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Investigating the dissolution performance of dipyridamole and cinnarizine spray dried amorphous solid dispersion using proton NMR

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Amorphous Solid Dispersions (ASDs) are of great interest as enabling formulations because of their ability to increase the bioavailability of poorly soluble drugs. However, the dissolution of these ASD based formulations results in highly supersaturated drug solution that can undergo different types of phase transition. We have investigated the dissolution performance of amorphous solid dispersions of poorly water-soluble dipyridamole (DPM) and cinnarizine (CNZ) spray-dried amorphous solid dispersions (ASDs) using polyvinyl pyrrolidone (PVP) and polyacrylic acid (PAA) as a carrier matrix. Dissolution studies were carried out under non sink conditions and solution phase drug-polymer interactions was characterized using proton NMR. It was found that the dissolution of ASDs led to sustained supersaturation, the duration of which varied depending on the drug loading and type of polymer used in the formulation. The main mechanism for drug supersaturation generation and prolongation was found to be anti-plasticization effect of polymers on amorphous drugs within spray dried ASDs and the ability of polymers to reduce the crystal growth rates of DPM and CNZ. To further understand the molecular mechanism behind supersaturation stabilization in the presence of polymer, we employed, Solution 1H NMR. The change in electron densities of proton and the relative intensities of peak shifts indicated the nature of interaction between drug and polymer in different systems are different. These different effects suggest that DPM and CNZ interacts in a different way with PVP and PAA in solution which goes some way towards explaining the different polymeric effect, particularly in terms of inhibition of drug recrystallization and dissolution of DPM and CNZ ASDs. . The overall supersaturation profile observed thus depended on a complex interplay between dissolution rate, polymer type, drug loading, crystallization mechanism of drugs and drug-polymer interaction in the solution state.

Biography

Shrawan Baghel is currently doing PhD in "Novel technologies and optimized formulations for delivery of solid dispersion of BCS class II drugs" at Pharmaceutical and Molecular Biotechnology Research Center (PMBRC), Waterford Institute of Technology. He is the winner of Science Foundation Ireland scholarship for this project in collaboration with Synthesis and Solid State Pharmaceutical Centre. The main aim of this project is to gain an insight into the mechanistic and molecular aspects of solid dispersion prepared by spray drying, hot melt extrusion and supercritical fluid process using DSC, XRD and NMR. He had also planned, conducted, interpreted nanotechnology and lipid based formulation approaches to increase the solubility and dissolution of poorly soluble drugs.

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