Formulation and Evaluation of Floating Microspheres of Ranolazine for the Treatment of Chronic Angina

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ABSTRACT
Ranolazine is indicated for the treatment of chronic angina alone or in combination with other cardiovascular agents. The objective of present investigation was to formulate floating microspheres of ranolazine to increase gastric residence time, increased bioavailability and reduce dose frequency of drug therapy. Novel o/w emulsion solvent diffusion technique was used for preparation of microspheres of ranolazine by using various polymers such as HPMC (hydroxypropyl methyl cellulose), ethyl cellulose and Eudragit L 100. Entrapment efficiency of drug was up to 80.16%. Eudragit L100 based microspheres were found to be hollow cavity, spherical and porous nature from the results of scanning electron microscopy. Micromeritic profile of these microspheres was found satisfactory. From the results of FTIR spectroscopy it was revealed that there was no drug–polymer interaction. Eudragit L100 based microspheres shows good in vitro buoyancy and sustained release profile for longer period of time (> 14 hours), suggesting the viability of floating microspheres of ranolazine for improved pharmacokinetics for treatment of chronic angina.

KEYWORDS: Ethyl cellulose; Ranolazine; Microspheres; Eudragit L100 and HPMC.

Introduction
Oral controlled release dosage forms have been developed over the past few decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and flexibility in formulation (Woo BH et al., 2001). Gastric emptying is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms (Shweta et al., 2005).

Several techniques are used to design gastro retentive dosage forms. These include floating, swelling, inflation, adhesion, high-density and low density systems that increase the gastric residence time. Gastric retention is useful for drugs which (i) act locally (ii) have a narrow absorption window in the small intestinal region; (iii) unstable in the intestinal environment (iv) low solubility at high pH environment (Sheth et al., 1984). Various dosage forms developed for gastric retention include, floating tablets, floating beads, pellets, floating granules, floating microspheres (Chien, 1993).

Microspheres are considered to be one of the most promising floating systems, because they combine the advantages of multiple unit systems, good floating properties and are prepared using assorted polymers (Curatolo et al., 1985). However, the success of these microspheres is limited owing to their short residence time at the site of absorption. It would, therefore, be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membranes. The floating microspheres have been developed in order to overcome frequent dosing to release the drug slowly into the GIT.

The objective of present study was to fabricate microsphere by using o/w emulsion–solvent diffusion technique in order to prolong the gastric residence time, in addition to enhance bioavailability and decrease the dose frequency of Ranolazine. The influence of several factors such as the particle size, drug entrapment efficiency, floating properties and dissolution of the resulting microspheres were investigated.

Materials and Methods
Drugs and Chemicals
Ranolazine was obtained as a gift sample from MSN Laboratories Ltd. Hyderabad; Eudragit L 100 was supplied by Degussa Pharmaceutical Ltd. Mumbai. Ethyl cellulose and HPMC was supplied by Colorcon Asia Pvt. Ltd. Goa. All ingredients and solvents used were of analytical grade Supplied by Loba chem. Mumbai.