Olanzapine Mesoporous Nanostructured Lipid Carrier: Optimization, Characterization, In Vivo Assessment, and Physiologically Based Pharmacokinetic Modeling

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Abstract

A promising approach has been emerging to enhance dissolution of hydrophobicdrugsby encapsulation in mesoporous silica materials. Olanzapine is a practically insoluble antipsychotic drug which is subjected to excessive first pass effect and shows inadequate oral bioavailability. Therefore, mesoporous silica was used to improve bioavailability of olanzapine incorporated in nano-structured lipid carriers (NLCs). These systems were characterized for their particle size, polydispersity index (PDI), zeta potential, entrapment efficiency (EE) and differential scanning calorimetry (DSC) as well asits release profile. The optimized mesoporous NLC system displayed nano-spherical particles (120.56 nm), possessed high entrapment efficiency (88.46%) and the highest percentage of drug released after six hours (75.13%). The biological performance of the optimized system was assessed in comparison with the drug suspension in healthy albino rabbits. The optimized system showed significantly ($P < 0.05$) prolonged MRT (8.47 h), higher C max (22.12Ñ 0.40 ng/ml) and T max (2.0 h) values compared to drug suspension. Physiologically based pharmacokinetic (PBPK) model was simulated and verified. All the predicted results were within 0.6 and 1-fold of the reported data. To set a conclusion, in vitro results as well as in vivo pharmacokinetic study and PBPK data showed an enhancement in bioavailability of the optimized NLCs system over the plain drug suspension. These results proved the potentiality of incorporating olanzapine in mesoporous NLC for a significant improvement in oral bioavailability of olanzapine.

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