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FORMULATION DEVELOPMENT AND EVALUATION OF FLOATING MICROBALLONS OF LAFUTIDINE

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ABSTRACT

Floating microballoons loaded with Lafutidine were formulated and evaluated for their potential as gastroretentive drug delivery systems. Various formulations (F1-F6) were prepared and characterized for yield, drug entrapment, buoyancy, and in vitro release kinetics. Among them, formulation F5 exhibited a high yield of 75.65% and efficient drug entrapment of 74.65% w/w. It demonstrated a short floating lag time of 52 seconds and high buoyancy (93%), indicating prolonged gastric retention. Particle size analysis confirmed uniform distribution, while SEM imaging revealed spherical morphology. In vitro release studies showed sustained drug release over 12 hours, fitting well with diffusion-controlled models ($R^2 > 0.98$). Formulation F5 holds promise for enhancing Lafutidine's bioavailability and therapeutic efficacy through controlled and sustained drug release.

Keywords: Floating microballoons, Lafutidine, gastroretentive drug delivery, buoyancy, sustained release.

INTRODUCTION

Lafutidine, a histamine H2 receptor antagonist, is widely recognized for its efficacy in treating peptic ulcers and gastroesophageal reflux disease (GERD) due to its potent acid-suppressive properties and relatively long duration of action compared to other H2 blockers (Kothari *et al.,* 2018). However, its bioavailability can be limited due to its absorption primarily in the upper gastrointestinal tract. This challenge has prompted the exploration of novel drug delivery systems, such as floating microballoons, to enhance Lafutidine's therapeutic efficacy.

Floating microballoons are gastroretentive drug delivery systems designed to remain buoyant on the gastric fluid surface, thereby prolonging gastric residence time and improving drug absorption (Streubel *et al.,* 2002). They typically consist of polymers that are buoyant in the stomach environment and encapsulate the drug, allowing sustained release over an extended period.

In recent years, research has focused on optimizing the formulation parameters of floating microballoons to achieve controlled drug release kinetics and enhance bioavailability. Factors such as polymer selection, drug loading efficiency, buoyancy properties, and release mechanisms play pivotal roles in determining the performance of these systems (Sharma *et al.,* 2020).

This study aims to develop and evaluate floating microballoons encapsulating Lafutidine, leveraging their potential to improve drug bioavailability and therapeutic outcomes. The formulation will be systematically optimized to achieve desirable characteristics, including buoyancy, sustained release, and stability. Evaluation will encompass physicochemical characterization,

in vitro drug release studies, and potentially *in vivo* pharmacokinetic assessments, providing comprehensive insights into the feasibility and efficacy of Lafutidine-loaded floating microballoons as a gastroretentive drug delivery system.

MATERIAL AND METHODS

Materials

In the formulation of floating microballoons containing Lafutidine, key materials include Lafutidine from Bioplus Life Sciences, Disodium Hydrogen Phosphate and Sodium Chloride from S. D. Fine Chem. Ltd., solvents like Methanol, Ethanol, and Chloroform from Qualigens Fine Chemicals, and polymers HPMC, Xanthan Gum, and Guar Gum from Loba Chemie Pvt. Ltd. Hydrochloric acid from Ozone International may also be used for pH adjustment.

Methods

Formulation of Lafutidine loaded microballoons

Floating microballoons containing Lafutidine with a central hollow cavity were prepared by the solvent evaporation technique (Yadav and Kumar, 2011). Weighed quantities of acebrophylline, HPMC, Guar Gum and Xanthan Gum were dissolved in a mixture of ethanol and DCM (1:1 solvent ratio) at room temperature. The polymer solution was poured into 250 mL distilled water containing 0.01% Tween 80 and the resulting solution was stirred with a propeller-type agitator at 300 rpm and 40°C for 1 hr to allow the volatile solvent to evaporate. The finely developed microballoons were then filtered, washed with distilled water, and dried in vacuum. The different ratios of polymers were used to prepare the microballoons.

Evaluation of microballoons

Percentage Yield

The prepared microballoons 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 microballoons (Azza and Marwa, 2015).

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

Drug Entrapment

The various formulations of the Floating microballoons were subjected for drug content. 10 mg of Floating microballoons from all batches were accurately weighed and crushed (Azza and Marwa, 2015).The powder of microballoons 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 microballoons were placed in 0.1 N HCl (100 mL). The mixture was stirred at 100 rpm in a magnetic stirrer (Porwal *et al.,* 2011). 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. Both the fractions of microballoons 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 microballoons 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 microballoons suspended in 5 ml of distilled water was used for the measurement (Joshi and Jaimini, 2013).

Determination of zeta potential

The zeta potential of the drug-loaded microballoons was measured on a zeta sizer (Malvern Instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water at 25°C in triplicate (Saneshan and Kanth, 2013).

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

From the formulated batches of microballoons, formulations (F3) which showed an appropriate balance between the percentage releases were examined for surface morphology and shape using scanning electron microscope Jeol Japan 6000 (Amrutha *et al.,* 2015). 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 microballoons was carried out using the USP type I (Electro Lab.) dissolution assembly. A weighed amount of floating microballoons 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 280nm to determine the concentration of drug present in the dissolution medium.

RESULTS AND DISCUSSION

The formulation and evaluation of floating microballoons loaded with Lafutidine represent a strategic approach to enhancing drug delivery efficiency and therapeutic outcomes. The study begins by assessing key formulation parameters, including yield and drug entrapment across formulations labeled F1 to F6. Among these, formulation F5 consistently demonstrates robust performance with a high yield of 75.65±0.32% and impressive drug entrapment of 74.65±0.15% w/w. These figures underscore efficient production processes and effective encapsulation of Lafutidine within the microballoons, crucial for optimizing drug delivery efficacy.

Buoyancy and floating lag time measurements further validate the formulations' suitability for gastroretentive applications. Formulation F5 exhibits a short floating lag time of 52 seconds and exceptional buoyancy at 93%, outperforming other formulations (F1-F6). These characteristics are pivotal as they prolong gastric residence time, potentially enhancing Lafutidine's bioavailability and therapeutic effectiveness by ensuring sustained drug release in the stomach.

Detailed characterization through particle size analysis and Zeta potential measurements provides insights into the physical properties and stability of the microballoons. Particle size data, particularly emphasized in Figure 1 for formulation F5, confirms a uniform distribution critical for consistent drug release kinetics and optimal gastric retention. Meanwhile, Zeta potential findings (Figure 2) for formulation F4 underscore the formulation's stability and interaction potential within biological environments, crucial for maintaining drug integrity and effectiveness.

Scanning Electron Microscopy (SEM) images, exemplified by Figure 3 for formulation F5, offer visual evidence of the microballoons' spherical morphology and surface characteristics. Such microstructural details are pivotal for assessing formulation integrity and potential interactions with gastrointestinal tissues, influencing overall drug delivery performance.

In vitro release studies (Table 5) across formulations F1-F6 and a marketed formulation reveal sustained drug release profiles over 12 hours, with formulation F5 demonstrating a gradual release pattern culminating in nearly complete drug release (99.12%) by 6 hours. This sustained release aligns with controlled drug delivery objectives, suggesting potential benefits such as reduced dosing frequency and improved patient adherence.

Regression analysis (Table 6) further supports the controlled release profile of formulation F5, showing strong correlations ($R^2 > 0.98$) with diffusion-controlled models like Higuchi and Korsmeyer Peppas. These findings validate the formulation's predictable release kinetics and underscore its potential for clinical applications requiring prolonged drug action and enhanced therapeutic outcomes.

Table 1: Formulations of the floating microballoons prepared

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

Table 2: Percentage yield for different formulation of Lafutidine floating microballoons

S. No.	Formulation	Percentage Yield*
1.	F1	67.85±0.15
2.	F2	69.98±0.32
3.	F3	71.21±0.22
4.	F4	66.74±0.45
5.	F5	75.65±0.32
6.	F6	72.32±0.74

***Average of three determinations**

Table 3: Drug entrapment for different formulations

S. No.	Formulation	Drug entrapment (% w/w) of prepared microballoons
1.	F1	66.32±0.22
2.	F2	68.85±0.35
3.	F3	70.32±0.45
4.	F4	63.32±0.32
5.	F5	74.65±0.15
6.	F6	70.52±0.32

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

Formulation	Floating Lag Time (Sec.)	Percentage Buoyancy
F1	73	75
F2	70	82
F3	68	80
F4	63	84
F5	52	93
F6	62	83

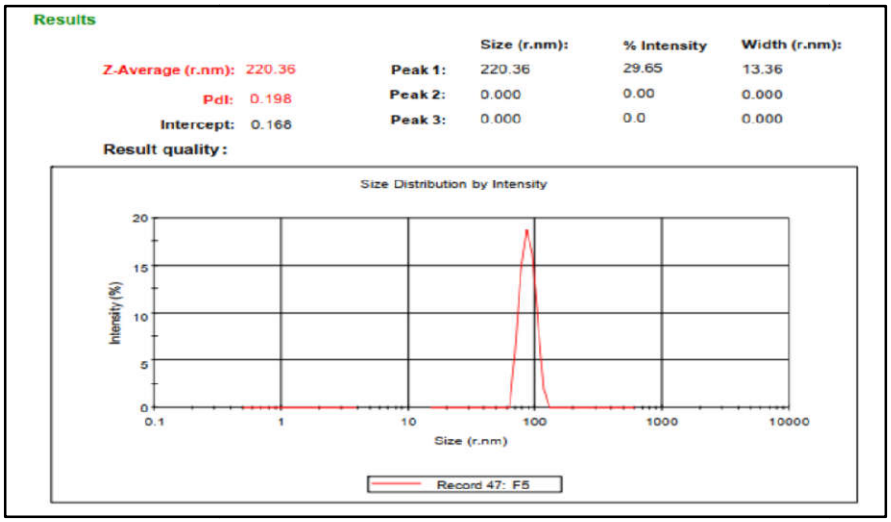

Figure 1: Particle size data of optimized microballoons formulation F5

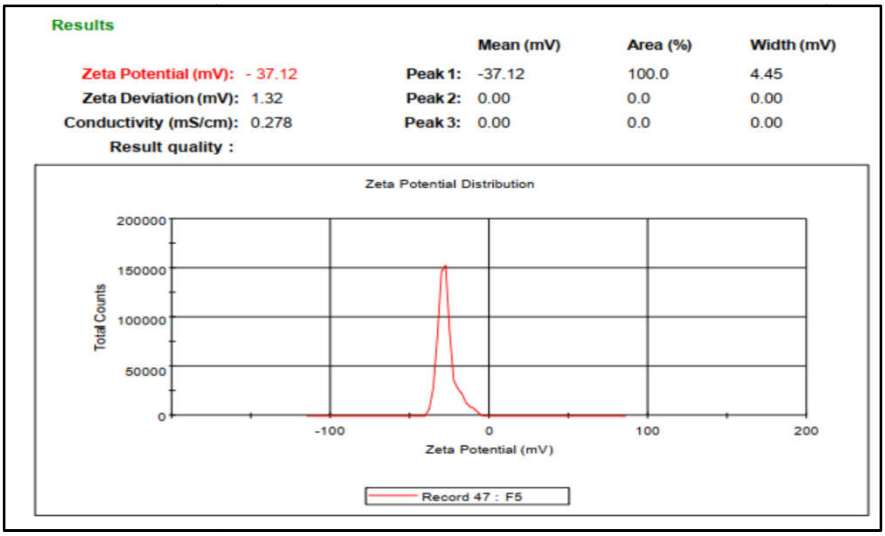

Figure 2: Zeta potential data of floating microballoons F4

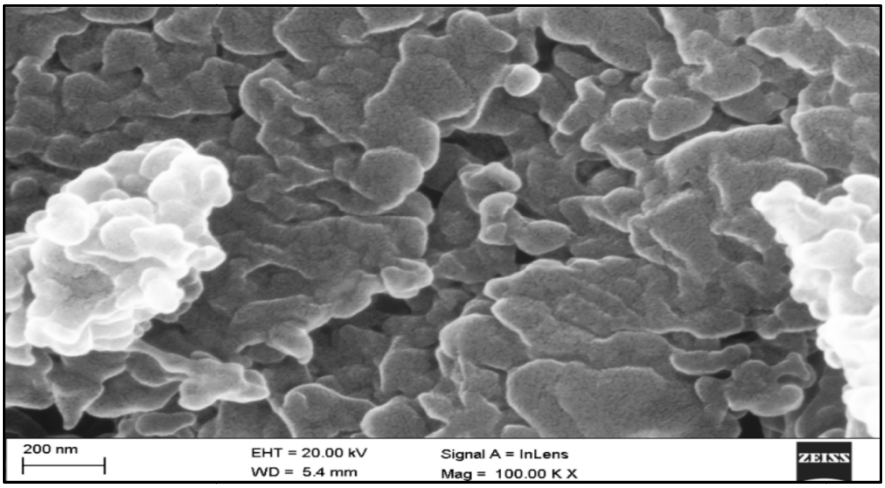

Figure 3: Graph of scanning electron microscopy (SEM) of formulation F5

Table 5: Release Study data of formulation F1-F6

Time (Hrs)	% of Drug Release						
	F1	F2	F3	F4	F5	F6	Marketed Formulation
0.5	39.98	36.65	32.25	30.25	26.65	22.12	44.65
1	56.65	55.45	52.23	46.65	36.85	30.45	76.65
2	73.32	69.98	68.85	65.45	49.98	43.32	98.85
4	82.23	76.65	75.41	69.98	59.98	55.45	99.74
6	99.12	88.85	86.65	82.23	68.78	63.32	-
8	99.85	98.85	97.78	96.65	76.65	74.45	-
10	99.92	99.45	99.45	99.74	89.98	88.85	-
12	99.98	99.74	99.88	99.85	99.12	91.32	-

Table 6: Comparative study of regression coefficient for optimized Formulation F5

Release Kinetics	Zero order	First order	Higuchi	Korsmeyer peppas
R^2	0.967	0.790	0.988	0.990

CONCLUSION

In conclusion, the comprehensive evaluation of floating microballoons loaded with Lafutidine, particularly formulation F5, highlights its advanced formulation characteristics and potential clinical benefits. Future research avenues could focus on refining its properties for specific patient populations or investigating its performance in vivo to validate its therapeutic efficacy and safety in clinical settings.

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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