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Original Research Article

FORMULATION AND CHARACTERIZATION OF GASTRORETENTIVE MICROSPHERE OF FAMOTIDINE

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ABSTRACT

This research focuses on the development and evaluation of gastroretentive microspheres of Famotidine, a drug used in the treatment of peptic ulcers. Gastroretentive drug delivery systems aim to prolong the residence time of drugs in the stomach, thereby improving their absorption and bioavailability. Microspheres, owing to their controlled release and ease of formulation, serve as a promising platform for drug delivery. The study involves the formulation of Famotidine-loaded microspheres using various polymers and cross-linking agents. Characterization of these microspheres includes assessment of particle size, morphology, drug loading, and release kinetics. The comprehensive analysis presented in this study provides insights into the formulation and evaluation of Famotidine floating microspheres, offering potential for enhanced therapeutic outcomes in the management of peptic ulcers.

Keywords: Famotidine, Microspheres, Gastroretentive drug delivery, formulation, Evaluation

INTRODUCTION

Gastroretentive drug delivery systems (GRDDS) have emerged as promising strategies to improve the bioavailability and therapeutic efficacy of drugs, especially those with limited absorption windows or requiring sustained release (Das *et al.,* 2021). One such drug is famotidine, a histamine H2-receptor antagonist widely used for treating gastric ulcers, gastroesophageal reflux disease (GERD), and related acid-related disorders (Hongo *et al.,* 2008). However, famotidine's short half-life and frequent dosing regimen present challenges in maintaining optimal drug levels, particularly in patients with gastric retention issues (Shaji *et al.,* 2008). To overcome these challenges, the development of gastroretentive microspheres of famotidine offers a compelling solution. By formulating famotidine into microspheres with buoyancy and mucoadhesive properties, these microspheres can prolong gastric residence time, thereby enhancing drug absorption and ensuring sustained release kinetics.

This study aims to formulate and comprehensively characterize gastroretentive microspheres of famotidine using appropriate polymers and manufacturing techniques. The physicochemical properties of the microspheres, including size, shape, surface morphology, and drug encapsulation efficiency, will be thoroughly evaluated. Additionally, the in vitro drug release profiles, buoyancy, and mucoadhesive properties of the microspheres will be assessed to determine their suitability for gastroretentive drug delivery. By optimizing the formulation parameters, such as polymer type, drug-polymer ratio, and manufacturing method, it is expected that the developed gastroretentive

microspheres will offer enhanced therapeutic outcomes for famotidine therapy. These microspheres hold promise for improving patient compliance, reducing dosing frequency, and ensuring consistent drug delivery, particularly in patients with gastric retention issues.

MATERIALS AND METHODS

Materials

The chemicals were obtained from various suppliers across India. Famotidine was obtained as a gift sample from Bioplus Life Science in Bangalore. Chloroform, Methanol, and Ethanol were supplied by Qualigens Fine Chemicals in Mumbai. Disodium Hydrogen Phosphate, Di potassium Hydrogen Orthophosphate, and Sodium Chloride were all acquired from S. D. Fine Chem. Ltd. in Mumbai. Lastly, HPMC, Ethyl cellulose, and Guar gum were obtained from Loba Chemie Pvt. Ltd. in Mumbai.

Preparation of gastroretentive microsphere of Famotidine

The research aims to develop and evaluate gastroretentive microspheres of Famotidine. Gastroretentive drug delivery systems are designed to prolong the residence time of the drug in the stomach, leading to better drug absorption and bioavailability. Microspheres are widely used in drug delivery due to their high surface area to volume ratio, controlled release, and ease of formulation. The research will involve the development of Famotidine-loaded microspheres using different polymers and cross-linking agents. The microspheres will be characterized for their particle size, morphology, drug loading, and drug release kinetics. The research is expected to provide a novel approach for the delivery of Gastroretentive microspheres loaded with Famotidine were prepared using solvent-evaporation method using HPMC, EC and Guar gum in different ratio table 1 as reported by Rao *et al.,* (2009) with slight modification. Drug and polymer in proportion of drug and polymers were dissolved in 1:2 mixture of solvent system of ethanol and dichloromethane. This clear solution was poured slowly in a thin stream into the aqueous solution of 1% polyvinyl alcohol. The emulsion was continuously stirred for 3 h at a speed of 500 rpm at 27±2°C. The floating microspheres were collected by decantation, while the non-floating microspheres were discarded. The microspheres were dried overnight at 40±2°C and stored in desicator.

Table 1: Formulations of floating microspheres of Famotidine

S. No.	Formulation Code	Famotidine (mg)	HPMC (mg)	EC (mg)	Guar gum (mg)
1.	F1	40	100	25	-
2.	F2	40	100	50	-
3.	F3	40	100	75	-
4.	F4	40	150	25	10
5.	F5	40	150	50	20
6.	F6	40	150	75	30

Evaluation of microspheres

Percentage yield

The prepared microspheres with a size range of 1µm to 1000µm were collected and weighed from different formulations. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the microspheres (Nila *et al.,* 2013).

$$\% \text{ Yield } = \frac{\text{Actual weight of product}}{\text{Total weight of drug and polymer}} x\ 100$$

Drug entrapment

The various formulations of the Floating microspheres were subjected for drug content. 10 mg of Floating microspheres from all batches were accurately weighed and crushed (Jain *et al.,* 2005). The powder of microspheres were dissolved in 10 ml 0.1 N HCl and centrifuge at 1000 rpm. This supernatant solution is than filtered through whatmann filter paper No. 44. After filtration, from this solution 0.1 ml was taken out and diluted up to 10 ml with 0.1 N HCl. The percentage drug entrapment was calculated using calibration curve method.

Floating behavior: Ten milligrams of the floating microspheres were placed in 0.1 N HCl (100 mL). The mixture was stirred at 100 rpm in a magnetic stirrer. After 10 h, the layer of buoyant microsphere was pipetted and separated by filtration. Particles in the sinking particulate layer were separated by filtration. Particles of both types were dried in desiccators until a constant weight was obtained (Jain *et al.,* 2009). Both the fractions of microspheres were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

$$\text{Percent buoyancy} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} x\ 100$$

Measurement of mean particle size

The mean size of the microspheres was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the microspheres suspended in 5 ml of distilled water was used for the measurement (El-Kamel *et al.,* 2001).

Determination of zeta potential

The zeta potential of the drug-loaded microspheres was measured on a zeta sizer (Malvern Instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell (Pandya *et al.,* 2011). All the samples were measured in water at 25°C in triplicate.

Shape and surface characterization of microspheres by scanning electron microscopy (SEM)

From the formulated batches of microspheres, formulations (F4) which showed an appropriate balance between the percentage releases were examined for surface morphology and shape using scanning electron microscope Jeol Japan 6000 (Jagdale *et al.,* 2009). Sample was fixed on carbon tape and fine gold sputtering was applied in a high vacuum evaporator. The acceleration voltage was set at 10KV during scanning. Microphotographs were taken on different magnification and higher magnification (200X) was used for surface morphology.

***In-vitro* release studies**

The *in vitro* drug release rate from Floating microspheres was carried out using the USP type II (Electro Lab.) dissolution paddle assembly. A weighed amount of floating microspheres equivalent to 100 mg drug were dispersed in 900 ml of 0.1 N HCI (pH=1.2) maintained at 37 ± 0.5°C and stirred at 55rpm. One ml sample was withdrawn at predetermined intervals and filtered and equal volume of dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. The collected samples analyzed spectrophotometrically at 264nm to determine the concentration of drug present in the dissolution medium.

RESULTS AND DISCUSSION

The study on Famotidine floating microspheres offers a meticulous investigation into various aspects crucial for their formulation and performance. Starting with the percentage yield (Table 2), which provides insights into the efficiency of the production process, the findings reveal consistent yields across different formulations, albeit with slight variations. This consistency suggests a robust manufacturing process, essential for scalability and reproducibility in industrial settings.

Moving on to drug entrapment (Table 3), the results elucidate the amount of drug effectively encapsulated within the microspheres. This parameter directly influences the drug loading capacity and, consequently, the therapeutic efficacy of the formulation. The data exhibit differences in drug entrapment among the formulations, highlighting the impact of formulation variables on drug encapsulation efficiency.

The buoyancy and floating lag time (Table 4) are pivotal characteristics of floating drug delivery systems. The observed variations in these parameters across formulations underscore the importance of formulation optimization in achieving desired floating behavior. Moreover, these findings offer valuable insights into the potential gastric retention capabilities of the microspheres, which are crucial for sustained drug release and improved bioavailability.

The release study data (Table 5) delineate the drug release profiles of the formulations over time. This information is instrumental in understanding the kinetics of drug release and assessing the suitability of the microspheres for controlled-release applications. Notably, the data exhibit distinct release profiles for each formulation, indicating the influence of formulation parameters on drug release behavior.

Lastly, the comparative study of regression coefficients (Table 6) provides a systematic evaluation of different release kinetics models. The high R2 values obtained for the Korsmeyer-Peppas model underscore its efficacy in describing the drug release kinetics of the microspheres. This finding aids in the selection of the optimized formulation and provides valuable insights into the underlying drug release mechanisms.

Table 2: Percentage yield for different formulation of Famotidine floating microspheres

S. No.	Formulation	Percentage Yield
1.	F1	68.85±0.35
2.	F2	67.98±0.25
3.	F3	65.58±0.31
4.	F4	71.12±0.45
5.	F5	65.65±0.33
6.	F6	68.54±0.20

Table 3: Drug entrapment for different formulations

S. No.	Formulation	Drug entrapment (% w/w) of prepared microsphere
1.	F1	67.85±0.32
2.	F2	65.56±0.45
3.	F3	63.32±0.65
4.	F4	70.32±0.25
5.	F5	64.47±0.36
6.	F6	66.36±0.14

Table 4: Percentage Buoyancy and floating lag time of floating microsphere

Formulation	Floating Lag Time (Sec.)	Percentage Buoyancy
F1	74±5	74±5
F2	65±4	69±8
F3	63±3	71±6
F4	55±6	83±6
F5	69±5	69±5
F6	73±3	70±3

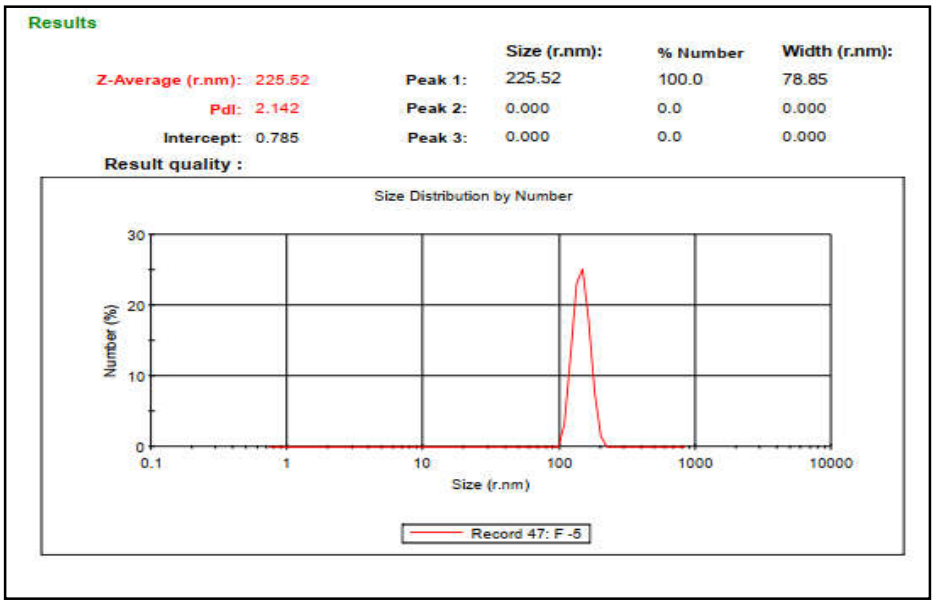

Figure 1: Particle size data of optimized microsphere formulation F4

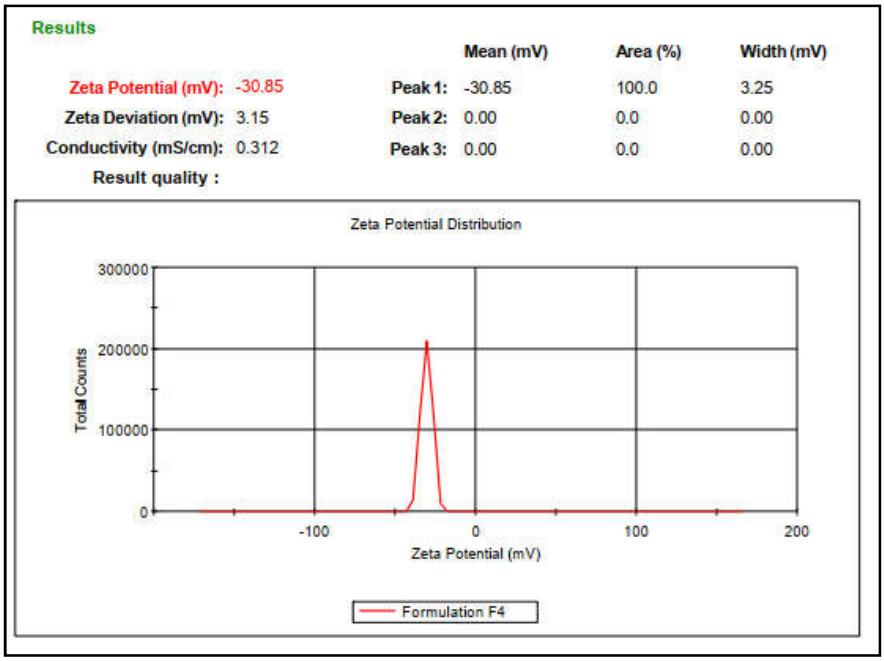

Figure 2: Zeta potential data of floating microsphere F4

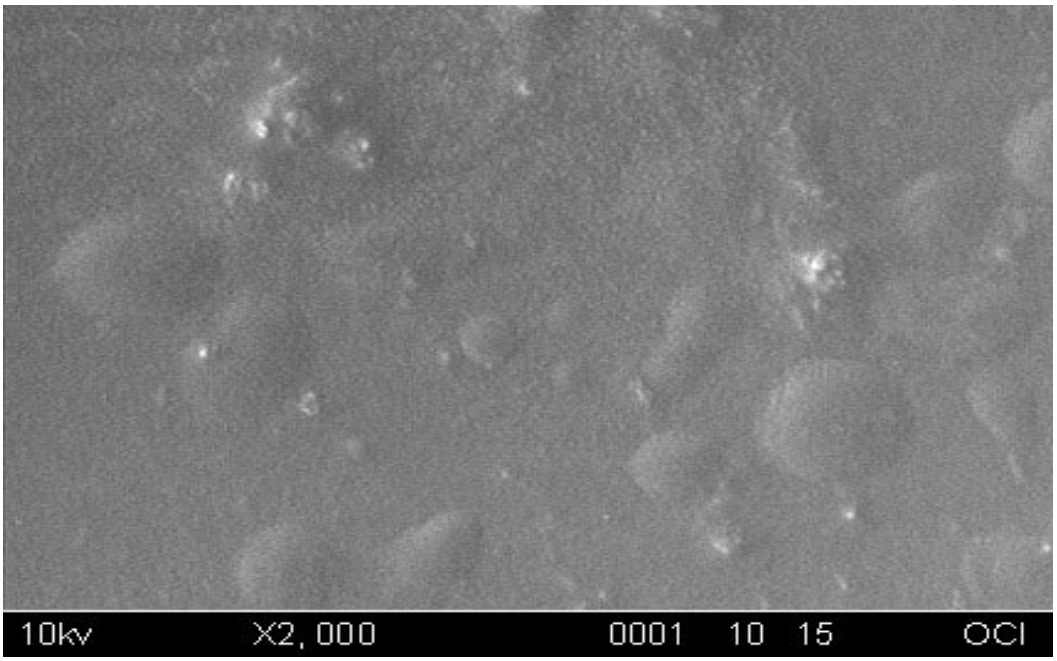

Figure 3: Image of scanning electron microscopy (SEM) of optimized formulation F4

Table 5: Release Study data of formulation F1-F6

Time (Hrs)	% of Drug Release					
	F1	F2	F3	F4	F5	F6
0.5	35.65	32.25	29.98	25.65	20.23	17.85
1	59.98	53.32	49.98	35.65	30.65	26.65
2	66.65	64.45	58.85	43.36	42.25	39.98
4	79.98	76.65	73.32	56.65	53.32	48.85
6	98.85	89.98	75.65	73.32	69.98	61.14
8	99.12	95.65	89.98	89.95	73.32	69.85
10	99.65	98.45	98.85	96.65	86.65	83.32
12	99.85	99.02	99.45	99.12	93.12	90.54

Table 6: Comparative study of regression coefficient of optimized Formulation F4

Release Kinetics	Zero order	First order	Higuchi	Korsmeyer peppas
R^2	0.962	0.930	0.986	0.988

CONCLUSION

The comprehensive analysis presented in this study sheds light on various aspects of Famotidine floating microspheres, including formulation characteristics, drug release behavior, and kinetics. These findings not only contribute to the understanding of floating drug delivery systems but also offer valuable insights for the development of optimized formulations with enhanced therapeutic efficacy and patient compliance.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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