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Gliclazide loaded PLGA-HPMC second generation nanocrystals for oral delivery: Design, development and in vitro performance characterization

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ABSTRACT

Introduction: Second generation functionalized nanocrystal is the advancement of nanocrystal technology with great potential to accommodate BCS (Biopharmaceutical Classification System) class II drugs to meet their formulation and drug delivery challenges. Gliclazide is a BCS class II drug used in the treatment of type 2 diabetes, shows poor water solubility and low rate of dissolution, leads to poor and variable oral bioavailability. The second generation poly(D,L-lactide-co-glycolide) (PLGA) Hydroxypropyl methylcellulose (HPMC) based functionalized nanocrystals of gliclazide were prepared by a combination method of emulsion diffusion-high pressure homogenization-solvent evaporation. **Methods:** Gliclazide second generation nanocrystals were fabricated with taguchi orthogonal experimental design in combination of step up and top down nanoformulation strategies using drug-polymer (PLGA) ratio at 1:0.5, 1:0.75, 1:1 with HPMC(0.5, 0.75, 1% w/v) as stabilizer. The formulated gliclazide PLGA-HPMC nanocrystals were investigated on particle size, polydispersity index, zeta potential, solubility study, drug entrapment efficiency, in vitro drug release, and surface morphology and compatibility studies. The gliclazide PLGA nanocrystals formulation was prepared with Drug : PLGA at 1: 1 ratio with concentrations 0.75% w/v HPMC at 3 homogenization cycles with 1000bar produce optimized gliclazide nanocrystals. **Results:** The optimized MSGNC8 formulation showed particle size of 239.9 nm, entrapment efficiency 98.62%, and drug release of 43.75%, 82.12% and 98.08% at 3hrs, 24hrs, and 48hrs compared to pure gliclazide % drug release of 28.73%, 67.51% and 78.41% at 3hrs, 24hrs, 48hrs respectively. The solubility study of optimized formulation shows eight folds increased in saturation solubility compared to pure drug. Scanning electron microscopy (SEM) analysis of the gliclazide nanocrystals revealed that gliclazide retained its crystal morphology in polymeric nanocrystals. Further, fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) studies on gliclazide PLGA-HPMC nanocrystals emphasize drug and excipient compatibility in development of gliclazide nanocrystals. **Conclusion:** The potential outcomes of research findings emphasize that the developed gliclazide second-generation nanocrystals, which resulted in increase in drug solubility and rate of dissolution with delayed modified release, can be explored in delivery of gliclazide for type 2 diabetes management.

Keywords: Second generation nanocrystals, Emulsion diffusion-High pressure homogenization-solvent evaporation, Gliclazide, D,L-lactide-co-glycolide(PLGA), Hydroxy propyl methylcellulose (HPMC), Type 2 diabetes management