration of stomach and pH 1-3, free drug is immediately released. Some drugs whose taste was masked using this technique are buflomedil and ciprofloxacin.[16, 17, 18, 19]

The types of ion exchange resins that have been successfully used to mask the taste of bitter drugs include Amberlite IRP 88 (an acrylic potassium resin), Amberlite IRP 69 (sodium polystyrene sulphonate) and Amberlite IRP 64 (a carboxylate form of the styrene polymer).[20]

Salt formation:

Salt formation for minimizing the bitter taste of drugs is by either decreasing solubility or by increasing hydrophobicity and thereby reducing contact of bitter drugs with the taste buds. If a less bitter tasting salt form or a tasteless derivative can be obtained, this would represent the best derivative to taste masking. Since there is no coating that can be broken during chewing, no problem will be encountered with respect to unpleasant after taste. Magnesium aspirin tablets are rendered tasteless by making magnesium salt of aspirin. D-chlorpheniramine maleate was also a taste masked salt of chlorphenaramine. The alkyloxyalkyl carbonates of clarithromycin have remarkably alleviated bitterness and improved bio absorbability when administered orally.[21]

Meglumine, an acid addition salt of ibuprofen, not only increases the water solubility of ibuprofen but also provides a significant taste masking effect. Hence, this salt of ibuprofen can be incorporated into palatable liquid formulations for oral administration. The acid addition salts are prepared by salifying the amino function of the meglumine with carboxylic acid function of the ibuprofen in approximate equal molar amounts.[22]

Micro encapsulation:

Micro encapsulation involves coating of drug particles using a natural or synthetic polymer or wax. Several techniques such as simple and complex coacervation, solvent evaporation, spray chilling, spray drying, annular jet, fluid bed and spinning disks methods have been successfully used to prepare microspheres.[23-31]

Polymers namely, Eudragit L-55 and RL were used to mask the taste of cefuroxime axetil. The drug was first encapsulated in the acrylic polymers using the solvent evaporation technique, and the resulting coated particles were then formulated as a suspension.[32] Ibuprofen is encapsulated using chewable methacrylic acid copolymers to reduce bitterness. A fluidized bed of ibuprofen crystals was spray coated with an aqueous dispersion containing Eudragit L-30 D, propylene glycol as plasticizer and talc. The encapsulated ibuprofen was mixed with mannitol and flavor and compressed into tablets.

Use of viscosifiers:

Viscosifiers are use to increase the viscosity of the preparation which reduces the contact of unpleasant tasting drug with the tongue. Viscosifiers such as acacia, tragacanth, Xanthan or synthetic polymers such as polyethylene glycols, hydroxy propyl methylcellulose and hydroxy ethyl cellulose can be used. Combination of polyethylene glycol (PEG) and sodium carboxy methyl cellulose (Na-CMC) were used to mask the unpleasant taste of drugs such as guifenesin, pseudoephidrine hydrochloride, dextromethorphan and ibuprofen.[33]

Use of Emulsions:

The use of multiple emulsions for masking the bitter taste of chloroquine was investigated in o/w/o and w/o/w emulsion systems. The multiple emulsions were prepared by a two-step procedure. The results indicated that the o/w/o system could mask the taste of chloroquine to some extent. Another classic example of only o/w type of emulsions of mineral oil, which is used as a lubricating cathartic. The oil has an unpleasant taste and hence formulating it into an oil-in-water type emulsion markedly improves its palatability.[5]

Use of Liposomes:

Therapeutic agents are used to entrap the bitter drugs into liposomes. For example, incorporating it into a liposomal formulation prepared with egg phosphatidycholine masked the bitter taste of an antimalarial chloroquinephosphate in HEPES (N-2, hydroxyethylpiperzine-N-2-ethane sulfonic acid buffer at pH 7.2.[34]

Use of excipients (Flavors and sweeteners):

Addition of flavors and sweeteners is the foremost and simplest approach for taste masking especially in the case of pediatric formulations. In the liquid formulation, where poorly water

soluble flavors are added to the alcoholic or other non aqueous solvent component of the formulation.

Fruit flavors are often used to mask sour taste, whereas bitter tasting drugs are often blended with salty, sweet or sour tasting agents. Various taste masking agents significantly suppress the perception of unpleasant organoleptic sensation such as bitterness or medicinal off taste of the volatile oils.[35] For taste masking Vanilla flavor, clove and honey are preferred.

Sweetening compositions containing D-fructofuranose are useful for dentifrices, mouth washes and foods.[36]Menthofuran and anethol not only mask the bitter taste but also improve the stability of the formulation.[37] Vitamin containing oral solutions are bitter in nature are reduced by adding sugars, amino acids and apple flavor.[38] Syrups that have been accomplishing the same task include orange syrup, citric acid syrup, cherry syrup, coca syrup, wild cherry syrup and raspberry syrup. Cinnamon syrup has been used to mask the excessive salty taste of drugs such as ammonium chloride and other salts. Clove oil has been found to be a good taste masking component for a number of medicaments because of its spicy and anesthetic effect.[39]

CONCLUSION

The review of various approaches of taste masking shows that the unpleasant taste is no longer a deterrent to formulating commercially viable liquid dosage forms. Applicability of all these techniques varies from drug to drug and hence a universal approach is desirable. A substance which is universal inhibitor of bitter taste is being researched for quite a long time. It is also suggested that sensory evaluation of the oral dosage forms of the bitter drug with taste inhibitors should take a more formalized structure for providing better and effective healthcare to the population, especially the pediatric segment.

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