ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES

Taste masking methods for bitter drug- A review

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Abstract

The problem of bitter and obnoxious taste of drug in pediatric and geriatric formulations is a challenge to the pharmacist in the present scenario. Molecule interacts with taste receptor on the tongue to give bitter, sweet or other taste sensation, when they dissolve in saliva. This sensation is the result of signal transudation from the receptor organs for taste, commonly known as taste buds. These taste buds contain very sensitive nerve endings, which produce and transmit electrical impulses via the seventh, ninth and tenth cranial nerves to those areas of the brain, which are devoted to the perception of taste.

Keywords: Taste masking, Bitter drugs, Methods

Introduction

There are numerous pharmaceuticals that contain actives, which are bitter in taste. With respect to OTC preparations, such as cough and cold syrups, the bitterness of the preparation leads to lack of patient compliance. The problem of bitter and obnoxious taste of drug in pediatric and geriatric formulations is a challenge to the pharmacist in the present scenario. In order to ensure patient compliance bitterness masking becomes essential. Molecule interacts with taste receptor on the tongue to give bitter, sweet or other taste sensation, when they dissolve in saliva. This sensation is the result of signal transduction from the receptor organs for taste, commonly known as taste buds. These taste buds contain very sensitive nerve endings, which produce and transmit electrical impulses via the seventh, ninth and tenth cranial nerves to those areas of the brain, which are devoted to the perception of taste.[1] An ideal taste masking process and formulation should have the following properties.[2]

1) Involve least number of equipments and processing steps.
2) Require minimum number of excipients for an optimum formulation.
3) No adverse effect on drug bioavailability.
4) Require excipients that are economical and easily available.
5) Least manufacturing cost.
6) Can be carried out at room temperature.
7) Require excipients that have high margin of safety.
8) Rapid and easy to prepare.

Methods of Taste Masking

Various methods are available to mask undesirable taste of the drugs. Some of these are as given below.

Coating of drug particles with inert agents[3-5]

Coating is an extremely useful technique for number of applications in the pharmaceutical field. By coordinating the right type of coating material it is possible to completely mask the taste of a bitter drug, while at the same time, it is not capable of adversely affecting the intended drug release profile. Any nontoxic polymer that is insoluble at pH 7.4 and soluble at acidic pH would be an acceptable alternative for taste masking.Taste masking of ibuprofen has been successfully achieved by using the air suspension coating technique to form microcapsules, which comprises a pharmaceutical core of a crystalline ibuprofen and methacrylic acid copolymer coating that provides chewable taste masked characteristics.

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ISSN: 0976-7126

Various inert coating agents like starch; povidone, gelatin, methylcellulose, ethyl cellulose etc. are used for coating drug particles. One of the most efficient method of drug particle coating is the fluidized bed processor.In this approach powder as fine as 50µm are fluidized in expansion chamber by means of heated, high velocity air and the drug particles are coated with a coating solution introduced usually from the top as spray through nozzle. The coated granules are dried with warm air.

Taste masking by formation of inclusion complexes[6]

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. Vaander Waals forces are mainly involved in inclusion complexes.B-cyclodextrin is most widely used complexing agent for inclusion type complexes. It is sweet, nontoxic, cyclic oligosacchride obtained from starch. Strong bitter taste of carbapentane citrate syrup was reduced to approximately 50% by preparing a 1:1 complex with cyclodextrin. The suppression of bitter taste by cyclodextrin was in increasing order of alpha, gamma, beta cyclodextrin.

Molecular complexes of drug with other chemicals[7-8]

The solubility and adsorption of drug can be modified by formation of molecular complexes. Consequently lowering drug solubility through molecular complex formationcan decrease the intensity of bitterness of drug.Higuchi and Pitman reported that caffeine forms complexes with organic acids that are less soluble than xanthine and as such can be used to decrease the bitter taste of caffeine.

Solid dispersion system[9]

Solid dispersion has been defined as dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting (fusion) solvent or melting solvent method. Solid dispersion is also called as co precipitates for those preparation obtained by solvent method such as co precipitates of sulphathiazale and povidone. Solid dispersions using insoluble matrices or bland matrices may be used to mask the bitter taste of drugs. Also using them as absorbates on various carriers may increase the stability of certain drugs.

Microencapsulation[10]

Microencapsulation as a process has been defined by Bokan as a means of applying relatively thin coating to small particles of solid, droplets of liquid and dispersion. This process can be used for masking of bitter tasting drugs by microencapsulating drug particles with various coating agents. Coating agents employed includes gelatin, povidone, HPMC, ethyl cellulose, Bees wax, carnauba wax, acrylics and shellac. Bitter tasting drugs can first be encapsulated to produce free flowing microcapsules, which can then be blended with other excipients and compressed into tablets. Microencapsulation can be accomplished by variety of methods including air suspension, coacervation, phase separation, spray drying and congealing, pan coating, solvent evaporation and multiorifice centrifugation techniques.

Multiple Emulsions[11-12]

A novel technique for taste masking of drugs employing multiple emulsions has been prepared by dissolving drug in the inner aqueous phase of w/o/w emulsion under conditions of good shelf stability. The formulation is designed to release the drug through the oil phase in the presence of gastrointestinal fluid.

Using Liposome's[13]

Another way of masking the unpleasant taste of therapeutic agent is to entrap them into liposome. For example, incorporating it into a liposomal formulation prepared with egg phosphatidyl choline masked the bitter taste of an antimalarial, chloroquine phosphate in HEPES (N-2-hydroxyetylpiperzine-N'- 2- ethane sulfonic acid) buffer at pH 7.2.

Prodrugs[14]

A prodrug is a chemically modified inert drug precursor, which upon biotransformation liberates the pharmacologically active parent drug. Examples of drug with improved taste are given below.

ISSN: 0976-7126

Table No.1: Prodrugs with improved taste

Sr. no.	Parent drug	Prodrug with improved taste
1	Chloramphenicol	Palmitate ester
2	Clindamycin	Palmitate ester
3	Triamcinolone	Diacetate ester

Complexation with Ion exchange resins.

Drugs are complexed with ion exchange resins. Depending upon the nature of the drug the resins are selected. In the present study the taste masking was done by two different methods.

- By complexation with ion exchange resins.
- By mass extrusion method (Dispersion coating)

Ion Exchange Resin[15-19]

Another popular approach in the development of taste masking is based on ion exchange resin. Ion exchange resins are solid and suitably insoluble high molecular weight polyelectrolytes that can exchange their mobile ions of equal charge with the surrounding medium. The resulting ion exchange is reversible and stiochiometric with the displacement of one ionic species by another. Synthetic ion exchange resin has been used in pharmacy and medicine for taste masking or controlled release of drug as early as 1950 s.The adsorption of bitter drugs onto synthetic ion exchange resins to achieve taste coverage has been well documented. Borodkin *et al.* prepared high potency adsorbates of methapyrilene, dextromethorphan, ephedrine, pseudoephedrine by column procedures using a polymethacrylic acid ion exchange resin. Taste evaluation of the adsorbates showed a significant reduction in the bitterness of the drugs. Coating the adsorbate particles with 4:1 ethyl cellulose - HPMC mixture reduced the bitterness further. Taste coverage was maintained after incorporation of the coated adsorbate into chewable tablets. Strong acid cation resins (sulfonated stynedivinylbenzene copolymer product) can be used for masking the taste of basic drugs. Polystyrene matrix cation exchange resins have been used to mask the bitter taste of chlorpheniramine maleate, ephedrine hydrochloride, and diphenhydramine hydrochloride. Extreme bitterness of quinolones has been achieved by ion exchange resin such as methacrylic acid polymer cross linked with divinylbenzene.

Results and Conclusion

There are number of technologies available which effectively mask the objectionable taste of drugs but require skillful application which does not affect the bioavailability of drug. With application of these techniques and proper evaluation of taste masking effect one can improve product preference to a large extent. Moreover, the development of taste masking methodology requires great technical skill, and the need for massive experimentation.

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