ABSTRACT

Pioglitazone (PG) and rosiglitazone (RG) are oral hypoglycemic agents, characterized by low solubility in gastric fluid, low dissolution rate, and low bioavailability. The objective of this study was therefore to design solid dispersion (SD) of PG and RG with hydrophilic carrier viz., poloxamer 188 and 407 (PXM) by kneading method and a novel particle engineering technique i.e. Melt Sono Crystallization (MSC) of drugs, in an attempt to enhance the aqueous solubility and therapeutic efficacy of the drugs. Phase solubility study with increasing PXM ratio (1:1 to 1:8) was done to study the influence of polymer concentration on solubility of PG and RG. All the prepared formulation of SDs as well as MSC gives high degree of dissolution and solubility enhancement as drug carrier ratio was increased in case of SDs. Furthermore SDs and MSC, significantly improved the solubility in comparison with pure drug or Physical Mixture (PM). The extent of drug dissolution particularly in SDs (Drug: poloxamer188, 1:5) approx. 60% in 15 min. at the pH 7.4. The XRPD study indicate amorphous nature of drug after entrapment in the poloxamer carrier in SDs and MSC. SEM studies examination showed formation of effective SDs. In case of MSC pure drug in form plate and needle shape resulted agglomeration of crystalline drug with number of shallow circular pits on the surface, reduction in the particle size surface roughness with porous nature. The DSC study in case of SDs shows amorphous precipitation of drugs and better solubilization in carriers and for MSC broadening and asymmetry in peaks, describe different crystals habit confirms changes in thermal properties of drugs. The stability studies data demonstrate marked stability of optimized formulation PG5 (PG: PXM 188). The in-vivo studies in rabbits indicated that the pharmacokinetic parameters like Cmax, Tmax, AUC of the optimized SD and pure PG were estimated and relative bioavailability for optimized formulation and found to be 120.98% depicting significant improvement in the efficacy of the drug. In conclusion, SD with (poloxamer 188 and 407) and melt sonocrystallization appeared to be promising to improve solubility, dissolution of poorly aqueous soluble drugs.