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Article

Development and Optimization of Proniosomal Formulation of Irbesartan Using a Box−Behnken Design to Enhance Oral Bioavailability: Physicochemical Characterization and *In Vivo* Assessment

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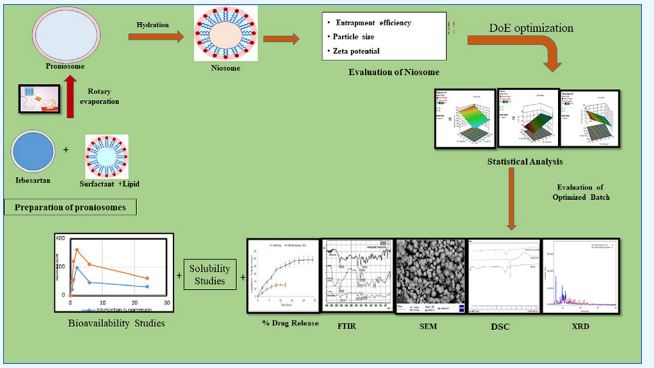
ABSTRACT: This research work aimed to develop and evaluate proniosomes for the oral delivery of the lipophilic drug Irbesartan (IRB) to improve its solubility and bioavailability. Proniosomes of Irbesartan were formulated using a lipid, surfactant, and carrier by a slurry method. Based on the prepared preliminary trial batches and their evaluation, the formulation was optimized by employing a Box−Behnken design (BBD) in which concentrations of span 60 (X_1), cholesterol (X_2), and mannitol (X_3) were used as three independent variables and the vesicular size (VS) (Y_1), % entrapment efficiency (% EE) (Y_2), and % cumulative drug release (% CDR) (Y_3) were used as dependent variables. The optimized batch B1 was obtained from the BBD experiment after validation of checkpoint analysis, and their characterization was done for VS, % EE, % CDR, Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), and X-ray diffraction (XRD) analysis. The optimized batch showed a VS of 199 ± 5.4 nm, a % EE of 99.25 ± 2.24%, and a % CDR of 97.36 ± 1.13% at 24 h. Scanning electron microscopy (SEM) study showed a smooth surface of batch B1. DSC and XRD studies indicated the amorphous nature of the proniosomal formulation. The proniosomal formulation showed increased solubility (2.65 ± 0.2 mg/mL) in phosphate buffer, pH 6.8, as compared to water (0.059 ± 0.02 mg/mL). The pharmacokinetic study in rats confirmed the increased bioavailability of the drug in optimized proniosomal formulation compared with its pure drug suspension. C_{max}, T_{max}, and $AUC_{0\text{-}t}$ of the drug also increased by 2-fold compared to those of drug suspension. Thus, in conclusion, the proniosomal formulation proved to be an efficient carrier for improved oral delivery of Irbesartan by improving the solubility and bioavailability of the drug.



1. INTRODUCTION

Recently, new potent chemical entities having poor water solubility are increasing, but they possess many problems like slow drug release, poor membrane permeability, poor bioavailability, and thus less efficacy in patients.[1] Active pharmaceutical ingredients with poor water solubility require special attention for selecting the appropriate formulations for oral bioavailability enhancement. These formulation strategies include the use of cosolvents,[2] the formation of salts,[3] cyclodextrin complexation,[4] solid dispersions,[5] nanosized formulations like nanosuspension,[6] nanoparticles,[7] and nanocrystals,[8] and lipid-containing drug delivery systems like microemulsions,[9] self-emulsifying drug delivery system,[10] solid lipid nanoparticles (SLN),[11] nanostructured lipid carriers (NLC),[12] liposomes,[13] niosomes,[14] etc. Out of these formulation strategies, niosomes and liposomes are points of greater attention as alternative options for colloidal lipid carriers. However, there are several issues with liposome dispersions in various applications such as expensiveness, purity difference of phospholipids, and the need for a vacuum atmosphere during preparation.[15] Niosomes correspond to liposomes as they involve the use of non-ionic surfactants,

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