Solubility enhancement of poorly water soluble atorvastatin calcium using solid dispersion techniques

Emanual Michael Patelia
University of Bedfordshire, UK

Abstract

Atorvastatin calcium (ATR), a cholesterol lowering agent, which is white to off white crystalline powder have poor aqueous solubility and bioavailability. It belongs to class II as per BCS classification system. ATR is a potent inhibitor of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase. Which catalyzes the conversion of HMG-CoA to mevalonate, this conversion is an early and rate-limiting step in the biosynthesis of cholesterol the drug is poorly absorbed from the gastrointestinal (GI) tract, therefore it is important to enhance aqueous solubility, dissolution rate and bioavailability from its oral solid dosage forms. The rationale of this study was to prepare and characterize solid dispersions of ATR for improving its solubility and dissolution rate and to formulate immediate release tablets. Solid dispersions of ATR were prepared with PEG 6000, PVP K-30 and HPMC K3LV. Saturation solubility study revealed the ability of PEG 6000, PVP K-30 and HPMC K3LV to form solid dispersions with ATR. Methods used for preparation of solid dispersions include kneading, solvent evaporation, fusion, and microwave irradiation fusion method. Solid dispersions were characterized by dissolution study, fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), differential scanning calorimetry (DSC) and X-Ray diffraction (XRD) to confirm conversion of crystalline ATR to amorphous form in solid dispersions. The immediate release tablets prepared using solid dispersions (ATR- PEG 6000) showed 99.19 %, solid dispersions (ATR- PVP K30) showed 99.12 % and solid dispersion (ATR- HPMC K3LV) showed 99.09 % drug release within 30 min. In vivo study was performed in terms of lipid-lowering efficacy, such as cholesterol, high density lipoprotein and triglyceride in (mg/dL) using a triton-induced hypercholesterolemia model in rats. The SD formulation significantly reduced serum lipid levels in phases I and II (18 and 24 h) of the triton test, as compared with ATR. The vivo result shows that the SD improves its bioavailability when compared with plain ATR. Stability studies were carried out for 90 days at 40°C/75% RH. Hence prepared solid dispersions lead to enhancement of solubility and dissolution rate of ATR.

Biography

Emanual M. Patelia is doing his M.Sc. in Pharmacology from University of Bedfordshire, London. His project mainly deals with Analytical method development. He has attended many seminars on analytical method development, pharmacy, systemic research methodology in medicinal plant research.