ABSTRACT

The purpose of this investigation was to develop a controlled release floating drug delivery system (tablets and hollow microspheres) of Losartan potassium, Verapamil hydrochloride and Rosiglitazone maleate.

The aim of the first study was to develop and evaluate non-effervescent floating matrix tablets. Drugs having narrow absorption window and those which are absorbed mainly in stomach were developed as floating delivery system. Losartan potassium, a class I anti-hypertensive agent, is well absorbed in stomach and upper part of small intestine. Hence there is need to develop floating dosage form. Floating matrix tablets were prepared by direct compression method employing polypropylene foam powder (Accurel® MP 1000), Karaya gum and Chitosan. Tablets were characterized by FT-IR, DSC studies and evaluated for floating lag time, duration of buoyancy, friability, hardness, thickness, weight variation, swelling studies, drug content, in vitro drug release studies and in vivo studies. FT-IR and DSC studies showed that there is no interaction between the drug and excipients. The tablets showed zero floating lag time and remained buoyant for more than 12 h achieving the gastric retention properties. All evaluation parameters were within the Pharmacopoeial limits. The in vitro drug release was sustained up to 12 h and release rates were fitted into an empirical equation to compute the diffusion parameter which indicates a super case II-transport mechanism. X-ray photographs confirm presence of tablet in rabbit stomach for more than 12 h. The studies concluded that floating matrix tablets could be used as floating drug delivery systems in view of their floatation in stomach.
The second study was to develop and evaluate floating tablets of Verapamil hydrochloride were engineered to extend gastric residence time and there by enhance its bioavailability. The floating matrix tablets were prepared by direct compression technique using a combination of hydroxyl propyl methyl cellulose (HPMC) and Karaya gum as polymers and sodium bicarbonate as gas generating agent. The prepared floating tablets were evaluated for weight variation test, hardness, thickness, swelling index, in vitro floating capabilities, floating lag time, compatibility studies and in vitro drug release. The swellable hydrophilic natural Karaya gum was used to control the release of drug. The results showed that the optimized formulation F8 containing 23.3 % of Karaya gum (70 mg) and 13.3 % of HPMC (40 mg) had good floating capability, shorter floating lag time, and sustained drug release for the period of 8 h. X-ray image at 12\textsuperscript{th} h indicated that the tablet was partially disintegrated but still remained in the stomach. The prepared tablets showed good floating capability and drug release.

The third work was to formulate floating hollow microspheres of Rosiglitazone maleate, which is soluble and shows better absorption in gastric pH. Microspheres were prepared by modified Quasi-emulsion diffusion technique using ethyl cellulose, eudragit S100, polyethylene oxide and HPMC K15M as polymers. The formulations were evaluated for micromeritic properties, in vitro, in vivo buoyancy, % yield, entrapment efficiency, in vitro and in vivo release studies. They were characterized by FT-IR and DSC. FT-IR and DSC studies indicated that there was no interaction between the drug and polymers. SEM photographs showed that the outer surface of microspheres was smooth and dense where as internal surface was porous which helped to prolong floating and increase residence time in stomach. The results showed that floating microspheres could be successfully prepared with better
yield (more than 54.5 ± 1.2 %), high encapsulation efficiency (53± 2.2 %) and narrow size distribution (223 ± 2.7- 446 ± 5.2 μm). All the formulations floated for more than 8 h. Results showed larger the particle size, longer was the floating time. *In vivo* evaluation in albino rabbit confirmed floating capability microspheres for more than 8 h. *In vitro* drug release studies showed controlled release of rosiglitazone maleate for over 12 h. The release behaviour best fitted mostly in Peppas and zero order equations. *In vivo* evaluation of blood glucose levels in albino rats showed that floating microspheres of rosiglitazone maleate had better glycemic control than conventional dosage form. From the results it can be concluded that gastric floating hollow microspheres can be successfully used for the delivery of rosiglitazone maleate to control blood glucose level.

**Key words:** Losartan potassium, Verapamil hydrochloride, Rosiglitazone maleate, Karaya gum, HPMC, Floating tablet, Release kinetics, Hollow microspheres, *In vivo* study.