Preparation, Characterization and in vivo Evaluation of Felodipine Solid-Lipid Nanoparticles for Improved Oral Bioavailability

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ABSTRACT

Felodipine is an antihypertensive drug with poor oral bioavailability due to the first pass metabolism. For improving the oral bioavailability, felodipine loaded solid lipid nanoparticles (SLNs) were developed using trimyristin, tripalmitin and glyceryl monostearate. Poloxamer 188 was used as surfactant. Lipid excipient compatibilities were confirmed by differential scanning calorimetry. SLN dispersions were prepared by hot homogenization followed by ultrasonication at a temperature, above the melting point. SLNs were characterized for particle size, zeta potential, drug content, entrapment efficiency and crystallinity of lipid and drug. In vitro release studies were performed in 0.1N HCl and phosphate buffer of pH 6.8 using dialysis method. Pharmacokinetics of felodipine-SLNs after oral administration in male Wistar rats was studied. The bioavailability of felodipine was increased by 1.75 fold when compared to that of a felodipine suspension.

KEYWORDS: Solid-lipid nanoparticles; felodipine; lipophilic; bioavailability; pharmacokinetics.

Introduction

Felodipine (FD) is a calcium channel blocker, and used as an antihypertensive drug. It is practically insoluble in water and has poor bioavailability (15%) because of extensive hepatic first pass metabolism (Capewell et al., 1998). Possible methods to avoid first pass metabolism include: transdermal, buccal, rectal and parenteral routes of administration.

Oral route is the most commonly used and preferred route for the delivery of drugs, although several factors like pH of GIT, residence time and solubility can affect this route. Lymphatic delivery is an alternative choice to avoid first pass metabolism in peroral drug delivery (Driscoll, 2002). Enhanced lymphatic transport of drugs reduces the hepatic first-pass metabolism and improves oral bioavailability, because intestinal lymph vessels drain directly into thoracic duct, further in to the venous blood, thus bypassing the portal circulation (Cavalli et al., 2003). The main function of the lymphatic system is to facilitate absorption of long chain fatty acids via chylomicron formation. Two different lipid based approaches are known to enhance the lymphatic transport, which include construction of a highly lipophilic prodrug and incorporation of drug in a lipid carrier (Charman and Porter, 1996).

Solid lipid nanoparticles (SLNs) are one of the carrier systems having more advantages than other colloidal delivery systems with regard to biocompatibility and scale up (Müller et al., 2000). Various methods, such as high-pressure homogenization, solvent emulsification/evaporation were reported in literature for preparing SLNs (Mehnert and Mäder, 2001).

Previously, the dissolution rate and oral bioavailability of FD was improved by nanosuspension technique (Bhanuand Malay, 2014). Improvement in the solubility of FD was reported by self-nanoemulsifying system approach (Pradeep et al., 2009). The bioavailability of felodipine was enhanced by targeting the M cells of Peyer's patches using PLGA nanoparticles (Shah et al., 2014). But, solid lipid nanoparticles of FD were not reported till now.

The aim of the present work was to study the improvement of bioavailability by incorporating felodipine in SLNs prepared with different lipids such as tripalmitin (TP), trimyristin (TM) and glyceryl monostearate (GMS). The SLNs were prepared by hot homogenization followed by ultra-sonication method. Drug excipient compatibility was assessed by DSC. The SLNs were characterized for particle size, zeta potential and in vitro release. Bioavailability study in rats was performed and was compared with that of felodipine suspension.

Materials and Methods

Materials: TP, Tripalmitin (glyceryl tripalmitate; Dynasan-116), TM, trimyristin (glyceryl trimyristate; Dynasan-114) were obtained from Sasol, Witten,