Preparation and Evaluation of Spray Dried Mucoadhesive Microspheres of Metoclopramide Hydrochloride for Nasal Delivery

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ABSTRACT
There is increasing interest in drug delivery through nasal mucosa because of the ability of drug particles to cross membrane due to their particle size in nano or submicron range. The present study was aimed to prepare and evaluate microspheres of metoclopramide hydrochloride (MH) by using HPMC E4M and Carbopol 934P. Microspheres were prepared using spray drying method and particle size was found in the range of 1.62 µm. Drug loaded microspheres of HPMC E4M and Carbopol 934P and combination of HPMC E4M: Carbopol 934P were evaluated for various parameters for optimized batch were drug entrapment (61.73%), mucoadhesive strength (1959.30 g/cms²), and in-vitro diffusion studies (95.61%). Optimized batch also evaluated for SEM, TEM, X-ray diffraction study. Amorphous form of optimized batch was confirmed by X-ray diffraction study. Particles were spherical and discrete confirmed by SEM study. Particle size range was confirmed by TEM. The drug release of optimized batch was carried out by using sheep nasal membrane. Histopathological studies have shown no toxicity to the sheep nasal membrane and hence optimized formulation was found to be safe. The optimized formulation was found to be stable in the accelerated stability studies. It was found that drug entrainment was in the order of HPMC E4M> Carbopol934P > Carbopol 934P: HPMC E4M, mucoadhesive strength Carbopol 934P: HPMC E4M > Carbopol 934P > HPMC E4M, In-vitro drug release Carbopol 934P: HPMC E4M > HPMC E4M > Carbopol 934P. In conclusion, these studies indicate the feasibility and superior pharmacokinetic profile of the metoclopramide nasal system.

KEY WORDS: Metoclopramide; Spray drying; Nasal delivery; Mucoadhesion; Microspheres.

Introduction
Nasal route is conventionally used for drug delivery for treatment of local and systemic diseases. In the recent years, this route has received special attention as a convenient and reliable method for the systemic delivery of drug, especially those that are ineffective by oral route due to their metabolism in the gastrointestinal tract being prone to first pass effect and must be administered by injection (Mainardes et al., 2006; Swamy et al., 2012) The nasal cavity as a site for systemic absorption of drugs has advantages such as porous endothelial membrane, large surface area, enhanced blood flow, avoidance of first pass metabolism due to lack of gastric and pancreatic enzymatic activity, highly vascularized epithelial layer, easy acceptability and neutral pH of the nasal mucus. (Krishnamoorthi et al., 1998; Jadhav et al., 2007; Swamy et al., 2012).

The limitation of nasal drug delivery is the mucociliary clearance (MCC) that provides a limited time available for adsorption within the nasal cavity (Soane et al., 1999; Swamy et al., 2012) Thus, mucoadhesive microspheres have been developed in order to decrease the effect of mucociliary clearance. Mucoadhesive preparations have been developed to achieve increased retention time of the dosage form with mucosal layers of nasal cavities resulting in enhanced drug absorptions. Spray drying is an alternative process that is cheaper and faster than other techniques to prepare nasal particles from mucoadhesive polymers (Mahajan et al., 2008).

The present study was aimed to prepare and evaluate microspheres of metoclopramide hydrochloride (MH) by HPMC E4M and Carbopol 934P as formulation additives. Our results indicate the feasibility and superior pharmacokinetic profile of the MH formulation.

Materials and Methods
Chemicals and Drugs
Metoclopramide hydrochloride was kindly gifted by Leben lab. Pvt. Ltd. (Akola). HPMC E4M was purchased from Signet Chemical, (Mumbai). Carbopol 934P was purchased from Ranq Remedies (Thane, Maharashtra). All other reagents used were of analytical grade.