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Development and evaluation of ethylcellulose floating microspheres loaded with ranitidine hydrochloride by novel solvent evaporation-matrix erosion method

Muniyandy Saravanan [a], Boddapati Anupama [b]

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Abstract

Ranitidine hydrochloride loaded floating microspheres were prepared by novel solvent evaporation-matrix erosion method using ethylcellulose and polyethylene glycol (PEG) blend. PEG employed as pore forming agent to induce buoyancy. Formulated microspheres were evaluated for various physicochemical properties. Drug loading, entrapment and encapsulation of microspheres were 23–32, 86–96 and 75–86% (w/w), respectively. The average particle sizes were between 45 and 106μm and reduced as % of PEG increases in the microspheres. Ethylcellulose microspheres prepared with 20–33.3% of PEG showed floating properties. Scanning electron microscopy revealed the presence of pores on the surface of floating microspheres due to matrix erosion, which are responsible for floating ability. Fourier-transform infrared spectroscopy, differential scanning calorimetry, X-ray diffraction studies indicated intact and amorphous nature of entrapped drug in the microspheres. The drug loaded microspheres could float 10h and sustain the drug release over 4–6h.

Introduction

Conventional oral drug delivery systems such as tablets and capsules guarantee a prompt release of the drug; but they fail to maintain the drug concentration within the therapeutically effective range for a required period. To maintain effective plasma drug concentration, these dosage forms must be administered frequently (Bruck, 1983). Presently, oral controlled drug delivery systems have emerged largely to overcome the problems experienced with the conventional dosage forms. Basically, oral controlled drug delivery systems consist of a drug reservoir from which the drug is released slowly during its transits in GIT, in a predetermined rate to maintain constant absorption of the drug. Drugs used in oral controlled drug delivery must have uniform absorption in the entire gastrointestinal tract.

The development of oral controlled drug delivery possesses a problem for drugs whose absorption changes due to various factors such as dissolution, solubility, pH, enzymes and microbial flora (Saravanan, Balaji, Kavitha, & Kingsley, 2009). Floating drug delivery system is one of the approaches (Lee et al., 1999, Singh and Kim, 2000) to increase gastric residence time and localize the drug at the stomach. This approach will enhance bioavailability of those drugs, which are poorly absorbed from the intestine. Drugs such as piroxicam (Joseph, Lakshmi, & Jayakrishnan, 2002), furosemide (Menon, Ritschel, & Sakr, 1994), theophylline (Stithit, Chen, & Price, 1998), acetohydroxamic acid (Umamaheswari, Jain, Bhadra, & Jain, 2003), 5-fluorouracil (Vaghani, Vasanti, Chaturvedi, Satish, & Jivani, 2010) and ranitidine hydrochloride (Mastiholimath, Dandagi, Gadad, Rashmi, & Kulkarni, 2008) were formulated as floating microspheres in order to retain them in the stomach.

Ranitidine hydrochloride (RH) is a H_2 receptor antagonist (Grant, 1989) used in the treatment of peptic ulcer. Since the biological half life of the drug is between 2 and 3 h, it is necessary to administer the drug frequently which may produce saw tooth kinetics and results in ineffective therapy. The drug can be preferably administered in controlled release dosage forms to obtain a better effect. RH has variable absorption in the gastrointestinal tract and particularly the absorption in the intestine is less due to microbial degradation (Basit and Lacey, 2001, Williams et al., 1992). Hence an oral controlled release preparation of ranitidine should be preferably placed in the stomach to achieve uniform drug absorption.

Ethylcellulose is one of the most utilized polymers in the development of microspheres for controlled drug delivery due to its biocompatibility, versatility and lower cost. Floating microspheres using ethylcellulose have received much attention recently (Mastiholimath et al., 2008, Vaghani et al., 2010) for controlled drug delivery in the stomach. These microspheres were prepared by evaporation of organic solvents to get porous microsphere

structure to float. In the present investigation, we are reporting an alternative, novel matrix erosion technique to formulate ethylcellulose floating microspheres for controlled and local delivery of drugs in the stomach. A blend of ethylcellulose and polyethylene glycol (PEG) 4000 was used to make floating microspheres. Matrix erosion due to dissolution of PEG from microsphere was exploited to produce floating microspheres.

In our previous work, we have reported (Saravanan et al., 2009) localization of RH loaded gelatin microspheres in the stomach using a magnetic field for stomach specific delivery. Application of a suitable magnet near the target area is the practical limitation of these formulations. Hence in the present work RH loaded ethylcellulose floating microspheres were developed for stomach specific drug delivery. Ethylcellulose microspheres were formulated with various proportion of PEG and characterized by drug loading, entrapment and encapsulation efficiency, buoyancy, particle size, scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), X-ray diffraction (XRD) and *in vitro* release studies.

Section snippets

Materials

Ethylcellulose (viscosity range 18–22 cp and ethoxy content of 48–49.5%) was purchased from Rainbow-2000, Chennai, India. Polyethylene glycol (4000) was purchased from Sisco Research Laboratories Pvt. Ltd. Mumbai, India. Ranitidine hydrochloride I.P., obtained from Cassel Research Laboratory Pvt. Ltd., Chennai, India. All other reagents used were of analytical grade. Simulated gastric fluid (pH 1.2) without enzymes was prepared with a composition of 0.2% (w/v) of sodium chloride and 0.7% (v/v)

Preparation, drug loading, entrapment and encapsulation efficiency of ethylcellulose microspheres

Formulation of ethylcellulose floating microspheres by a novel solvent evaporation/matrix-erosion method was reported in the present investigation. Solvents such as methanol, ethanol, acetone, dichloromethane and chloroform in single/combination were tried to dissolve RH, ethyl cellulose and PEG. No such single solvent could dissolve polymer and drug. RH is soluble in methanol and sparingly soluble in ethanol. Mixture of acetone:methanol (1:1) was found to be suitable solvent for

Conclusions

Microspheres formulated with ethylcellulose/PEG blend by novel solvent evaporation and matrix erosion method were able to float 12 h without and 10 h with RH. SEM revealed the presence of pores on floating microspheres due to matrix erosion, which are responsible for the floating ability. FT-IR, DSC and XRD indicated intact and amorphous nature of entrapped drug. The microspheres sustained the drug release over a period of 4–6 h. The above results revealed the possibility of development of

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