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School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Dissolution enhancement of glybenclamide by a supercritical fluid-based solvent -antisolvent technique

M. Tabbakhian[1], F. Hasanzadeh[2], N. Tavakoli[1], Z. Jamshidian[3,*]

[1]Department of Pharmaceutics and Novel Drug Delivery Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Medicinal Chemistry and Novel Drug Delivery Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[3]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Aims: Glybenclamide has formulation-dependent bioavailability due to its poor aqueous solubility. The aim of this study was to enhance glybenclamide dissolution by a supercritical fluid-based solvent-antisolvent (SAS) technique.
Methods: A D-optimal mixture design was used to investigate the effects of varied ratios of PEG6000 (20-40%), and Poloxamer407 (0-20%) at fixed amount of HPMC-E5 (60%) on drug dissolution from different solid dispersion formulations obtained by SAS. Glybenclamide, polymer and surfactant were dissolved in dichloromethane: ethanol (1:1) followed by sonication for 15 min to degas the solution. The drug solution and supercritical CO2 were pumped into the particle formation vessel at speeds of 0.2 and 2 ml/min, respectively. The pressure was kept at 1500-3000 PSI. The powder obtained was characterized using FTIR spectroscopy, differential scanning calorimetry (DSC) and X-ray diffraction (XRD). Drug dissolution studies were performed in compendia-recommended media and various parameters including the drug mean dissolution time (MDT), dissolution efficiency (DE2%), and percent release in 45 min were calculated.
Results: FTIR spectra indicated chemical integrity of glybenclamide. Little or no change in endotherm from 164.9 C confirmed FTIR results. The differences observed in XRD patterns of glybenclamide powder and glybenclamide solid dispersions obtained in the supercritical SAS process were, however, suggestive of less crystallinity of the latter due to partial transformation of drug crystals to amorphs. The analysis of dissolution data indicated that enhanced drug dissolution can be achieved where the solid dispersions obtained in the supercritical fluid process were consisted of HPMC (60%), PEG (30%), and poloxamer (10%).
Conclusions: The current study indicated the potential of supercritical fluid-based technologies in enhancing the dissolution rate of poorly-soluble drugs from the solid dispersion of drugs and polymers and ingredients commonly-used in pharmaceutical industry.

Keywords: Glybenclamide; Glyburide; Dissolution enhancement; Solid dispersion; Supercritical fluid technology; Solvent-antisolvent (SAS)