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Taste Masking Approaches for Unpleasant Taste Drugs

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Abstract

Improving patient compliance with significant therapeutic value is highly important to be in concern while developing an oral dosage form. Undesirable taste of the drug can influence patient compliance and product quality. Health care providers are dealing with bitter drug issues while orally administering to each pediatric patients and elderly patients. Masking the unpleasant taste of bitter drugs is a potential tool for the enhancement of patient compliance and success of the product. Various approaches and methodologies of development for masking the undesirable taste of drugs with consideration of applications, evaluations, and technologies for taste masking. This review covers the factors need to be considered for taste masking, different taste masking approaches and recent technologies developed for taste masking. The brief overview provided in this review will helps readers to explore further in a particular aspect of their interest.

Keywords

Taste masking, Inclusion complexes, Resins, Microencapsulation

Introduction

Pediatrics and elderly patients specifically; are difficult to control while administering the unpleasant taste of specific drug, leading to administer fewer doses, which cause less efficiency. Taste masking is the proper way to improve the quality of the treatment [1]. The taste masking defined as a perceived decrease of an unpleasant taste of active pharmaceutical ingredients [2]. There are several applications and methodologies of taste masking, and each method has specific advantages. The easiest method involves the use of flavor enhancers and in case no results found with this method, then complex methodologies comes on the board. The techniques found to be effective on taste masking are; inclusion complex formation with cyclodextrin, ion exchange resins, granulation, liposome, microencapsulation, multiple emulsions, prodrug approach, polymer coating, solubility limiting methods, and the use of anesthetic agents [3]. Then evaluation of the taste masking is essential, such as evaluation of liquid and solid dosage forms, evaluation of microspheres, recent innovations, recent trends (AdvaTab ODT Technology), recent trends (Microcaps ODT Technology), liquitard ODT Technology, for multiplex and formulcoat, and linecaps. Moreover, a recent innovation tastes masking by using electronic tongue.

Factors Taken into Consideration of Taste Masking Formulation

Extent of bitter taste

Strongly bitter taste medicines have the ability even with the least exposure; to perceive the bad taste. The optimum efficient technology for strong bitter drugs is coating, nevertheless, it reduces the efficiency of the technique. Moreover, microencapsulation of a potent bitter drug is not enough to provide the taste masking of liquid oral suspensions [4,5].

Specific dose load

As the dose is small, it is easy to mask the taste of the specific medicine with the flavoring agents. While in the case of high doses required, flavoring agents may fail to mask the taste. An ideal taste masking is coating with sweeteners for the suitable final dosage form size [1,4].

Shape of the drug

The characteristics of the drug can reduce the efficiency of the taste masking. For instance, when the shape of the drug is irregular, taste masking will be insufficient and less effective. Moreover, the small particle size as well can affect the taste masking overcome [1,4].

Taste Masking Techniques

Taste masking with flavors, sweeteners and amino acids

The simplest approach for masking the taste of active pharmaceutical ingredients is

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using flavors, sweeteners and amino acids technique. While in the case of highly bitter drugs, this technique is not effective enough. The importance of using taste masking techniques with artificial sweeteners is to improve the efficiency of the techniques. An excipient such as flavors, act by enhancing the formulation with better taste. Example of flavors is; menthol and bitterness inhibitors. An additional excipient is sweeteners such as Sucrose, Glucose, Fructose, Sorbitol, Mannitol; and they are highly water soluble dissolving in saliva with coating the taste buds [6-8].

Polymer coating of the drug

The best technique for taste masking is a polymer coating, due to its acts as a physical barrier to the drug particles, which result in minimizing the interaction between the drug and the taste buds. The various polymer coating can be as hydrophobic polymers, hydrophilic polymers, lipids, and sweeteners [6-8].

Formation of inclusion complexes

Usually, the formation of inclusion complex method is used when low dose drug is required. This technique works by the host and guest link, where the host is the complexing agent; and the guest is the active moiety. The purpose of the complexing agent is to mask the unpleasant taste of specific drug either by reducing its oral solubility or reducing the amount of the drug particles to taste buds. The most common use complexing agent is cyclodextrin, due to its sweet in taste, non-toxic, and cyclic oligosaccharide acquired from starch. In inclusion complexes, the Vander Walls forces are predominantly involved [5-8].

Ion exchange resin complexes

The ion exchange resins groups have the ability to exchange charge counter ions, therefore absorbing the ions into the polymer matrix. They are high molecular weight water insoluble polymers and synthetic organic polymers containing a hydrocarbon chain. According to the taste masking, it depends on the nature of drug whether weak cation exchange; such as carboxylic acid moieties or weak anion exchange; such as predominantly tertiary amine substituents [5-8].

Solid dispersion

Dispersion of one or more active ingredients; in an inert carrier of solid state prepared by the melting-solvent method is known as a solid dispersion. This technique is used for masking the bitter drug taste with the help of polymers, sugar, and other suitable agents. Various carriers are used in a solid dispersion method; consist of ethylcellulose, hydroxypropyl methylcellulose, mannitol, polyethylene glycols, povidone, and urea [5-8].

Microencapsulation

The method of coating active pharmaceutical ingredients either solid or liquid droplets with a polymeric material; is called Microencapsulation. There are various types of coating agents such as; beeswax, carnauba wax acrylics, ethylcellulose, gelatin, hydroxyethyl cellulose, povidone, and shellac. By using Microencapsulation method, different techniques are used for achieving taste masking; such as phase coacervation, polymerization, solvent evaporation, and ionization [6-8].

Liposomes and multiple emulsions

Masking the bitter taste of the drug using multiple emulsions technique is a good approach. This technique is achieved by dissolving the active pharmaceutical ingredient in the inner aqueous phase of w/o/w emulsion. Those are in which internal aqueous phase and the external aqueous phase are separated by the oil phase. Another type is o/w/o emulsion, in which water globules are containing oil globules. The effectiveness of masking the bitter taste using both types of multiple emulsions of chloroquine phosphate is high. Liposomes are also good taste masking methods, and they are carrier molecules containing different layers of lipids; in which the unpleasant taste of specific drug is entrapped within the lipid molecule. The bitterness of the active drug can be inhibiting by phospholipids. Different examples of phospholipids; are phosphatidic acid, phosphatidylinositol, soya lecithin [9].

Prodrug method

Prodrug approach is known as chemically inactive molecules, but due biotransformation happens to the prodrug, it converts to the active compound. Prodrug method achieved by changing the molecular formation of the initial molecule, and the amount of the unpleasant taste receptor –substrate adsorption can be modified [6-9].

Taste Masking with Lipophilic Vehicles

Masking the taste with lipids, oils, polyalcohols, and surfactants; results in increasing the viscosity which coat the taste buds. While formulation, a large excess of lecithin substances required to control unpleasant taste drugs [5-10].

Formation of salt and derivative

Salt preparation tends to decrease the solubility of the drug by altering the chemical group which is responsible for the unpleasant taste. To form an ionized drug molecule, many salts of organic compounds are formed by addition or by removal of the proton. After formulation, it neutralized with a counter ion [4,7,10].

Taste masking with effervescent formulations

Sodium bicarbonate is used to form an effervescence effect to release carbon dioxide. When the effervescent preparation is added to water, the sodium bicarbonate reacts with the acid and the remaining solution known as carbonated water. The drug dissolves in the carbonated water which helps to mask the unpleasant taste [3,7,11].

Evaluation of the Taste Masking

Evaluation of liquid and solid dosage forms

E-tongue is a multi-channel taste sensor, and it acts as a human tongue. It provides a fast and simple assessment of oral formulation. The taste sensor contains a transducer that consists of polymer and lipid membrane, which act by transforming taste information into electrical signals of the membrane [11-13].

Evaluation of microspheres

When the rate of the drug release from microspheres is known, the index of the degree of taste masking is achieved [11,14,15].

Recent Innovations

Alpha MOS is a taste analyzing system; that contains a taste sensor composed of silicon transistors with an inorganic coating that manages the selectivity and sensitivity of each sensor. The sensor can approximately last for one year [4,16].

AdvaTab ODT technology is developed by APTALIS Pharmaceutical technologies, which features with high physical stability, stable during package and transport, pleasant taste, and good patient compliance. Also, coating method is used for **Microcaps ODT**technology. The coating is a polymer membrane which eradicates the unpleasant taste of the drug. There are several advantages with Microcaps ODT technology, such as taste masking in a precise way, good release, and patient [18]. **Liquated ODT** technology provides an effective, suitable, and taste-masked powder formulation in a single dose sachet; which can be administered as a suspension or sprinkle [4,18].

Formulplex and Formulcoat is another technology that masks the taste by coating the micro or nano-sized particles with a non-organic solvent at room temperature [11,18] .**KLEPTOSE® Linecaps technology uses** pea maltodextrin for masking the unpleasant taste of the drug by reducing the total amount of drug particles exposed to the taste buds [19,20].

Conclusion

Masking the obnoxious taste must be in consideration toenhance the patient compliance. The aim of the techniques mentioned in the

review is to have an effective taste masking. Researches of maskingthe taste drug delivery system are essential for the treatment quality. An ideal taste masking technique should have excellent patient compliance, additionally avoidance of interaction with drug release.

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