

Nanoprecipitation with Ultrasonication for Enhancement of Oral Bioavailability of Furosemide: Pharmacokinetics and Pharmacodynamics Study in Rat Model

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Abstract : Furosemide is a weakly acidic diuretic indicated for treatment of edema and hypertension. It has very poor solubility but high permeability through stomach and upper gastrointestinal tract (GIT). Due to its limited solubility it has poor and variable oral bioavailability of 10-90%. The aim of this study was to enhance the oral bioavailability of furosemide by preparation of nanosuspensions. The nanosuspensions were prepared by nanoprecipitation with sonication using DMSO (dimethyl sulfoxide) as a solvent and water as an antisolvent (NA). The prepared nanosuspensions were sterically stabilized with polyvinyl acetate (PVA). These were characterized for particle size, ζ potential, polydispersity index, scanning electron microscopy (SEM), differential scanning calorimetry (DSC), X-ray diffraction (XRD) pattern and release behavior. The effect of nanoprecipitation on oral bioavailability of furosemide nanosuspension was studied by in vitro dissolution and in vivo absorption study in rats and compared to pure drug. The stable nanosuspension was obtained with average size range of the precipitated nanoparticles between 150-300 nm and was found to be homogenous showing a narrow polydispersity index of 0.3 ± 0.1 . DSC and XRD studies indicated that the crystalline furosemide drug was converted to amorphous form upon precipitation into nanoparticles. The release profiles of nanosuspension formulation showed up to 81.2% release in 4 h. The in vivo studies on rats revealed a significant increase in the oral absorption of furosemide in the nanosuspension compared to pure drug. The AUC₀₋₂₄ and C_{max} values of nanosuspension were approximately 1.38 and 1.68-fold greater than that of pure drug, respectively. Furosemide nanosuspension showed 20.06 ± 0.02 % decrease in systolic blood pressure compared to 13.37 ± 0.02 % in plain furosemide suspension, respectively. The improved oral bioavailability and pharmacodynamics effect of furosemide may be due to the improved dissolution of furosemide in simulated gastric fluid which results in enhanced oral systemic absorption of furosemide from stomach region where it has better permeability.

Keywords : furosemide, nanosuspension, bioavailability enhancement, nanoprecipitation, oral drug delivery

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