Supersaturated controlled release matrix for delivery of BCS Class-II compound Glipizide
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INTRODUCTION
Amorphous systems are of interest to pharmaceutical scientists as a robust way to achieve enhanced solubilization and greater bioavailability due to their higher enthalpy, entropy and free energy relative to crystalline structures. However enhanced solubilization of poorly soluble compounds based on amorphous property of the drug-carrier for inclusion into a controlled release delivery system remains a challenge. Problems such as dissolution stability and potential precipitation from a supersaturated state to equilibrium solubility level within the delivery system itself as well as during prolonged dissolution, transit in the GI tract and exposure to GI milieu are of chief concerns during delivery system development and evaluation.

OBJECTIVES
The goal of this study was to develop spray-dried dispersion (SDD)-based matrix tablet in order to enhance both rate and extent of dissolution of BCS Class-II compound (glipizide) while maintaining the supersaturation state in the matrix during 20 hours dissolution study.

RESULTS
Powder XRD analysis demonstrated the amorphous state of glipizide within SDDs up to 60% drug loading level. Supersaturated micro-dissolution testing of SDDs in fasted state simulated intestinal fluid (FaSSIF, pH 6.5, non-sink) showed prolonged supersaturation state (up to 180 minutes) with solubility increases of 5.2 to 13.9 fold relative to crystalline drug under same conditions. Plot of the most desirable SDDs in terms of relative dissolution AUCs (AUC(SDD)/AUC(crystalline)) versus stable supersaturated concentration ratio (C180/Cmax) were determined (Figure 4).

CONCLUSIONS
Non-sink in-vitro dissolution tests of SDDs revealed distinct release profiles. Measured dissolution results (SDDs or crystalline drug) indicate that SDDs provide stable supersaturated concentration within the hydrated matrix with increased rate and extent of dissolution over 20 hours. Study further confirms the successful application of SDD-based HPMCAS/HPMC matrix tablet as an effective way to increase the dissolution rate and extent of water-insoluble drug intended for controlled release purpose while maintaining the supersaturation state.

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