Preparation, Characterization and In vivo Evaluation of Rosuvastatin Calcium Loaded Solid Lipid Nanoparticles

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ABSTRACT

Rosuvastatin calcium (RC), is a hypolipidemic drug, and has poor oral bioavailability of about 20% due to first-pass effect. For improving the oral bioavailability of RC, solid lipid nanoparticles (SLNs) were developed using triglycerides (tristearin, tripalmitin, and trimyristin). Hot homogenization followed by ultrasonication method was used to prepare RC-SLNs. The prepared SLNs were characterized for particle size, PDI, zeta potential (ZP), entrapment efficiency (EE) and drug content. In vitro release studies were performed in 0.1N HCl and pH 6.8 phosphate buffer of by open tube method. Physical stability the SLNs was observed at refrigerated temperature and room temperature for 60 days. Pharmacokinetics of RC-SLNs after oral administration, in male Wistar rats was studied. SLNs prepared with tristearin (Dyanasan-118) having size of 207.3 ± 8.52 nm, PDI of 0.344 ± 0.084, ZP of − 20.9 ± 4.88 mV with 97.06 ± 0.210 % EE were optimized. Differential scanning calorimetric (DSC) study revealed that no interaction between drug and lipid. In vitro release studies showed that more cumulative release of RC in pH 6.8 phosphate buffer than in 0.1N HCl during 24 hours. The lyophilized SLN formulation was used in knowing morphology of SLNs and was found to have spherical shape with increased polydispersity by Scanning electron microscopy. Pharmacokinetic studies showed the relative oral bioavailability of this drug by minimizing first pass metabolism.

KEYWORDS: Rosuvastatin calcium; Solid lipid nanoparticles; Triglycerides; Oral bioavailability; Pharmacokinetics.

Introduction

Oral route of drug delivery offers challenges for drugs having poor solubility, chemical instability in the gastrointestinal tract, poor permeability through the biological membranes or sensitivity to metabolism. The limiting factors of the oral bioavailability of drugs include first-pass metabolism, permeability, lack of the drug solubility and dissolution. Poorly soluble compounds tend to be eliminated from the GIT before they had opportunity to fully dissolve and absorb into the circulation. The inherent problems associated with the drug, in some cases, can be solved by modifying the formulation or changing the routes of administration.

Controlled release behavior of colloidal systems is reported to enable the bypass of gastric and intestinal degradation of the encapsulated drug and their possible uptake and transport through the intestinal mucosa (Arik and Amnon, 2008). Absorption of nanoparticles occurs through mucosa of the intestine by several mechanisms, namely through the Peyer’s patches, by intracellular uptake or by the paracellular pathway (Üner M and Yener G, 2007). Solid lipid nanoparticles (SLNs) are an alternative nanoparticulate carrier system to polymeric nanoparticles, liposomes and o/w emulsions (Mehnert W and Mañer K, 2001; Müller RH et al., 1995; Müller RH et al., 2000). Aqueous SLN dispersions are composed of lipid which is solid both at body and room temperature, being stabilized by a suitable surfactant. SLNs possess distinct advantages compared to other carriers, e.g., polymeric nanoparticles, lipids used in topical and oral drug delivery can be used as matrix material, including the long list of different surfactants/stabilizers employed in these traditional formulations. Thus, there is no problem with the regulatory accepted status of excipients (Souto EB et al., 2007). Lipid nanoparticles were studied for percutaneous drug delivery (Driscoll MC, 2002; Souto EB and Müller RH, 2007; Müller RH et al., 2005). SLNs also enjoy more advantages over other colloidal delivery systems with regard to biocompatibility, scale up and also the release of drugs from SLNs can be modulated in order to optimize their performance (Zur Mühlen A et al., 1998). These features make lipid nanoparticles an interesting carrier system for optimized oral delivery of drugs. There are very few reports in literature describing the use of SLNs for bypassing first pass metabolism. When all-trans-retinoic acid was loaded into SLNs, the oral bioavailability in rats was increased four to five fold.