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FAMOTIDINE LOADED FLOATING BIOMATERIAL GELLAN GUM BEADS IN -VITRO CHARACTERIZATION

***[1]Jogu Sowjanya, B. Rama M. Pharm, phD and M. Swetha[2] M. Pharm**

[1]Department of Pharmaceutics, Mallareddy Institute of Pharmaceutical Sciences, JNTU Hyderabad, Telangana, India.

[2]Holymary institute of technology and Sciences College of Pharmacy, Keesara, Hyderabad, Telangana, India.501301.

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***Corresponding Author**
Jogu Sowjanya
Department of Pharmaceutics, Mallareddy Institute of Pharmaceutical Sciences, JNTU Hyderabad, Telangana, India.

ABSTRACT

Famotidine has been the most broadly utilized drug for the treatment of peptic ulcer for a long time. The present examination concerns the formulation and evaluation of floating tablets of famotidine which after oral administration, to drag out the gastric residence time, increment medicate bioavailability and focus on the gastric ulcer. A gliding drug delivery system was created gellan gum. Every one of the formulations were subjected for preformulation evaluation. After effects of preformulation examines, FTIR, SEM, molecule size and size dissemination, % yield, drug content, buoyancy time, entrapment efficiency, in vitro dissolution and release kinetics. The FTIR Spectra uncovered that, there was no cooperation among polymers and Famotidine. Based on release information of Famotidine plan F5 demonstrated a decent controlled release profile with most extreme ensnarement effectiveness as a result of ideal polymer fixation i.e., 1:3 proportion (Gellan gum) with sodium alginate than other drug: polymer proportions. The invitro dissolution studies for best formulation F5 were fitted in various kinetic models i.e, zero order, first order, Higuchi and korsemeyer-peppas models. optimized formulation F5 demonstrates zero order sedate release with Super case II transport system.

KEYWORDS: Famotidine, Gellan gum, FTIR, SEM.

INTRODUCTION

Pharmaceutical invention and research are gradually more focusing on delivery systems

which enhance desired therapeutic objectives while lowering side effects. Recent trends specify that multiparticulate drug delivery systems are specifically suitable for achieving controlled formulations with smallest amount risk of dose dumping1.Multiparticulates offer greater advantages over single unit system as they disperse uniformly in GI tract, possess more predictable gastric emptying, offer flexibility and show less inter and intra individual variability in formulation process.[1-2]

Over the past decades, hydrogel polymers have attracted a great deal of attention for use as Potential carriers in controlled and sitespecific delivery of drugs.[3-5]

Hydrogels are the hydrophilic, three-dimensional network structures having the natural property to absorb large quantity of water or biological fluids and they resemble those of biological tissues. The ability of hydrogels to swell in the presence of water or biological fluids regulates the release of the encapsulated drugs. By controlling the degree of swelling due to cross linking makes them potential carriers of drugs for controlled release applications.[6]

Hydro gels from natural polymers, especially polysaccharides, have been widely used because of their advantageous properties over synthetic polymers such as non-toxicity, biocompatibility, biodegradability, ability to modify the properties of aqueous environments, and capacity to thicken, emulsify, stabilize, encapsulate, swell, and form gels and films.[7]

Gellan gum (GG) is an extracellular anionic heteropolysaccharide consisting of a linear structure of repeating tetrasaccharide units of glucose, glucuronic acid, and rhamnose in a molar ratio of 2:1:1. It has a characteristic temperature and ionic-dependent gelling property. The mechanism of gelation involves the formation of double helical junction zones followed by aggregation of double helical segments to form a three-dimensional network by complexation with cations such as calcium and zinc and hydrogen bonding with water.[8]

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the GRT of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestine. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.

Famotidine has been the most widely used drug for the treatment of peptic ulcer for many decades. The present investigation concerns the formulation and evaluation of floating tablets of famotidine which after oral administration, to prolong the gastric residence time, increase drug bioavailability and target the gastric ulcer. A floating drug delivery system was developed using gellan gum. The concept of formulating floating hydrogel beads containing Famotidine offers a suitable, practical approach to achieve a prolonged therapeutic effect by continuously releasing the medication over extended period of time.

MATERIALS AND METHODS

Famotidine was procured from B.M.R. chemicals pvt. Ltd., Sodium alginate was procurewd from S D fine chemical Ltd, Mumbai. Gellan gum, Calcium chloride, were procured from Loba chemie Pvt. Ltd., Mumbai.

Preformulation studies[9-10]

Preformulation studies includes solubility studies, determination of UV spectrum, Calibration curve of Famotidine in 0.1N HCL. Drug polymer interactions were studied by FT-IR spectroscopy.

Preparation of Famotidine Hydro gel beads[11]

Method used – Ionotropic gelation method

Accurate quantity of polymer was dissolved in 25ml of distilled water and stirred to form dispersion. Drug was added to the above dispersion and again stirred for uniform distribution. and stirred until a homogenous mixture was obtained. The mixture was extruded through a 23G syringe needle into calcium chloride solution. The beads were allowed to remain in the same solution for 30 min to improve their mechanical strength. The formed beads were separated, washed with water and allowed to dry at room temperature overnight.

Evaluation of Famotidine Loaded Floating Gellan Gum Beads[12-16]

Surface morphology (SEM)

Scanning electron microscopy has been used to determine particle size distribution, surface topography, texture, and to examine the morphology of fractured or sectioned surface. SEM is probably the most commonly used method for characterizing drug delivery systems, owing in large to simplicity of sample preparation and ease of operation. SEM studies were carried out by using JEOL JSM T-330A scanning microscope (Japan).

Percentage yield

Percentage practical yield of Famotidine hydrogel beads was calculated to know about percentage yield or efficiency of any method, thus it helps in selection of appropriate method of production. Practical yield was calculated as the weight of Famotidine beads recovered from each batch in relation to the sum of starting material.

The percentage yield of Famotidine beads prepared was determined by using the formula.

$$\text{Percentage yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

Buoyancy behavior[17]

The time between the introduction of the FDDS into the medium and its buoyancy to the upper one third of the dissolution vessel (floating lag time) and the floating ability was determined using USP dissolution tester apparatus II (Paddle method). Fifty beads were put in the vessel and the paddles were rotated at 50 rpm in 900 ml 0.1 N HCl pH 1.2, maintained at 37±0.5 °C for 12 hours. The floating ability of the beads was measured by visual observation. The preparation was considered to have buoyancy, only when all beads floated on the test solution immediately or within a lag time which did not exceed 2 min.

Drug Entrapment Efficiency[18]

20mg of prepared floating alginate beads of Famotidine were dissolved in 50 ml of 0.1N HCl (pH 1.2) and the drug content was analyzed at 266nm using a UV/visible spectrophotometer (PG Instruments T60). Encapsulation efficiency was calculated as the percentage (w/w) of the theoretical drug content.

EE (%) = Actual Drug Content/ Theoretical Drug Content X 100

In-vitro dissolution studies[19-20]

Procedure for In-vitro dissolution study

The release rate of Famotidine Hydrogel beads was determined by employing USP apparatus II (Paddle method). The dissolution test was performed using 900 ml 0.1N HCL, in 37 ±0.5°C at 50 rpm. Famotidine hydrogel beads equivalent to 20 mg of Famotidine was used for the study. At various time points (hourly) 5ml of the sample solution was withdrawn from the dissolution apparatus for upto 12 hrs, and the samples were replaced with fresh dissolution medium. The samples were filtered and the absorbance was determined at 266nm. Dissolution profiles of the formulations were analyzed by plotting

cumulative percentage drug release versus time.

The data obtained were also subjected to kinetic treatment to understand release mechanism.

RESULTS AND DISCUSSION

Drug polymer interaction (FTIR) study

FTIR Spectra were obtained for Famotidine, physical mixture, Famotidine and polymers. The characteristic peaks of the Famotidine were compared with the peaks obtained for physical mixture of Famotidine and polymer. From the obtained spectra it appeared that there were no interaction between Famotidine and polymers.

Surface morphology (SEM)

The surface morphology of the Famotidine beads was studied by SEM. SEM photographs of the optimized formulation was shown in the Fig.7.5. Surface morphology of the Famotidine beads revealed that the beads were found to be spherical with rigid nature, which was formulated using Gellan gum.

Particle size analysis

As the ratio of polymer was increased, the mean particle size of Famotidine beads had also decreased. The significant decrease may be due to the increase in the viscosity of the droplets. Famotidine beads having a size range of 1.6 to 1.7 mm.

Buoyancy

The floating ability of prepared beads were evaluated. The beads remained a float throughout the study period (7-12hrs). It was observed that varying the polymer concentrations in the bead formulations did not affect the floating lag time or the floating duration of the beads in the dissolution media.

Percentage yield

The percentage yield for Famotidine floating hydrogel beads were given in table 7.5.

Percentage drug entrapment efficiency

Entrapment efficiency increased with increase in the polymer concentration. From the results it can be inferred that there is a proper distribution of Famotidine in the beads and the deviation were within the acceptable limits.

By increasing the polymer concentration, the encapsulation efficiency was increased. The entrapment efficiency of high in beads that were formulated by using xanthan gum.

***In vitro* dissolution studies**

The *in vitro* performance of Famotidine floating hydrogel beads showed prolonged and controlled release of Famotidine. The results of the *in vitro* dissolution studies showed controlled release in a predictable manner. As the polymer concentration was increased, the drug release from the floating hydrogel beads were found to decrease. Compared to Gellan gum beads of formulations containing 1:1, 1:2 & 1:3 & 1:4. 1:3 ratio showed sustained drug release even by changing the external phase ratios and also with changes in RPM. So F5 formulation was considered as the best formulation based upon the in vitro drug release.

The *in vitro* release profiles of all the formulations F1 to F10.

CONCLUSION

The concept of formulating floating hydrogel beads containing Famotidine offers a suitable, practical approach to achieve a prolonged therapeutic effect by continuously releasing the medication over extended period of time. In present work, floating hydrogel beads of Famotidine were prepared successfully by ionotropic gelation method using gellan gum in different ratios.

From the above experimental results it can be concluded that:

Preformulation studies like melting point, solubility and UV analysis complied with standards. The FTIR Spectra revealed that, there was no interaction between Famotidine and polymers. Surface smoothness of the Famotidine beads was confirmed by SEM. As the ratio of polymer was increased, the mean particle size of Famotidine floating beads was decreased. Famotidine floating beads with normal frequency distribution were obtained.

Entrapment efficiency increased with increase in the polymer concentration upto 1:3 ratio, in 1:4 ratio entrapment efficiency was found to be decreased due to the increased polymer concentration the drug entrapment was decreased.

The study also indicated that the amount of drug release decreases with an increase in the polymer concentration. The *in vitro* performance of Famotidine Floating hydrogel beads showed prolonged and controlled release of drug, with Gellan gum.

Based upon the preliminary data and in vitro dissolution studies of Famotidine floating hydrogel beads it was concluded that the formulation of floating hydrogel beads was successfully formulated by using sodium alginate along with Gellan gum in 1:3 ratio.

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