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Research Article

FORMULATION OF PRIFINIUM BROMIDE AND PRIFINIUM BROMIDE –DICLOFENAC SODIUM COMBINATION AS ORODISPERSIBLE TABLETS

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ABSTRACT

Oro-dispersible tablets (ODTs) are solid dosage forms that are designed to be placed in the mouth, disintegrated in the saliva, and then swallowed without the aid of additional water in less than one minute; thus, enhance patient compliance especially for paediatrics and geriatrics. The aim of this study was to develop a simple and inexpensive method of manufacturing ODTs of Prifinium Bromide (PBr) using direct compression method and study the effect of different types and concentrations of superdisintegrants (SD) and diluens on the tablets characteristics. Then a combination of Prifinium Bromide-Diclofenac Sodium (PBr-DcNa) ODTs was to be prepared using the best formula of PBr ODTs.

Different formulas of PBr were prepared using different types and concentrations of SD as well as different diluents. The resulted tablets were evaluated to select the best formula especially regarding disintegration and dissolution. Then a combination of PBr-DcNa formula was prepared using the best PBr ODTs and evaluated.

Results showed that the formula contained crosscaramellose sodium (CCS) as SD, Avicel-mannitol combination as diluents gave the best results concerning disintegration (12), dissolution where total drug release was achieved in 2 minutes , and physical characteristics of the resulted tablets. In addition, combination of the two drugs was successful. No interaction between the two drugs was detected and the combination orodispersible tablets showed high release of both drugs (> 80%) in pH 6.8 in 20 minutes.

Keywords: Orodispersible tablets, Prifinium bromide, Diclofenac sodium, Superdisintegrant, Direct compression, Combination therapy.

INTRODUCTION

Solid dosage forms are convenient to patients as they are self-administered, medication is already in a distinctive measure, and therefore, accurate dose is given. They are also easier to package, distribute, and store.[1] One of the disadvantages of solid dosage forms is that particular classes of patients including geriatrics and paediatrics have difficulty in swallowing tablets or capsules. Furthermore, conventional tablets usually take longer time for disintegration, dissolution and drug absorption.[2]In view of that, scientists have developed Oro-dispersible drug delivery system, offering the convenience of a solid dosage form with the rapid onset of action[3]

Many processes are usually applied in the development of ODT. The most widely used methods are: Freeze drying, molding and conventional methods which include: direct compression, wet granulation and dry granulation.[4]

Oro-dispersible tablet (ODT) is "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue.[25]

Despite the advantages and the wide acceptance of ODTs in the market, many factors should be taken in consideration in their development process. Fast disintegration is the major specification of ODT which is attributed to quick access of water into tablet matrix resulting in rapid disintegration. Therefore, the basic approaches to develop ODTs include the use of highly water-soluble excipients, incorporating the appropriate disintegrating agent(s) and maximizing the porous structure of the tablet matrix.[5,6]

In addition, the physicochemical and organoleptic properties of the active drug substance such as solubility, chemical stability, and taste along with the intended dose can potentially affect the performance of ODTs.[7]

Combination therapy has been used to maximize therapeutic outcomes and enhance patients' compliance. For employers and healthcare insurers, it reveals that the combination therapy is more economic regarding packaging needed and less time consuming for the manufacture of products; which provides an industrial rationale for producing such combinations.[8]

Prifinium Bromide is an anticholinergic drug used to relieve smooth muscle spasms. Diclofenac Sodium (DcNa) is a non-steroidal anti-inflammatory drug (NSAID) with analgesic activity [26]

From a clinical therapeutics point of view, the rationale for using drug combinations to obtain a greater therapeutic effect with the combination that can be achieved with either drug alone and to obtain the same therapeutic effect as could be obtained with only one of the two drugs, but with fewer deleterious side effects or dose-limiting toxicities. Presumably, an ideal combination therapy would accomplish both of these goals.[9]

The aim of this study is to formulate directly compressible rapidly disintegrating tablets of PBr and investigates different factors affecting the formula like the effect of diluents, the type and concentration of superdisintegrant (SD) on the characteristics of the resulted ODTs, and perform physical and chemical evaluation of the prepared formulas. Also, to prepare ODTs that contain combination of PBr and DcNa for the use in diseases that need anticholinergic beside analgesic effect.

MATERIALS AND METHODS

Materials

PBr, DcNa, Crospovidone (CP), Mannitol, Lactose, Dibasic calcium phosphate (DCP), Aspartam, Magnesium Stearate (MgSt) and Mint flavor were kindly supplied by Hikma Pharmaceuticals. Avicel® PH102 (AZ Chem for chemicals, Germany). VIVA Sol® Crosscarmellose Sodium, VIVA Star® Sodium Starch Glycolate and VIVA Pharm®. Banana and Pineapple flavors (Bell Flavors & fragrances, Germany). Hydrochloric Acid 37% (Biosolve chimie SARL, France), and chloroform (VWR® Prolabo, EC).

Methods

Formulation of PBr ODT

Different formulas of ODT were prepared by accurately weighing the active pharmaceutical ingredient (API) and other excepients. Composition of each tablet is given in table 1 and the batch size was 200 gm.

The weighed PBr was added to diluent(s), SD, sifted colloidal silicon dioxide (Aerosil™), in polyethylene bag and mixed manually for