**ABSTRACT**

Ziprasidone HCl is an atypical antipsychotic agent, which has 60 % bioavailability and has relatively good solubility at gastric pH. Rapid gastrointestinal transit could result in incomplete drug release from the drug delivery system leading to diminished efficacy of the administered dose. Hence the objective of the present research work was to formulate and optimize the gastroretentive drug delivery system containingZiprasidone HCl as a model drug. The tablets were prepared by direct compression technique, using polymers Hydroxypropyl methylcellulose (HPMC) of different grades and Xanthan gum were used as matrix forming agent. A simplex lattice design was applied to investigate the combined effect of formulation variables i.e., amount of HPMC K4M (A), Xanthan gum (B), HPMC K15M (C). The floating lag time, drug release for 1, 2, 8, 24 h (%) was taken as responses. Results indicated that low level of(C) and (B) and high level of (A) should be used to manufacture the tablet formulation with desired in vitro floating time and dissolution. The optimized formula was also developed using simplex lattice design and evaluated for various kineticmodels of drug release. There was no significant difference observed between the predicted values and experimental values. The correlation coefficient was higher for Peppas model and “n” value was found to be between 0.45 and 0.89 which indicates the drug release pattern follows the non-Fickian diffusion mechanism.

**Keywords:** Ziprasidone, Simplex lattice design, Peppas model, Diffusion mechanism.