Review article

TASTE MASKING IN PHARMACEUTICALS: AN UPDATE

Jha Kumar Sajal*[1], Sharma Raj Uday[1] and V Surendra[1]
[1]Acharya & B.M. Reddy College of Pharmacy, Soldevanahalli, Bangalore-56009

For correspondence: Sajal kumar Jha,Acharya & B M Reddy College of Pharmacy, Soldevanahalli,Bangalore-560090.
E-mail: jha_sajal@indiatimes.com
Received on: 19-08-2008; Accepted on :18-09-2008

Abstract
Taste is an important factor in the development of dosage form. Nevertheless it is that arena of product development that has been overlooked and undermined for its importance. Taste masking technologies offer a great scope for invention and patents. Several approaches like adding flavors and sweeteners, use of lipoproteins for inhibiting bitterness, numbing of taste buds, coating of drug with inert agents, microencapsulation, multiple emulsion, viscosity modifiers, vesicles and liposomes, prodrug formation, salt formation, formation of inclusion and molecular complexes, solid dispersion system and application of ion exchange resins have been tried by the formulators to mask the unpleasant taste of the bitter drugs. The present review attempts to give a brief account of different technologies of taste masking with respect to dosage form and novel methods of evaluation of taste masking effect.

Key words: Taste masking, microencapsulation, multiple emulsion, viscosity modifiers, Liposomes, prodrug, un pleasant taste.

INTRODUCTION

Taste is one of the most important parameters governing patient compliance. Undesirable taste is one of several important formulation problems that are encountered with certain drugs. Oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers, especially for pediatric patients. Several oral pharmaceuticals, numerous food and beverage products, and bulking agents have unpleasant, bitter-tasting components. So, any pharmaceutical formulation with a pleasing taste would definitely be preferred over a competitor's product and would translate into better compliance and therapeutic value for the patient and more business and profits for the company. The desire of improved palatability in these products has prompted the development of numerous formulations with improved performance and acceptability. This article reviews the earlier applications and methodologies of taste masking and discusses the most recent developments and approaches of bitterness reduction and inhibition for oral pharmaceuticals [1].

The methods most commonly involved for achieving taste masking include various chemical and physical methods that prevent the drug substance from interaction with taste buds. The simplest method involves use of flavor enhancers. Where these methods fail more complex methodologies are adopted. Various techniques have been identified for taste masking which include polymer coating, inclusion complex formation with cyclodextrin, use of ion exchange resins, solubility limiting methods, liposome, multiple emulsions, use of anesthetic agents, etc. The present review attempts to give a brief account of different technologies of taste masking with respect to dosage form along with novel methods of evaluation of taste masking effect.

Two approaches are commonly utilized to overcome bad taste of the drug. The first includes reduction of drug solubility in saliva, where a balance between reduced solubility and bioavailability must be achieved. Another approach is to alter the ability of the drug to interact with taste receptor. An ideal taste masking process and formulation should have the following properties [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.

TASTE MASKING TECHNOLOGIES:

Polymer coating of drug:

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, not adversely affecting the intended drug release profile [3]. 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 [4].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's as fine as 50µm, are fluidized in expansion chamber by means of heated, high velocity air and the drug particles are coated with a coating solution introduced usually from the top as spray through nozzle. The coated granules are dried with warm air [5] **.**

Formation of 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. Beta-cyclodextrin is most widely used complexing agent for inclusion type complexes. Strong bitter taste of carbapentane citrate syrup was reduced to approximately 50% by preparing a 1:1 complex with cyclodextrin [6].

Solid dispersion

Solid dispersions using insoluble matrices or bland matrices may be used to mask the bitter taste of drugs[7-8]. Also using them as absorbates on various carriers may increase the stability of certain drugs.

Microencapsulation

This process can be used for masking of bitter tasting drugs 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. The bioavailability of flucoxacillin preparation micro-encapsulated for taste abatement with 17% ethyl cellulose found to be better compared to commercially available flucoxacillin preparation [9].

Mass extrusion

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets.

Ion exchange resin complexes:

Ion exchange resins (IER) have received considerable attention from pharmaceutical scientists because of their versatile properties as drug delivery vehicles. In past few years, IER have been extensively studied in the development of Novel drug delivery system and other biomedical applications. Several ion exchange resin products for oral and peroral administration have been developed for immediate release and sustained release purposes. Bitter tasting drugs can be absorbed

onto ion exchange resins, thus effectively removing them from solution during the transit through the mouth, at salivary pH 6.7, remains in intact form making the drug unavailable for the taste sensation. Various studies have revealed that ion exchange resins are equally suitable for drug delivery technology [10].

- **Kyron T-104:** Kyron T104 is derived from Crosslinked polymer of Methacrylic acid. Kyron T104 has carboxylic acid functionality which enables its use as a TASTE MASKING AGENT, while the Crosslinked porous nature makes it suitable as a SUSTAIN RELEASE AGENT.

- **Kyron T-134:** Kyron T134 is derived from crosslinked polymer of acrylic acid and has a K+ ionic form. Kyron T134 is a very high purity polymer finding use in pharmaceutical formulations as a TASTE MASKING AGENT.

- **Kyron T-154:** Kyron T154 is derived from crosslinked polymer of Styrene and Divinylbenzene form. Kyron T154 has Sulphonic Acid functionality which enables its use as a TASTE MASKING agent while the cross linked porous nature makes it suitable as a Sustained Release Agent.

- **Kyron T-114:** Kyron T114 is derived from crosslinked polymer of Methacrylic acid. Kyron T114 has carboxylic acid functionality which is enables its use as a TASTE MASKING AGENT. Kyron T114 is a very high purity polymer finding use in pharmaceutical formulations as a TASTE MASKING of certain drugs, particularly B-lactam antibiotics.

Multiple Emulsions

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 [11-12].

Development of Liposome

Another way of masking the unpleasant taste of therapeutic agent is to entrap them into liposome. For example, incorporating into a liposomal formulation prepared with egg phosphatidyl choline masked the bitter taste of chloroquine phosphate in HEPES (N-2-hydroxyetylpiperzine-N'- 2- ethane sulfonic acid) buffer at pH 7.2 [13].

Prodrug concept

A prodrug is a chemically modified inert drug precursor, which upon biotransformation liberates the pharmacologically active parent drug [14]. Examples of drug with improved taste include conversion of chloramphenicol to palmitate ester.

Use of flavor enhancers:

The materials for taste masking purpose have often been classified depending upon the basic taste that is masked. Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices and distilled fractions of these. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups or spirit [2]. Apart from these conventional materials many compositions have been found to show effective taste masking abilities with improved flavor such as alkaline earth oxide, alkaline earth hydroxide or an alkaline hydroxide. Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and mixtures thereof. Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution. Unlike natural flavors are usually stable. Aspartame is used as a prominent sweetener in providing bitteness reduction [15].

Techniques Employed for Taste Masking of Different Dosage Forms

Tablets:

Most of the tablets can be effectively masked for their taste by applying inert polymer coatings that prevent the interaction of the drug substance with the taste buds. Nevertheless, attempts have been made time and again by several workers to investigate and explore

the use of newer materials in bad taste abatement and good taste enhancement.

Granules / Powders:

Granules for reconstituting as liquids (e.g. sachets, sprinkle capsules & powders) hold a high share of pediatric and geriatric market. A large number of patents on the topic highlight the significance of the same. Thus taste masking of granules becomes an important priority in product development and varied technologies and methodologies exist for the same as illustrated below. Hayward *et al*. have reported a granular composition for taste masking comprising of drug core of a NSAID and methacrylate ester copolymers as coating agents for taste masking [16]. The method comprises of coating the drug cores with separate layers of aqueous dispersions of the copolymers. Granules of the invention could be used in the preparation of chewable tablets, which had good palatability and bioavailability.

Liquids:

They present a major challenge in taste masking because the majority of pediatric preparations are syrups and suspensions although, the aforementioned methodologies have- also had been used for improving liquid taste and few patents in this area are worth mentioning. Nakona *et al*.masked the bitter taste of vitamin B1 derivatives such as dicethimine by formulating with menthol and or polyoxyethylene, polyoxypropylene for formulating oral liquids [17].Meyer *et al*. used prolamine , applied as single coating in weight ratio 5% to 100% relative to active substance being coated result in the production of a liquid suspension which effectively masked the taste of orally administered drugs which are extremely bitter [18]. Prolamine coating does not restrict the immediate bioavailbility of the active substance Prolamine coating is effective in masking the taste of antibiotics, vitamins, dietary fibers, analgesic, enzymes, and hormones.

Evaluation of Taste Masking Effect

Sensory analysis has been used in developed countries for years to characterize flavors, odors, and fragrances. Historically expert provided formulation scientist with subjective data on the composition of one product with another. Soutakagi, *et al*. invented a multichannel taste sensor whose transducer is composed of several kinds of lipid/polymer membrane with different characteristics, which can detect taste in manner similar to human gustatory sensation [19]. Taste information is transformed into a pattern composed of electrical signals of membrane potential of the receptor part. It was reported that suppression of bitterness of Quinine and a drug substance by sucrose could be quantified by using multi channel taste sensor. The present method can be expected to provide new automated method to measure the strength of drug substance in place of sensory evaluation. Evaluation of the taste masking effect from coated microsphere can de done by determining the rate of release of the drug from the microspheres. Similarly for evaluating the taste masking effect by ion exchange resin, the drug release rate can serve as an index of the degree of masking achieved. Other methods include evaluation by a trained flavor profile panel and time intensity method in which a sample equivalent to a normal dose was held in mouth for 10 seconds. Bitterness level are recorded immediately and assigned values between 0-3 [20].

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.

References:

1. Sohi H. Sultana Y and Khar RK. Taste masking technologies in oral pharmaceuticals: recent developments and approaches. Drug Dev Ind Pharm. 30(5), 2004, 429-48.
2. Chatap V K. A Review on Taste Masking Methods of Bitter Drugs. Pharmainfo.net.
3. Mauger JW. Robinson J R. and Dennis H. US Patent, 1998, 5,728,403.
4. Shen R.W. US Patent, 1996, 5,552152
5. Davis J D. Drug Cosmet. India. Encyclopedia of Pharmaceutical Technology, Volume II (2000).
6. Kurusumi T. Imamori K.and Isawa A. Japan Patent, 1991,03236616

7. Lachman L. Theory and practices of Industrial pharmacy, Third Edition, 1986,450.
8. Liberman H A. Lachman L. Pharmaceutical Dosage forms, Tablet volume 1989, 11-14, 99-101,136,159-160,198-199,210-212.
9. Maccari M. Controlled Release Technologies Method, Theory and Applications, 1stEd. Volume II 1980,113.
10. Jain N K. Advances in controlled and Novel Drug delivery, 1stEd 2001, 290-306.
11. Rosoff M. Pharmaceutical dosage form disperse system, vol I, Marcel the Dekker, New York 1988, 245-283.
12. Rao Y M. Bader F. and Leon Maura. Masking the taste of chloroquine by multiple emulsion. The East Pharm, 11, 1993,123.
13. Kasturagi Y. Sugiura Y C. Lec. Otsugi K. and Kurihara., Selective inhibition of bitter taste of various drugs by lipoprotein. Phram.Res. 12, 15, 1995, 658-662.
14. Brahmankar D M. and Jaiswal S B. Biopharmaceutics and pharmacokinetics, 1stEd. Vallabh Prakashan, New Delhi1995; 162-163.
15. Mastsubara Y., Kawajan A., Ishiguro F., Granules with suppressed bitterness, Jp patent 1990;02,056,416.
16. Hayward, M., U.S. Patent, 37277, 1998.
17. Nakano, H., Hasegawa, K., Japan Patent, 11139992, 1999.
18. Meyer, G., Mazer, T., U.S. Patent, 5599556, 1997.
19. Soutakagi K T. Koichiwada H Y. and Kenzo T. J. Pharm. Sci. 1998; 87(5): 552.
20. Roy G M. Pharm. Tech. 1994; 62.

Source of support: Nil, Conflict of interest: None Declared