Abstract

A controlled drug delivery system with prolonged residence time in the stomach can be of great practical importance for drugs with an absorption window in the upper small intestine. Floating microspheres are specially gaining attention due to their wide applicability in the targeting of drugs to stomach. Gabapentin and acyclovir dosage forms could be designed to release the drug in the stomach at a rate providing the maximum amount of drug absorbable by the upper intestinal segment using the multiple-unit floating system to increase the gastric residence time (GRT) of the dosage forms. The purpose of the present study was preparation and in vitro evaluation of the floating microspheres of two drugs (gabapentin and acyclovir) as gastroretentive drug delivery systems. The floating microspheres of those drugs were prepared by the solvent evaporation methods (W/O/W double emulsification- solvent

evaporation method, O/O and O/W single emulsion solvent evaporation) using polymers like ethyl cellulose, cellulose acetate, HPMC, HEC, PVP, PVA and chitosan. In addition, the gelation method was used for preparing alginate beads of gabapentin using combination of sodium alginate, HPMC and EC polymers.

The prepared floating microspheres were evaluated for their particle size, shape, percentage yield, drug entrapment, buoyancy ratio, drug-polymer interaction (physically and chemically) and in-vitro drug release kinetics. In addition, the effects of polymer type, polymer: drug ratio (1:1, 1:2, 1:3 and 1:4), dispersed phase compositions (Single or combined solvent type), emulsifying agent used (tween 80, span 60 or span 80) , stirring speed (200-700 rpm), temperature (30-45C°), addition

of magnesium stearate (at different amounts and sites of incorporation) and method of preparation on the floating microspheres characteristics were studied.

The (O/O) single emulsion-solvent evaporation is the best method used for preparation of floating microspheres of both drugs using ethyl cellulose and cellulose acetate as coating polymeric materials into different polymer: drug ratios (2:1, 3:1 and 4:1). By which, high microencapsulation yields and encapsulation efficiencies (reach 100%) as well as, high buoyancy ratios (reach 98%) were obtained. Investigations using optical and scanning electron microscopes revealed spherical shape floating microspheres, with an average particle size range of (130-960μm). and no drug-polymer physical and chemical interactions were detected depending on the results obtained using differential scanning calorimetry and Fourier transform infra red instruments respectively.

A modified release pattern (for ten hours) was obtained for some floating microspheres formulas of gabapentin (formula FGS11) and acyclovir (FAS5 and FAS6) which were significantly affected by the type of polymer used. The data obtained from the release kinetics of gabapentin indicating the mechanism of the drug release to be a fickian diffusion controlled and dominates the drug release through the swelling matrix and hydrophilic pores. While for acyclovir, an anomalous (nonfickian) mechanism of release (mediated diffusion and erosion) is mainly obtained. More stabilization and protection (the percent of degradation was not exceed 1%) were obtained for both drugs by encapsulation of their particles within hydrophobic polymeric materials.