ABSTRACT

The aim of the present work was to prepare self emulsifying drug delivery systems (SEDDS) of Efavirenz, Atorvastatin calcium and Rosuvastatin calcium. These drugs exhibit poor aqueous and low bioavailability. Based on the solubility study, Labrafac PG (oil), Tween 80 (surfactant), PEG 200 (cosurfactant) were selected for preparation of Efavirenz SNEDDS (self nanoemulsifying drug delivery systems). Capmul MCM (oil), Tween 20(surfactant), Propylene Glycol (co-surfactant) were used for Atorvastatin calcium (AC). While for Rosuvastatin Calcium (RC), Capmul MCM (oil), Tween 20 (surfactant), PEG 200 (cosurfactant) were used. Pseudo-ternary phase diagrams were constructed to evaluate the area of self-nanoemulsification. FT-IR studies were carried out to identify interaction between drug and excipients. The prepared formulations were subjected to thermodynamic stability, dispersibility, robustness to dilution, globule size, zeta potential, refractive index, percent transmittance, viscosity, drug content and In vitro drug release. The optimized formulations were adsorbed on solid carrier. The Solid-SNEDDS were characterized by SEM, DSC and XRD studies. The loaded Solid-SNEDDS were prepared as tablet by applying $2^3$ factorial design using Design-Expert 8.0.6.1 software. The pharmacokinetic parameters were determined after oral administration of pure drug and SNEDDS tablets into wistar rats.

FT-IR studies showed that there is no interaction between drug and excipients. The thermodynamic tests and robust to dilution test rules out the selection of metastable formulation. The refractive index and percent transmittance data indicated that the formulations were transparent. The optimized Efavirenz SNEDDS yielded nanoemulsion of mean globule size 142.8 nm, AC SNEDDS yielded nanoemulsion of mean globule size 42.21 nm and RC SNEDDS yielded nanoemulsion of mean globule...
size 35.27 nm. *In vitro* release studies showed remarkable increase in drug release from SNEDDS as compared to pure drug due to its increased surface area. *In vitro* release studies showed that all the SNEDDS released more than 90% of drug at the end of 30 min.

Aerosil loaded SNEDDS were used for preparation of tablets because of its high loading capacity and better flow properties compared to Accurel MP 1000 and Porous polystyrene beads. The SEM of the S-SNEDDS showed smooth granular particles. The DSC thermograms of S-SNEDDS indicate presence of drug in molecularly dissolved state in the lipid excipients and the result was supported by XRD studies. The optimized Efavirenz tablets were prepared using MCC (278.75 mg), PVP (12 mg) and SSG (15.88) that give hardness of 4, disintegration time of 78 sec and drug release of 97%. The optimised AC tablets were prepared using MCC (250.02 mg), PVP (10.08 mg) and SSG (13.37). While the optimised RC tablets were prepared using MCC (267.73 mg), PVP (10.08 mg) and SSG (14 mg).

The Cmax of drugs in SNEDDS tablets was higher in all the formulations compared to the pure drugs. The \((AUC)_{0}^{1}\) for Efavirenz SNEDDS tablets was 388.39 mcg/ml.h whereas for pure drug it was 95.39 µg/ml.h. For AC SNEDDS tablets, \((AUC)_{0}^{1}\) was 386.2 µg/ml.h whereas for pure drug it was 73.56 mcg/ml.h. For RC SNEDDS tablets, \((AUC)_{0}^{1}\) was 418.6 µg/ml.h, whereas for pure drug it was 52.9 µg/ml.h. The optimized formulation did not undergo any significant change during the stability study confirming the stability of the formulations. The obtained results suggested that, solid SNEDDS tablets could be an effective oral solid dosage form to improve the bioavailability of poorly water-soluble drug (Efavirenz, AC and RC).

**Keywords:** Self emulsifying drug delivery systems, Pseudo-ternary phase diagrams, Factorial designs and Bioavailability.