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Review

Film coatings for taste masking and moisture protection

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ABSTRACT

Taste masking and moisture protection of oral dosage forms contribute significantly to the therapeutic effect of pharmaceutical and nutraceutical formulations either by ensuring patient compliance or by providing stability through shelf life of the dosage form. Among different types of taste, bitter taste is the most relevant for patient acceptance because of the extremely high sensitivity. As hydrolysis is the most common mode of degradation of an active ingredient, moisture protection plays a vital role in the stability of the active during manufacturing and storage. Optimized oral dosage forms need to reliably hinder the release of bitter drug molecules in the mouth or ensure stability of the active compound, while also ensuring fast drug release in the stomach to enable early therapeutic onset. Besides different formulation concepts, film coating is found to be the most effective and commonly used approach for taste masking and moisture protection. Film coating can be achieved through the use of water-soluble, cationic, anionic or neutral insoluble polymers from different chemical structures. Cationic polymers provide efficient moisture protection as well as taste masking without influencing the release of the drug in the gastric fluids. Polymers may be sprayed onto various types of cores from dispersions or solutions in organic, solvents or water in drum or fluidzed bed coaters. Applied quantities need insuring complete coating thickness ranging from 0.5 to 50 μm or more finally. Insulating excipients, such as hydrophobic plasticizers, lipids, pigments or other insoluble substances will influence the functionality of films. Organoleptic tests are still common in testing the quality of taste-masked formulations. Recently, multi-channel taste sensors have been developed to quantify different types of taste. Dynamic vapor sorption technique and studies at elevated temperature provide effective concepts study the efficacy of the formulations. Efficient taste masking and reliable moisture protection of solid oral dosage forms can be achieved by film coating implementing the options of pharmaceutical polymers and processes.

Contents

1. Introduction: needs and concepts

1.1. Need and concepts of taste masking

The beneficial therapeutic effect of pharmaceuticals is dependent on regular dosing following manufacturer advice. The oral,

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self-dosage route is the most common method for the application of many drugs. However, patients tend to neglect instructions when they are inconvenient or unpleasant. Particularly for oral pharmaceuticals, disagreeable taste – besides frequent daily dosing – is one of the main reasons for patients to refrain from regular dosing. Among the different taste sensations, bitterness is the most repellent. For oral dosing in particular, compliance depends significantly on the taste of the dosage form. Thus, masking bitter taste is the key parameter to improving patient compliance as well as the therapeutic efficiency of oral pharmaceuticals (Valleri et al., 2004). Measures to mask the taste of oral dosage forms must include efficiency, but also avoid any negative effect of sensory awareness, such as mucosa irritation, roughness in the mouth or hindered swallowing. Another important aspect is to not negatively affect the bioavailability of the active compound by hindering its release or delaying its effect. This can be accomplished by designing a release kinetic which functions over an extended time period after ingestion.

Several concepts of taste masking for pharmaceuticals have been developed and put into practice. Molecular concepts include chemical modifications, such as the prodrug approach (i.e. esterification with fatty acids, Brahmankar and Jaiswal, 1995), or salt formation using either anions (i.e. organic acids, Sohi, 2004; JP, 1992) or cations such as magnesium (Nanda et al., 2002a) or interaction with ionogenic polymers, such as (meth)acrylates (EP, 2003; WO, 2003a; Sharma and Lewis, 2010). Physical taste masking on a molecular basis may be achieved by complexation (i.e. inclusion in cyclodextrins, Swarbrick and Bolan, 1990), its derivatives (i.e. hydroxypropyl-beta-cyclodextrin). Additionally practiced are concepts of binding to ion exchange resins, which have been revealed to be effective taste masking agents. Cross-linked polymers and copolymers of methacrylic acid are available in pharmaceutical grades – and optimized variations for different classes of drug may be tested (Jain, 2001). Formulation concepts for taste masking include the incorporation of specific flavor enhancers. Examples may be sweeteners, i.e. aspartame (JP, 1990), amino acids and their phosphate derivatives, natural products including fruit juices, aromatic oils, herbs, alkaline earth oxides, hydroxides and spices in forms such as high concentrated extracts or dried solids, as well as either alcoholic or aqueous solutions (Chatap, 2007). Further functional excipients, which improve the organoleptic perception of unpleasant oral formulations, are effervescent agents or rheological modifiers, such as gel forming gums.

The type of taste masking suitable for final formulation is very much influenced by the selected manufacturing process. Processes for applying taste masking are melt and liquid extrusion, spray or freeze drying to form solid dispersions or agglomerates, coating with lipids or waxes, formation of lipid vesicles or multiple emulsions (preferably for oils, Rossof, 1988 or liposomes). Coating processes are preferably used for taste masking of tablets or minitablets. Commonly applied processes include liquid melt or powder coating with lipids, waxes and polysaccharides. Compression coating is an unconventional, alternative method with limited practical relevance. A modern variation of coating techniques is film coating particularly suitable for microencapsulation of small particles to form taste masked multi-unit dosage forms. The functional coating is applied by spray processes from organic or aqueous solutions or preferably from aqueous solutions or dispersions including natural or synthetic polymers. Among these varieties of formulation designs, film coating provides the highest efficiency and has thus gained the broadest importance.

1.2. Need and concepts of moisture protection

An active pharmaceutical ingredient in a dosage form needs to be stable until the end of its shelf life, in order to ensure its efficacy and safety for the patient. Degradation of the active ingredient can occur though hydrolysis, thermal degradation, oxidation, light, microorganisms or any other chemical reaction that renders the active ineffective for its intended purpose (Ahlneck and Zografi, 1990). Of the various modes of degradation, hydrolysis is most commonly found to influence the stability of the active. Amorphous forms of a material, which have a high internal energy and a specific volume, are thermodynamically in a metastable form. They are converted to a more stable crystalline form, which has lower solubility and bioavailability as compared to the amorphous states. Moisture influences the glass transition temperature and thus affects the stability of such systems. Therefore, moisture is considered to be one of the most important factors influencing the stability of a pharmaceutical formulation.

Atmospheric humidity is one of the main sources of moisture that influences the active ingredient chemically or physically. However, a formulator also needs to consider the inherent moisture of some of the excipients, which could be potential contributors of water molecules for hydrolysis. Many active ingredients are hygroscopic in nature and need to be protected from moisture. In addition, moisture protection is often needed when the cores are hygroscopic (Prinderre et al., 1997a), as is the case with many herbal products. Special attention needs to be given to the designing of such formulations in order to prevent degradation due to hydrolysis (Luftensteiner et al., 1999). For most powders, residual humidity modifies their mechanical and rheological properties. Hence, the concept of water adsorption on the surface of solids is of utmost importance in pharmaceutical studies.

A number of formulation approaches have been developed to reduce hydrolytic degradation as well as to mask the taste of the active pharmaceutical ingredient. These approaches have been described below in detail.

Protecting a formulation from hydrolytic degradation is also possible through appropriate packaging, however it does not exclude moisture from seeping into the container during multiple openings. Protecting the cores with a moisture barrier film is found to be more appropriate, since it also eliminates the problem caused by multiple openings of the container. Thus, of all the alternatives available, coating the formulations is found to be the most appropriate and widely used technique.

Moisture-protective polymer coatings are often used to prolong the storage stability of water-sensitive drugs, including many herbal extracts (Haleblian and Goodhart, 1975; Rudnic and Kottke, 1996; Du and Hoag, 2001).

While developing a coating formulation for a moisture sensitive drug, the following strategies need to be considered during the entire development process:

- Designing the dosage form with non-hygroscopic/low water-activity excipients.
- Formulating the core with the least amount of inherent moisture.
- Providing the dosage form with a moisture protective coating.
- Packaging the dosage form with an appropriate moisture-resistant material.

1.3. Mechanism of taste sensitivity and moisture uptake

To protect it, evolution has provided the body with taste in response to dissolved substances in the oral cavity. Taste buds, located primarily on the tongue, consist of open pores on the surface. These are onion shaped organelles of receptor cells carrying G-protein coupled receptors (GPCRs). The taste of compounds is perceived by the binding of tastants (e.g. medicines or food) with GPCRs in the taste buds. Interactions of tastants with the receptor induce the release of the G-protein gustucin, which