Abstract

In present study three drugs Ondansetron HCl, Ketoprofen and Glipizide were selected for design of various floating drug delivery systems. All three candidates were required to be designed as floating drug delivery system for sustained action of them. For Ondansetron HCl Floating matrix tablet was prepared using natural gums to retain it in stomach for longer time, from where its absorption is better. For Ketoprofen floating drug delivery system were designed, since it is absorbed better from upper part of duodenum and microspheres were prepared to minimize its gastric irritation by reducing the mucosal contact. For Glipizide floating bilayer tablets were developed, since its absorption is unpredictable in diabetic patients due to impaired gastric motility or gastric emptying. So the efficacy of the drug was improved.

Various formulation batches were developed for Ondansetron Hydrochloride floating tablet by $3^2$ full factorial design using Xanthan gum and Karaya gum. Preformulation study of drug and polymers were done by performing IR. Powders mixtures were evaluated for angle of repose, Carr’s index, bulk density and tapped density. Ondansetron Hydrochloride floating tablet formulations were prepared and evaluated for floating lag time, buoyancy duration, dissolution study and accelerated stability study were performed.

Tablets containing Xanthan gum (27.27%, w/w), Karaya gum (21.81%, w/w), NaHCO3 (18.18%, w/w) and tartaric acid (9.09%) (formulation F4)showed satisfactory results with respect to total floating duration, floating lag time, swelling ability, and controlled drug release rates. Drug release profiles on model fitting of optimised formulation F4 followed Kosymer-Peppas model as best fit model which indicated that drug release was Anomalous Transport or Non Fickian through the pores. Stability study that was carried and concluded that there was no much effect of the temperature and moisture on the hardness, drug content, floating lag time and drug release from floating matrix tablet.

Sustained release microspheres of Ketoprofen were prepared by using ionotropic gelation technique. Various batches were developed by applying $3^2$ full factorial design. The prepared batches of microsphere were evaluated for micromeritics study such as particle size determination, tapped density, bulk density, Carr’s index, hausner ratio and angle of repose. Moreover they were also evaluated for percentage yield, drug entrapment and in-vitro drug release.
All batches of microspheres studied shown good floating behavior. However, based on the drug entrapment, % yield and release rate studies of the formulations, it was observed that the formulation containing 75 mg of Ketoprofen and 150 mg sodium bicarbonate with 150mg of sterculia gum and 200mg sodium alginate i.e. batch F4. This batch released 94.08% drug over a period of 12 hours, also shown good drug entrapment efficiency and % yield. SEM study confirmed spherical shape and smooth surface of microspheres. Accelerated stability study also showed that formulations were stable for a month at $40 \pm 2^\circ C/75 \pm 5 \%$ RH.

Sustained release bilayer floating tablets of glipizide were developed by applying $2^3$ factorial design using HPMC K4M, HPMC K15M, Xanthan gum, HPMC K100M, Sodium bicarbonate and starch 1500. Among all sustained release layer formulations studied it was observed that, Glipizide release from the matrix was largely dependent on the polymer swelling, drug diffusion and matrix erosion. Formulation A2 was able to retard drug for 12hrs, releasing 98.22% drug in 12hrs. Formulation A6 was able to retard drug for 12hrs, releasing 96.39% drug in 12hrs. Polymer to drug ratio 2:1 shown better retardation due to higher concentration of polymers, while polymer to drug ratio 1:1 was unable to retard the release for 12hrs. When HPMC K15M and HPMC K 4M used in ratio of 9:1 with xanthan gum, they shown more retardation and less than 75 % drug released in 12hrs, but when these polymers used in ratio 1:1 with xanthan gum shown better control over release pattern of the drug.

Sustained release layer formulations A2 and A6 were optimized and used for preparation of bilayer tablets. Optimized floating layer composed of HPMC K100M (46mg), Sodium bicarbonate (45mg) and starch1500 (49mg). These bilayer tablets shown satisfactory drug release pattern, floating time, floating lag time and followed Higuchi release kinetics indicating the drug release is controlled by Fickian diffusion of drug.

It can be concluded from the forgone studies that Xanthan gum act as good drug release retardant for matix floating tablet of Ondansetron HCl. Also it was observed that swelling of the microsphere is affected by the reaction parameters such as concentration of the sterculia, alginate and crosslinker. At the same time floating nature of beads can make the retention of drug delivery systems in the stomach for longer time and could improve the bioavailability and therapeutic efficacy of the Ketoprofen. The present work also showed promising sustained-release floating matrix tablets of Glipizide using HPMC K grade and Xanthan gum.