NOVEL APPROACHES FOR ENHANCEMENT OF DRUG BIOAVAILABILITY

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Mrs. Bijal Prajapati

[Enrollment No.: 150800402005]

Research Guide

Prof. (Dr.) Abhay Dharamsi, M.Pharm, Ph. D

Dean, Faculty of Pharmacy

Parul University

DEPARTMENT OF PHARMACY, PARUL UNIVERSITY

LIMDA, WAGHODIA-391760, VADODARA, GUJARAT-INDIA

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ABSTRACT

Schizophrenia is a serious brain disorder that alters the way a person acts, thinks, expresses emotions, make out reality and relates to others. Schizophrenia can be the most chronic and disabling disorder, characterized by changes in mental function where thoughts and perceptions become disordered, and there is a loss of contact with reality. Drugs used for the treatment of Schizophrenia are reported to have low bioavailability pertaining to high first pass metabolism, high protein binding and enzymatic metabolism. They also show low permeability across blood brain barrier. In the present study, Microemulsion (ME) and Nanostructured lipid carriers (NLC) of Asenapine maleate (ASNM) and Ziprasidone hydrochloride (ZPR) were prepared with the objective to provide increased permeability as well as protection to drug by biocompatible lipidic content and nano-scale size and thus to develop formulation having potential for enhanced bioavailability and brain targeting. Water titration method was used to prepare microemulsion and phase digram were constructed using CHEMIX Software and evaluated for particle size, polydispersity index (PDI), zeta potential, rheology, conductivity and drug content. ME of ASNM and ZPR were developed with globule size of 118.17 ± 0.154 nm with PDI 0.224 ± 0.002 and 107.14 ± 0.114 nm with PDI 0.178 ± 0.004 respectively. High pressure homogenization technique was optimized and used to prepare Nanostructured lipid carriers (NLC) using a systematic approach of design of experiments and evaluated for particle size, polydispersity index (PDI), zeta potential and entrapment efficiency. NLC of ASNM and ZPR of average size 169.7 ± 1.80 nm having PDI of 0.256 with 72.54 ± 2.11 % entrapment efficiency and 168.5 nm ± 1.21 with PDI 0.232 with 80.25± 2.43 % entrapment efficiency respectively, were produced. The formulations were found stable. Microscopic evaluation and the histopathological studies respectively indicated spherical shape and non-irritant nature of the formulated nanoformulations. The optimized formulations were further evaluated for various parameters like *in-vitro* and *ex-vivo* release studies. The *in-vivo* pharmacokinetic and pharmacodynamic studies showed increased concentration of ZPR in brain, when administer through intranasal route indicating its potential for an attempt towards cure of Schizophrenia.

Keywords: Asenapine maleate, Ziprasidone hydrochloride, Nanostructured lipid carriers, Microemulsion, High pressure homogenization, DoE, Bioavailability, Nose-to-brain, Brain targeting.