Research Paper

Formulation, Physicochemical Evaluation, and Dissolution Studies of Carbamazepine Solid Dispersions

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Received April 26, 2012; accepted May 10, 2012

ABSTRACT

Carbamazepine is a water-insoluble antiepileptic drug. Being a BCS class-II drug, its absorption is dissolution rate limited. Solid dispersions were prepared to enhance the dissolution rate of the drug. Crospovidone and croscarmellose sodium were used as the hydrophilic carriers. Solid dispersions showed a remarkable enhancement in the dissolution rate of the drug. In the present research work, the solid dispersions were formulated into fast dissolving tablets. The prepared tablets were evaluated for hardness, friability, drug content, disintegration time, and the in vitro dissolution rate. The solid dispersions were characterized by Fourier Transform Infrared Spectroscopy (FTIR), differential scanning calorimetry (DSC) and thermo-gravimetric analysis (TGA). The DSC study revealed a marked reduction in the crystallinity of the drug. The faster dissolution rate of the solid dispersion is attributed to a marked reduction in the crystallinity of the drug. The FTIR and DSC studies demonstrated the absence of drug-polymer interaction. The formulated tablet (F2) achieved a 7 fold faster dissolution rate compared to the marketed tablet.

KEYWORDS: Carbamazepine; solid dispersions; dissolution; fast dissolving tablets.

Introduction

The progress in treatment of diseases has been evident with the upsurge in the development of new drugs. An estimated 40% of these drugs are poorly water soluble. The enhancement of oral bioavailability of such poorly water soluble drugs remains one of the most challenging aspects of drug development. The development of solid dispersions as a practically viable method to enhance the bioavailability of poorly water-soluble drugs can overcome the limitations of the previous approaches such as salt formation, solubilization by cosolvents, and the particle size reduction (Chiou and Riegelman, 1971). Much of the research that has been reported on solid dispersion technologies involves drugs that are poorly water-soluble and highly permeable to biological membranes, as with these drugs, the dissolution is the rate limiting step to absorption (Ford, 1986).

Solid dispersion technologies are particularly promising for improving the oral absorption and bioavailability of BCS Class II drugs (Sinha et al., 2010). The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles. Solid dispersion technology is the science of dispersing one or more active ingredients in an inert matrix in the solid state in order to achieve increased dissolution rate, sustained release of drugs, altered solid state properties and enhanced bioavailability (Leuner and Dressman, 2000; Sheu et al., 1994). The solid dispersion approach has been widely and successfully applied to improve the solubility, dissolution rate and consequently the bioavailability of poorly soluble drugs (Craig, 2002; Sudha et al., 2002; Varma and Pandit, 2005). Many hydrophilic excipients like PVP, cyclodextrins, PEG 4000, PEG 6000, mannitol, and poloxamers can be used to enhance the dissolution of poorly soluble drugs (Dahlberga et al., 2010). When the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug releases as fine colloidal particles. The resulting enhanced surface area produces higher dissolution rate and bioavailability of poorly water-soluble drugs.

The carbamazepine is an anticonvulsant and mood-stabilizing drug used primarily in the treatment of epilepsy and bipolar disorder, as well as trigeminal neuralgia (Raid et al., 1986). It is practically insoluble in water. Being a BCS class-II drug, it has dissolution dependent oral bioavailability. The absorption of carbamazepine from immediate-release tablets is slow, erratic and unpredictable (Aldenkamp et al., 1988; Martindale, 2005). Solid dispersions of carbamazepine in sodium starch glycolate and HPMC have been developed to increase the dissolution rate (Rane et al., 2008).