Research Paper

Physicochemical Properties of Glimepiride in Solid Dispersions with Polyethylene Glycol 20000

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ABSTRACT: The aim of this study was to investigate the physicochemical properties of glimepiride in SDs with PEG 20000. The phase solubility behavior of glimepiride in presence of various concentrations of PEG 20000 in pH 7.4 buffer was obtained at 37°C. The solubility of glimepiride increased with increasing amount of PEG 20000 in pH 7.4 buffer. Gibbs free energy ($\Delta G^\circ$) values were all negative, indicating the spontaneous nature of glimepiride solubilization and $\Delta G^\circ$ decreased with increase in the PEG 20000 concentration, demonstrating that the reaction conditions became more favorable as the concentration of PEG 20000 increased. The SDs of glimepiride with PEG 20000 were prepared at 1:1, 1:3 and 1:5 (glimepiride: PEG 20000) ratio by melting method. Evaluation of the properties of the SDs was performed by using dissolution, Fourier-transform infrared (FTIR) spectroscopy and X-ray diffraction (XRD) studies. The SDs of glimepiride with PEG 20000 exhibited enhanced dissolution rate of glimepiride, and the rate increased with increasing concentration of PEG 20000 in SDs. Mean dissolution time (MDT) of glimepiride decreased significantly after preparation of SDs and physical mixture with PEG 20000. The FTIR spectroscopic studies showed the stability of glimepiride and absence of well-defined glimepiride-PEG 20000 interaction. The XRD studies indicated the amorphous state of glimepiride in SDs of glimepiride with PEG 20000.

KEYWORDS: Glimepiride; Solid dispersion; PEG 20000; Dissolution; Solubility

Introduction

Glimepiride, 1-(p-(2-(3-ethyle-4-methyl-2-oxo-3-pyrroline -1-carboxamido) ethyl) phenyl) sulfonyle)-3-(trans-4-methylcyclohexyl) urea is a third generation hypoglycemic sulfonylurea which is useful in the treatment of non-insulin dependent diabetes mellitus (NIDDM) (Fig 1) (Massimo, 2003: Kouichi et al., 2005). Glimepiride is a white crystalline powder, relatively insoluble in water, but the predicted water solubility is 3.84e-02 mg/mL (pK$_a$=6.2). Glimepiride exhibits slow GI absorption rate and inter individual variations of its bioavailability (Frick et al., 1998). The slow absorption rate of drug usually originates from either poor dissolution of drug from the formulation or poor permeability of drug across GI membrane. The slow dissolution can be attributed, at least in part, to hydrophobicity of glimepiride powder as evidenced by poor wetting of powder surface by water. For poorly water soluble and highly permeable (class -II) drugs the rate of oral absorption is often controlled by the dissolution rate in the gastrointestinal tract (Lobenberg R and Amidon, 2000).

The increased GI absorption of glimepiride could be achieved by use of solid dispersions with hydrophilic polymers such as polyethylene glycol which enhance dissolution and solve inter individual variation of its bioavailability.

Fig. 1 Structure of glimepiride.

Polyethylene glycols (PEGs) with molecular weights of 1500-20000 are used for the preparation of solid dispersions (SDs). Their solubility in water is generally good, but decreases with increase in molecular weight (Leuner and Dressman, 2000). A particular advantage of PEGs for formation SDs is that they also have good solubility in many organic solvents. Additional attractive features of the PEGs include their ability to solubilize some compounds, and increase in solubilization capacity with increase in molecular weight (Betageri and Makarla, 1995). The SDs of drugs with PEG 20000 may be useful to solve various problems such as stability, solubility and dissolution rate (Anguiana-Igea et al., 1995; Greenwald, 2001).