A REVIEW ARTICLE ON FORMULATION AND EVALUATION STUDY OF ODT

Kumar Dinesh*, Kamble P.R.
Department of Quality Assurance, B.N College of Pharmacy, Udaipur, Rajasthan, India (313001)

ABSTRACT

Cefpodoxime Proxetil (CP) is a third generation cephalosporin antibiotic given orally, used in the treatment of respiratory and urinary tract infections. It is also used in children for treating pharyngitis or tonsillitis. However it is very bitter in taste and practically slightly soluble in water. Hence, the main objective of the present work is to mask the bitter taste of Cefpodoxime proxetil and formulate it into Orally Disintegrating Tablets (ODTs). Such taste masked and easy to use formulations have been found to be more patient compliant with a profound application especially in the pediatric and geriatric populations. Ion exchange resins (polacrillin potassium) have been employed as taste masking agents to achieve the purpose. Ion exchange resins are also known to be useful as disintegrating agents superior to other conventional agents. Hence, the study undertaken was aimed at using ion exchange resins for the dual purpose of taste masking as well as rapid disintegration in context of formulating taste masked Orally Disintegrating Tablets (ODTs). Such a dosage form may be swallowed in the form of dispersion, as it is expected to disintegrate quickly when in contact with saliva. But the bitter taste may not be perceived because the ion exchange resin complex does not release the drug at the salivary pH due to the lack of cations which can exchange with the drug, resulting in no direct contact of the drug with the taste buds. Further when it comes in contact with acidic environment of the stomach, the complex will be broken down due to presence of large number of exchangeable cations (H+) hence, quickly releasing the drug which may then be absorbed.
1. INTRODUCTION

The development of Orally Disintegrating Tablets (ODT’s) has received an escalating interest among pharmaceutical researchers and industries, especially over the last decade. The new European regulations on pediatric medicines and recent WHO recommendations have stressed on an increased need for research into novel pediatric-appropriate dosage forms.  

At present, ODTs are the only quick-dissolving dosage form recognized by FDA which has been listed in Approved Drug Products with Therapeutic Equivalence Evaluations (also called the Orange Book).  

The ODT’s are designed to completely disintegrate or dissolve rapidly on coming in contact with saliva, in the absence of additional water hence, more patient compliant as compared to the traditional dosage forms. The U.S Food and Drug administration Center for Drug Evaluation and Research (CDER) terms the fast dissolving/dispersing oral dosage form as Orally Disintegrating Tablets (ODT) and defines as “a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.”

Oral fast-disintegrating dosage forms, also known as ‘fast-melt’, ‘fast-disintegrating’, ‘Mouth dissolving’ or ‘fast-dissolving’ dosage forms, are a relatively novel dosage form technology that involves the rapid disintegration or dissolution of the dosage form, which is either a tablet (the most common form) or a capsule, into a solution or suspension in the oral cavity, without the requirement of water. The dosage form begins to disintegrate immediately and rapidly after coming into contact with the salivary fluid, with complete disintegration normally occurring within 30–50 seconds after administration. The solution containing the active ingredients is swallowed and during the intestinal transit, the active ingredients

The major advantage of ODTs include improved patient compliance, including safe administration to patient who cannot swallow, such as the elderly, stroke victim and bed ridden patients and patients who refuse to swallow such as pediatrics, geriatric, and psychiatric patients.

The various taste masking approaches can be divided into the following methods:

1. Addition of flavoring and sweetening agents.
2. Microencapsulation.
3. Ion exchange resins.
4. Inclusion complexes.
6. Adsorption.
7. Prodrug approach.
8. Bitterness inhibitors.
9. Multiple emulsions.
10. Solid dispersion.

**Ion exchange resins.**

[Diagram of ion exchange process]

**Fig 1: Reproduced from Ref 9**

**ION EXCHANGE RESINS**

IE is the reversible interchange of ions (of like charge) between a liquid and a solid phase, involving no radical change in the structure and properties of the solid. The solid phases in the IE process are referred to as IER, and are usually the polymers with integrated ionic moieties. Based on the nature of the ionic species being interchanged, the IE process is known as either cation exchange (CE) or anion exchange (AE). The IER used in these processes are referred to as cation-exchange resin (CER) or anion-exchange resin (AER), respectively.

In practice, drug in an ionic form (usually in solution) is mixed with the appropriate IER to form a complex, known as ‘resinate’. The performance of resinate is governed by several factors, such as:

- pH and temperature of the drug solution;
Molecular weight and charge intensity of the drug and IER;
Mixing speed;
Ionic strength of the drug solution;
Degree of cross linking and particle size of the IER;
Nature of solvent and contact time between the drug species and the IER.

The chemistry of the resinate is such that the drug retains its characteristics, but is immobilized on a solid support. The interactions between the IER and drug, although primarily chemical in nature, are also partially a result of physical adsorption. These interactions are commonly referred to as ‘adsorption on IER’, rather than complexation on most occasions. The IE process, therefore, is generally regarded as a double-decomposition process, in which the IER used are able to provide the type of ion required to replace the one that is adsorbed from the solution. The ion of the IER, which can be exchanged for a drug counterpart, is called a ‘counter ion’. The affinity of counter and drug ions towards the IER is competitive. When resinate from the delivery system reaches the site of delivery, the exchange process is reverted, resulting in the liberation of free-drug ions. Therefore the ionic strength and pH at the site of delivery plays a key role in the liberation of immobilized drug from the resinate. Drug delivery at the desired target via the IE process occurs because of the presence of highly activated counter ions at the site, resulting in the exchange of ions and drug release. The IER devoid of drug is eliminated or biodegraded from or at the site of delivery. Figure 1 depicts the factors that affect the IE process involved in the delivery of a cationic drug.

The taste of pharmaceutical preparations is an important parameter governing patient compliance and commercial success in the market. The scope of IER for masking the undesirable taste of pharmaceuticals is unlimited. At salivary pH (6.8), resinate remains in intact form, making the drug unavailable for the taste sensation. As the formulation enters the upper segment of the GIT the environment changes to acidic and drug release takes place. Polystyrene matrix CER have been used to mask the bitter taste of chlorpheniramine maleate, ephedrine hydrochloride and diphenhydramine hydrochloride. The ionic binding of the drugs to polymeric materials such as Carbopol is emerging as an important mechanism of taste masking. However, as IER could also retard the release of drugs, a proper and careful selection of IER is essential to yield optimal taste masking without affecting the bioavailability. Generally, less cross-linked IER are helpful in taste masking. In present work, Cefpodoxime Proxetil was considered for taste masking and further
formulating it into an ODT formulation. Cefpodoxime proxetil is a third generation cephalosporin antibiotic given orally and most widely in the treatment of respiratory and urinary tract infections. It is also commonly prescribed for children in treating pharyngitis or tonsillitis. Hence an ODT formulation of the drug candidate would prove extremely beneficial for the pediatric and geriatric patients who commonly suffer from swallowing difficulties (Dysphagia). But the extremely bitter taste of this drug limits its direct utilization into an ODT. Hence, masking its taste becomes necessary while formulating it into an oral dosage form. The marketed formulations also suffer from the major drawback of unacceptable taste. Hence to overcome the drawback of existing formulations and to obtain effective taste the approach attempted in this study are formulation of orally disintegrating tablet with taste masked Drug-Ion Exchange Resin complexes.

REFERENCES