ABSTRACT

The objective of the present study was to develop a novel lipid based drug delivery system to enhance the solubility, dissolution rate and ultimately the oral bioavailability of poorly water soluble drugs, fenofibrate & simvastatin. Approximately 40% of new drug candidates have poor water solubility and the oral delivery of such drugs is frequently associated with implications of low bioavailability, high intra- and inter subject variability, and lack of dose proportionality. Hydrophobic drugs can often be dissolved in lipid based systems allowing them to be encapsulated in the form of fine globules. So that the drug remains undissolved in the gut avoiding the dissolution step, which frequently limit the rate of absorption of hydrophobic drugs from the crystalline state. This can lead to improved bioavailability. Phase solubility studies were conducted using various oils for the maximum solubility of simvastatin & fenofibrate. Ternary phase diagrams were constructed to evaluate the emulsion regions and were also for the optimum concentrations of oil and surfactants and in the formulation. The globule size analysis and zeta potential of all the developed formulations were studied using Nano ZS 90, Horiba, Japan. In vitro release studies are conducted using USP Type II dissolution test apparatus. FTIR analysis for investigating the drug-excipients interactions and SEM studies for the size, shape and morphology of the globules after the emulsification process was performed. The formulation of lipid based systems was compared with commercial formulations (Simvas 10mg tablet and Lofibra 50mg capsule). The in-vivo studies were performed in rat models.

The Results of the studies indicated that, the rate of dissolution of the developed lipid based systems formulations containing simvastatin & Fenofibrate was 2.5 to 3 folds increased compared with that of commercial formulations. The mean globule size (n=3) was observed to be below 200nm for the optimized formulations and the zeta potential was negative which may not interfere in the absorption of the formulation. There were no interactions between the drug, oil and surfactants, that was confirmed from the results of FTIR studies. Therefore the developed lipid based systems formulation improved the Solubility and in-vitro drug release of simvastatin & fenofibrate when compared with commercial formulation. The in-vivo study was performed to evaluate the pharmacodynamic potential of an optimized formulation against plain drug using a triton
induced model. Hypolipidemic activity of Simvastatin and fenofibrate causes reduction in elevated total CH, LDL-CH and TG levels.