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Original Article

TASTE MASKING OF PRIFINIUM BROMIDE IN ORODISPERSIBLE TABLETS

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ABSTACT

Objective: In previous work, Prifinium Bromide had been successfully formulated as oro-dispersible tablets. However, Prifinium Bromide, a quaternary ammonium compound, has a bitter taste; therefore, taste masking was necessary to produce acceptable oro-dispersible tablets and enhance patients' compliance.

Methods: In this work, several attempts had been made to mask the bitterness of this drug. β-cyclodextrin inclusion complexes, solid dispersions of the drug in ethyl cellulose and methyl cellulose as well as loading the drug on Eudragit E100 have all been used. The selected granules were used to prepare oro-dispersible tablets and were evaluated.

Results: Drug-Eudragit granules E3 prepared by mass extrusion method gave less than 10% of drug in simulated saliva fluid and almost complete release in simulated gastric fluid after 2 minutes. Therefore, it was used to prepare oro-dispersible tablets formulas. In vitro disintegration time of formula T2 was 45.5 ± 7.7 seconds showed a complete drug release of Prifinium Bromide in phosphate buffer (pH 6.8) and (94%) in SGF (pH 2.1).

Conclusion: Loading of Prifinium Bromide on Eudragit E100 using mass extrusion method was the best method to overcome the disagreeable taste of the drug. They gave the least amount of drug released in simulated saliva fluid and passed the quality control tests of tablets after formulation as oro-dispersible tablets. They also gave good taste when tested in vivo.

Keywords: Prifinium Bromide, Orodispersible tablets, Taste masking of active ingredient, Mass extrusion method, Eudragit E100, β - Cyclodextrine.

INTRODUCTION

Oro-dispersible tablets (ODTs) entered the market in the 1980s as an alternative to tablets and other conventional dosage forms. ODT is defined as a tablet that disperses or disintegrates in less than one minute in the mouth before swallowing. It results in quick dissolution and rapid absorption, which provide rapid onset of action. It also provides an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules [1].

There are some challenges in the formulation and production of successful ODTs like the fast disintegration, tablet strength and porosity, moisture sensitivity, amount of drug and the size of tablet in addition to the drug organoleptic properties like solubility, stability and taste [2]. For drugs having disagreeable taste, several taste masking techniques were introduced to overcome this problem. Addition of Sweeteners and flavors is a well known technique that uses artificial sweeteners instead of natural sugars. Saccharin Sodium, Aspartame, Sucralose have all been used as sweeteners [3].

Layering process is another technique used to overcome the disagreeable taste of active pharmaceutical ingredient (API) which involves deposition of serial layers of API onto the granules of an inert starter seeds such as sugar spheres or microcrystalline cellulose beads and using a polymer that's usually not dissolve in pH of saliva [4].[5]

Taste masking could also be achieved by granulation to decrease the surface area subjected to the taste buds. [6]. Spray drying, on the other hand, serves to coat the API particles with polymers as done by Dionysios, *et al.* Where Cetirizine HCl taste-masked ODT using Eudragit® RL30-D in different ratios were prepared using a fluidized bed coating machine. [7].

Complexation is used to mask the bitter taste of API 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 [8]. Cyclodextrin is one of the widely used complexing agent in masking taste by inclusion complexes [9].

Other approaches are coaservation phase separation [10], ion exchange resins [11], solid dispersions [12] and extrusion method [13] have all been used to mask the disagreeable taste of the API.

The aim of this study is to develop a successful method to cover the bitter taste of previously prepared Prifinium Bromide (PBr) ODT [14] by trying different techniques and the preparation of a taste masked ODT using a previously prepared formula.

MATERIALS AND METHODS

Prifinium Bromide, Mannitol, Ethocel, Aspartam, Sucralose, Magnesium Stearate and Mint flavor were kindly supplied by Hikma Pharmaceuticals. Eudragit E100 (Evonik industries, Germany). β-Cyclodextrin (Sigma- Adrich, USA).

Avecil® HFE- 102 (AZ Chem for chemicals, Germany). VIVA Sol® Crosscarmellose sodium, VIVA Star®, HPMC hypromellose (JRS Pharma GMBH & Co., Germany). Banana and Pineapple flavors (Bell Flavors & fragrances, Germany).

Compatibility study

The compatibility of PBr with each of the used polymers (ethylcellulose, methylcellulose, mixture of ethyl and methyl cellolose, β-cyclodextrin and eudragit E100) has been investigated using differential scanning calorimetry (DSC). Each of the mentioned materials was scanned individually and then the PBr -polymer loaded granules were also analyzed. Each sample was weighed and subjected to heat range from 25°C to 300°C at a heating rate of 10°C/min under a (80 ml/min) flow of nitrogen [15].

Preparation of taste-masked granules

Preparation of inclusion complex

Prifinium Bromide and β-cyclodextrin were mixed in the ratio (1:3) and (1:6) (w/w) ratio to prepare granules B1 and B2, respectively, as in table 1. Ethanol 50% added with continuous mixing until a suspension is formed. The solvent was evaporated under reduced pressure by using rotary evaporator for 45 minutes. After solvent evaporation, PBr - β- cyclodextrine granules obtained where stored in a desiccator for further use [16].