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FORMULATION AND EVALUATION OF MICROBALLONS OF FAMOTIDINE FOR THE TREATMENT OF GASTRIC ULCER

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ABSTRACT

In the present research envisaged was to prepare gastro retentive micro balloons to increase the retention time in stomach and to modulate the release pattern of drug. The formulation were prepared by solvent diffusion evaporation method in which different concentration of polymers Eudragit S 100, Hyaluronic acid were used to get the optimized formulations, These prepared formulations were subjected for further characterization were done by determining particle size, Percentage yield, percentage entrapment efficiency, surface morphology in percent buoyancy, vitro drug release. These observations suggested that floating microballoons were promising as a carrier for intragastric floating drug delivery of famotidine.

KEYWORDS: Famotidine, Floating Drug Delivery Systems, Gastric Residence Time.

INTRODUCTION

Conventional oral formulations such as tablets, capsules, pills give a specific drug concentration in systemic circulation but do not release at the drug in constant rate for prolonged period of time in to increase the bioavailabily of formulation.

Controlled release drug delivery system (CRDDS) provides drug release at a controlled and predictable rate either systematically or locally for desired duration and provide best therapeutic effect of a drug. Controlled-release drug delivery system increases activity of duration for short half-life drugs, reduce side effects and gives better bioavailability.[1] Floating drug delivery systems (FDDS) or hydro-dynamically balanced systems like microballoons have a bulk density lower than gastric fluids and therefore they floating in the stomach without affecting the gastric-emptying rate for a prolonged period.[2]

Microballoons are one of the most widely used buoyant systems with the unique advantages of multiple unit systems exhibits better floating properties, due to central hollow space inside the microsphere. These formulations are characteristically free flowing powders comprising of proteins or synthetic polymers.[3] Famotidine is a histamine H_2-receptor antagonist. It is majorly prescribed in gastric ulcers, and gastro esophageal reflux disease. It is incompletely absorbed from GI tract, the low bioavailability (40-45%) and short biological half-life (2.5-3.5 h) of famotidine following oral administration is the basic reason for the development of a sustained release formulation of this drug.[4]

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MATERIAL AND METHODS

Drug Famotidine was obtained as a gift sample. Eugdragit S 100, hyaluronic acid, Poly vinyl alcohol were purchased from CDH cheicals New Delhi other solvent used in the work were of analytical grade.

PREPARATION AND OPTIMIZATION OF FLOATING MICROBALLOONS

PREPARATION OF FLOATING MICROBALLOONS BY SOLVENT DIFFUSION-EVAPORATION METHOD

Floating microballoons were prepared by solvent diffusion evaporation method. Accurate quantity of polymer mixture i.e. Eudragit S 100 and Hyaluronic acid was dissolved in ethanol followed by the addition of dichloromethane (1:1). The drug was homogeneously dispersed in this polymer solution. This solution was slowly introduced into polyvinyl alcohol (0.75%w/v) solution with stirring at 400-500 rpm using a mechanical stirrer (Remi India). The solution was stirred for 3-4 hrs and floating microballoons were collected by filtration, washed three times with distilled water and dried at room temperature for 24 hrs.

CHARACTERIZATION OF PREPARED FLOATING MICROBALLOONS

The prepared floating microballoons were characterized for shape and surface morphology, size and size distribution, percent drug loading and *in vitro* drug release.

Table 1.Optimized formulation on the basis of Formulation & process variables

S. No.	Optimized parameter	Formulation code	Final code for optimized preparation
1.	Polymer ratio	1:1	FF1
2.	Surfactant concentration (0.75)	0.75	
3.	Stirring speed	450rpm	
4.	Drug polymer concentration (60mg)	60mg	

SHAPE AND SURFACE MORPHOLOGY

The floating microballoons were examined by optical and scanning electron microscopy. Floating microballoons were suspended in water and than a drop having microballoons was placed on a glass slide, covered with a cover slip and viewed under the optical microscope (Leica -Biomed, Germany) to examine their shape.

In order to examine the surface morphology, the further formulations were analyzed scanning electron microscope.

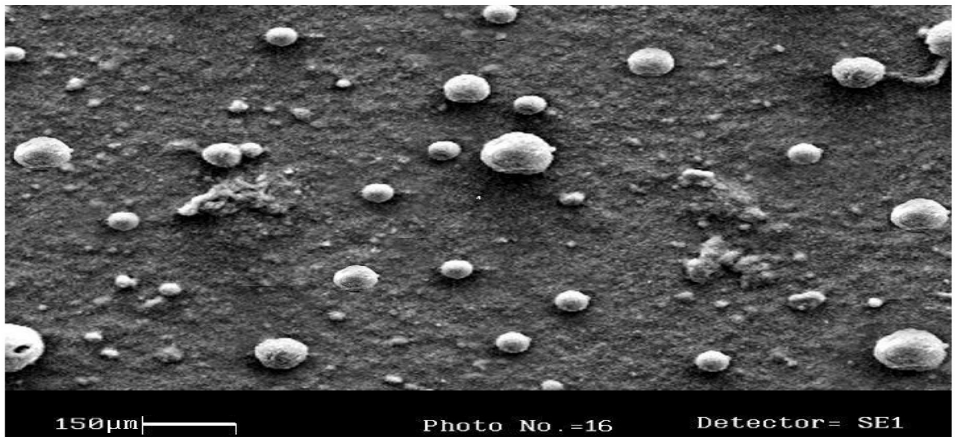

Figure 1.SEM photograph of Famotidine floating microballoons

PARTICLE SIZE AND SIZE DISTRIBUTION

Floating microballoons were studied microscopically for their size and size distribution using calibrated ocular micrometer. Least count of the ocular micrometer was calculated as 16.2 μm. Around 100 particles from each formulation were observed and the data for each formulation were recorded.

DRUG CONTENT

The drug content was measured by extracting 100 mg of microballoons using 0.1 N HCl with aggitaion for 8 hrs. The dispersion was sonicated for 15 min. and filtered . After appropriate dilution with 0.1N HCl, absorbance was taken in UV spectrop-hotometer at 264 nm. The percentage drug content was calculated from the formula :

Drug Content **(%)**

$$= \frac{\textbf{Weight of drug in floating microballoons}}{Weight\ of\ Microballoons}$$

ENTRAPMENT EFFICIENCY

Drug entrapment efficiency represents the proportion of the initial amount of drug ,wich has been incorporated in to the microballoons it was calculated using the formula

Entrapment Efficiency

$$= \frac{Calculated\ drug\ content}{Theoretical\ Drug\ content} x100$$

IN VITRO BUOYANCY

Floating microspheres (equivalent to 100 mg) were dispersed in 900ml of 0.1 N hydrochloric acid solution (pH 1.2) containing tween 20 (0.0 2 W /V %) to simulate gastric fluid at 37°. The mixture was stirred with a paddle at 100 rpm and after 12 hr, the layer of buoyant microspheres (Wf) was pipetted and separated by filtration simultaneously sinking microspheres (Ws) was also separated. Both microspheres type were dried at 40°C overnight Each weight was measured and buoyancy was determined by the weight ratio of the floating microsphers to the sum of floating and sinking microsphers.

YIELD OF FLOATING MICROBALLOONS:

The prepared floating microballoons were collected and weighed. The measured weight was divided by total amount of all non-volatile components which were used for the preparation of microballoons.

Percentage Yield

$$= \frac{Actual\ weight\ of\ Product}{Total\ weight\ of\ excipient\ and\ drug} X100$$

Table 2.Different evaluation parameters of Preparedmicroballoons

Formulation code	% yield	Entrapment efficiency	% buoyancy
F1S2R3D5	83.13	73%	62

IN VITRO DRUG RELEASE STUDY IN SIMULATED GASTROINTESTINAL FLUID

Best formulation of floating microballoons was evaluated for the *in vitro* drug release study by the paddle type dissolution apparatus specified in USP XXIII.

50 mg of Famotidine loaded floating microballoons was weighed accurately and gently spread over the surface of 900 ml of dissolution medium. The content was rotated and thermostatically controlled at 37±0.5°C. Condition was prevailed during the drug dissolution. The release was tested in dissolution medium of pH 1.2. An aliquot was withdrawn at predetermined time intervals and an equivalent amount of fresh medium was added to the release medium. The collected samples were analyzed spectrophotometrically.

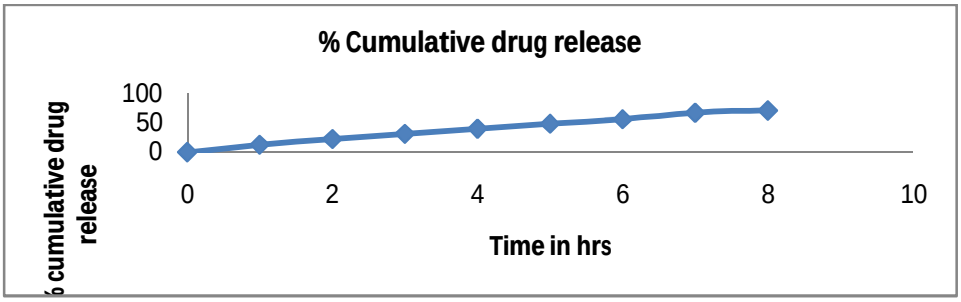

Figure 2.Cumulative percentage drug release and per hour of the microballoons

RESULT AND DISCUSSION

The microballoons of famotidine was prepared by solvent diffusion evaporation Method. The effect of formulation variables e.g. drug concentration, solvent ratio of internal phase (ethanol/DCM), surfactant concentration and process variables e.g. stirring speed were studied in order to optimize the formulation. The results suggested that these variables influence the shape, size and size distribution, total drug loading efficiency and *in vitro* drug release. Hence these parameters were optimized to prepare microballoons of small size with narrow size distribution, good drug loading efficiency, good release at the gastrointestinal pH and good surface morphology.

Effect of polymer concentration was found to influence the particle size by increasing concentrationof polymer it was observed that size of microballoons were found to be increased. The surfactant concentration was optimized on the basis of particle size of microballoons. In case of 0.50%w/v surfactant concentration, the particle size was slightly more than that of F1S2. The reason behind this is that 0.50% w/v surfactant concentration was not sufficient to reduce the surface charge so that the particles were aggregated and resulted in increase in particle size. Due to this reason 0.75% w/v surfactant concentration was used

Stirring speed was optimized to get optimum particle size. The results confirmed that stirring speed of 400 and 500 rpm results in approximate same particle size. The microscopic examination of microballoons revealed that the mean diameter of Eudragit S100-PVA complexedmicroballons varied from 121.24μm to 143.24μm by varying the concentration of all variables. Thus it may be concluded that the prepared microballons were of spherical shape with good entrapment efficiency. The optimized formulation FF1.

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