Formulation Development and Characterization of Itraconazole Granules

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ABSTRACT

Itraconazole is practically insoluble in water; large inter-individual and intra-individual variations of its oral bioavailability are reported. The main purpose of this study was to prepare and evaluate itraconazole granules for immediate release as drug delivery formulations. As a part of formulation optimization, different concentrations of hydroxypropyl-methyl cellulose (HPMC) E5 were taken for the preparation of itraconazole granules, and were optimized with different characteristics like size, shape, surface roughness, density, moisture content, assay and dissolution. Formulation optimization includes a detailed study of itraconazole granules with different concentrations of polymer. The results of the study showed that 6% of HPMC E5 is sufficient as a binding agent and gave good shape and surface, low moisture content, 100% assay and 98.24% drug release within one hour. Based on these results, it can be concluded that 6% HPMC E5 is suitable for formulation of itraconazole granules.

KEYWORDS: Granules; HPMC E5; itraconazole.

Introduction

Itraconazole is an oral antifungal agent with a broad-spectrum of activity. Itraconazole is most effective when drug concentration is maintained above the minimum effective concentration. Itraconazole is weakly basic (pKa = 3.7) and highly hydrophobic (octanol/water partition coefficient at pH = 8.1, log P = 5.66) (Grant et al., 1989). It is practically insoluble in water. Itraconazole belongs to the Biopharmaceutical Classification Systems Class II drugs categorized with low water solubility and high permeability (Amidon et al., 1995).

Granules are agglomerates of fine powders or granules of bulk drugs and excipients with sizes ranging from about 0.1-2.0 mm. The term “pelletization” is used synonymously with granulation, but in pharmacy, this term usually refers to the manufacturing of aggregates, preferably spherical, with a narrow size distribution in the range of about 0.5-1.5 mm. They consist of small, free-flowing, spherical or semi-spherical solid units, typically about 0.5-1.5 mm, and are intended usually for oral administration (Swarbrick et al., 1992; Aulton, 2002). Granules can be prepared by many methods. The most common techniques of granulation are dry granulation, which includes roller compaction and slugging, and wet granulation, which includes wet massing, fluid bed granulation, spray drying, pan granulation, extrusion and palletizing, and other granulation processes such as humidification and melt pelletization (Conine et al., 1970; Ghebre et al., 1985; Leon et. al., 1991; Niskanen, 1992; Parikh, 1997a; Parikh, 1997b).

The layering process comprises of the deposition of successive layers of drug entities from solution, suspension or dry powder on the nuclei which may be crystals, granules of the same material or inert starter seeds (Gamlen, 1985; Jackson et al. 1989). Itraconazole is most effective when drug concentration is maintained above the minimum effective concentration. The main purpose of this study is to prepare itraconazole granules that release the maximum possible amount of drug within one hour.

Materials and Methods

Drugs and Chemicals

Itraconazole was procured from Metrochem API Pvt. Ltd (Hyderabad, India). HPMC E5 supplied by Ruitai Pharmaceutical Company, China. Crospovidone, calcium carbonate, sodium lauryl sulphate were supplied by Loba Chemie Pvt Ltd (Mumbai, India). Tween-80, diethyl phthalate, isopropyl alcohol and dichloromethane are procured from S.D. Fine Chemicals Ltd (Mumbai, India). All the reagents used in this study were of analytical grade.