Original Article

Floating Microspheres of Lafutidine: Formulation, Optimization, Characterization, *in-vitro* and *in-vivo* Floatability Studies Using Eudragit Grades

Sunil Kumar[1,2,*], Abhishek Tiwari[3], Naveen Goyal[4]

[1]Uttarakhand Technical University, Dehradun, Uttarakhand, INDIA.
[2]Vaish Institute of Pharmaceutical Education and Research, Rohtak, Haryana, INDIA.
[3]Devsthali Vidyapeeth College of Pharmacy, Rudrapur, Uttarakhand, INDIA.
[4] Deputy Registrar, Gurugram University, Gurugram, Haryana, INDIA.

ABSTRACT

Aim/Background: The objective behind this study was to develop a Microspheres of Lafuditine using central composite design for gastroretentive drug delivery. **Materials and Methods:** Gastroretentive Microspheres were prepared by Emulsion Solvent Evaporation method. The present investigation will study the effect of formulation variables (polymer concentration etc) on the floating behaviour and drug release characteristics for developing mathematical relationship between them and optimize the formulation with an aim to minimize onset of floatation, maximize the duration of floatation in stomach in order to achieve maximum bioavailability and therapeutic efficacy of selected drug. Microspheres were evaluated for shape, size, melting point, buoyancy time, floating capacity, % yield, swelling index, and *in-vitro* drug release and in-vivo kinetic studies. **Results:** Results showed that selected independent variables significantly affect the yield (66-85%), particle size (3.78-10.62 μm), buoyancy (42.68-95.75%), encapsulation efficiency (69.32–94.05%), and cumulative drug release from the microspheres (79.02-96.92%). The interface and quadratic terms were also affect the process variables, it can be said that to develop and optimize gastroretentive system of Lafuditine with central composite design (CCD) is a valuable second-degree design which is effective treatment of *H. pylori* mediated infection and also provides a base to localize the drug release in the gastric region. **Conclusion:** The gastroretentive floating Microparticulate system of Lafutidine will enhance the patient compliance and play a vital role in improving patient's quality of life.

Keywords: Lafutidine, Eudragit, Central composite design, *In-vitro* drug release, Microparticulate system, Sodium bicarbonate.

Submission Date: 23-08-2021;
Revision Date: 02-12-2021;
Accepted Date: 03-03-2022.

DOI: 10.5530/ijper.56.3.116

Correspondence:
Prof. Sunil Kumar
[1]Research Scholar, Uttarakhand Technical University, Dehradun-248007, Uttarakhand, INDIA.
[2]Assistant Professor, Vaish Institute of Pharmaceutical Education and Research, Rohtak-124001, Haryana, INDIA.
E-mail: esabi@ksu.edu.sa

www.ijper.org

INTRODUCTION

Oral route remains the preferred route for the administration of therapeutic agents owing to ease of administration, low cost of therapy and easy fabrication at industrial scale along with better patient compliance.[1,2] An effective oral drug delivery may depend upon many factors such as gastric emptying process, drug release from the dosage form besides pKa, gastrointestinal transit time of the dosage form and site of absorption of drug.[3] Oral controlled release (CR) dosage form had to overcome a number of physiological difficulties such as inability to restrain and locate the dosage form within the desired region of the GIT due to variable gastric motility and emptying. Furthermore, through the major absorption zone for certain drugs the relatively brief gastric emptying time in human which normally averages 2-3 hr and incomplete drug release can result in stomach and upper part of the intestine from the drug delivery system prominent to reduce efficiency of the administered dose.[4] Gastroretentive drug delivery systems are intended to remain in stomach for prolonged periods. They include floating, bioadhesive,

and high density, magnetic and expandable systems. The diversity in these systems is owed to the numerous benefits obtained from designing them. These benefits include increased drug bioavailability, decreased side effects and dosing frequency, in addition to increased patient compliance. Gastroretentive delivery systems are mainly intended for drugs having a narrow absorption window, a biological half-life ranging from 2–8 hr and drugs taken in multiple daily doses.[5] The GRDDS greatly improves the pharmacotherapy of the stomach through local drug release, leading to high drug concentrations at the gastric mucosa.[6]

Micro particulate drug delivery system has recently attracted a lot of attention of scientists working in the area of drug delivery as in addition to other advantages associated with gastro-retentive drug delivery, they also avoid all or none effects associated with unit dosage forms thereby ensuring the success of therapy.[7,8] Many researchers have attempted to formulate floating microcapsules and evaluated them for gastric retention and other characteristics. Present investigation aims to study the effect of formulation variables (polymer concentration etc) on the floating behaviour and drug release characteristics and optimize the formulation parameters with an aim to minimize onset of floatation, maximize the duration of floatation in stomach in order to achieve maximum bioavailability and therapeutic efficacy of selected drug.[9]

Lafutidine is a H_2 Antagonistic agent acting on the H_2- receptor shows site-specific absorption in the stomach and in the upper part of GIT. This drug is very much effective in the treatment of gastric ulcer, gastroesophageal reflux disease and pathological hypersecretory conditions. The drug has plasma half-life range from 1.92 hr and it is given orally at a dose of 10-20 mg, two or three times a day. Lafutidine thus has all the requisite characteristics for developing a gastroretentive drug delivery dosage form which would increase its oral bioavailability. Eudragit is a derivative of acrylic and methacrylic acids. For the preparation of floating microspheres there are several grades of eudragit which were utilized. For the preparation of floating microspheres Eudragit RL, E, and RS grade are used. In those grades, RL 100 and RS 100 are in granular forms and used widely than any other polymer which are pH independent swelling polymer with mucoadhesive properties. To increase the bioavailability and sustain release are the main advantages of these type of polymers.[10]

MATERIALS AND METHODS

Materials

Drug (Lafutidine) has been obtained as a gift sample from Unichem Lab. and other excipients were purchased from Loba Chemie, Mumbai, India.

Methods

Different methods are used here for the characterization and evaluation of microspheres such as; preformulation studies, Scanning elctron microscopy, dissolution profile, anti-ulcerative activity etc.

Calibration Method

Determination of λ_{max}

- 10 mg of Lafutidine was weighed and transferred into a 10 mL of volumetric flask containing approximately 5 mL of acetic acid. Flask was then gently shaken and volume was finally made up to 10 mL using 0.1N HCl.
- 1 mL of this solution was pipette out in another volumetric flask and volume was made up to 10 mL (100 µg/mL) and similarly (10 µg/ mL) and absorbance was measured from 200 nm to 400 nm for determination of λ_{max} of Lafutidine by using UV spectrophotometer.
- Same procedure was repeated for phosphate buffer (pH 6.8) and distilled water.
- The peaks were observed at 286 nm in 0.1N HCl, at 285 nm in phosphate buffer (pH 6.8) and at 276.5 nm in distilled water. The calibration plots were made for all these.

Identification of Formulation Variables and Responses

Fabrication of GRDF with Eudragit (RL 100 and RS 100)

The factors selected were (a) Drug: Eudragit ratio (b) Eudragit RL 100: RS 100 ratio at three levels -1, 0, and +1 where first formulation variable will have drug polymer ratio as 1:1 (+1), 1:1.5 (0) and 1:2 (-1) and second formulation variable will be ratio of Eudragit RL and RS as 25% : 75% (+1), 50% : 50% (0) and 75% : 25% (-1).

The responses variables selected were (a) Particles size, (b) drug entrapment efficiency, (c) *in-vitro* buoyancy studies (d) Dissolution studies.

A total of 13 formulations for 2 factors and 3 levels central composite design as generated by design expert are prepared (Batches EF1 to EF13) as given in Table 1.

Preparation of Microsphere with Eudragit (RL 100 and RS 100)

Gastroretentive Microspheres were prepared by Emulsion Solvent Evaporation.[13] The formulations from EF1-EF13 are same as the design gives these formulations and compostion of all formulations are given in Table 2.

RESULTS AND DISCUSSION

The microspheres were evaluated for flow properties. Bulk density and Tapped Density for all the formulations were found in the range between 0.2046 ± 0.0063 to 0.2609 ± 0.0068 and 0.2331 ± 0.0062 to 0.2989 ± 0.0032 g/ml respectively.

Carr's index of all formulations was found in the range of 11.19 ± 0.54 % to 13.90 ± 0.66 %, indicating that the studied powder blend have an good flow properties.

Table 1: Formulation code with coded factor levels.

Formulation Code	Coded Factor Levels	
	X1	X2
EF1	-1	-1
EF2	-1	0
EF3	-1	+1
EF4	0	-1
EF5	0	0
EF6	0	+1
EF7	+1	-1
EF8	+1	0
EF9	+1	+1
EF10	0	0
EF11	0	0
EF12	0	0
EF13	0	0

Translation of coded levels in actual units

Coded level	-1 (low)	0 (middle)	+1(high)
X1 : Drug: Eudragit Ratio	1;1	1:1.5	1:2
X2 : Eudragit RL: Eudragit RS	1:3	2:2	3:1

Hausner's ratio of all formulation was in the range 1.12 ± 0.022 to 1.16 ± 0.0013, hence the produced powder blends have a good flow property. Angle of repose was found to be in the range of 20.07 to 26.80. The values of angle of repose were less than 30, indicating good flowability. These values indicate the prepared blend exhibited good flow properties. The drug was confirmed by DSC analysis and there was a sharp peak at 102.67°C corresponding to its melting point. The absence of interaction between physical mixtures was further confirmed by DSC analysis. The IR spectra of Lafutidine showed characteristics peaks at 3278cm due to -NH Stretch, 3094-2940 cm due to C-H Stretch, at 1641cm due to C=C Stretch, 1263 cm at due to N-C Bending, 1222-1139 cm due to C-O stretching.

Micromeritics Studies of Prepared Microspheres

Following micromeritic parameters has been carried out. a. Bulk density(BD)/tapped density(TD): Both BD and TD were determined by taking the powdered material into 10mL measuring cylinder after breakage of any agglomerates. The initial volume was noted and then according to USP method II the cylinder is placed in the density tapper instrument and it is measured (upto125 taps). The tapping was continued until a constant volume was observed and final volume of packing after was noted.[11]

BD and TD were calculated by using following Equations

BD = weight of the powder / volume of the packing

TD = weight of the powder / tapped volume of the packing

b. Compressibility index: Compressibility index or Carr's index values of granules were calculated according to the following equation.[12]

Carr's index (%) = [(tapped density – fluffy density) × 100]/tapped density

c. Hausner's ratio: It is the ratio of tapped to bulk density and was calculated by using the following equation.[13,14]

Hausner's ratio = tapped density/ bulk density

Table 2: Composition of formulations (Quantity, in mg).

Ingredients	EFI	EF2	EF3	EF4	EF5	EF6	EF7	EF8	EF9	EF10	EF11	EF12	EF13
Lafutidine	500	500	500	500	500	500	500	500	500	500	500	500	500
Span 60	750	750	750	750	750	750	750	750	750	750	750	750	750
Mag. Stearate	750	750	750	750	750	750	750	750	750	750	750	750	750
Eudragit RL 100	750	500	250	562.5	375	187.5	375	250	125	375	375	375	375
Eudragit RS 100	250	500	750	187.5	375	562.5	125	250	375	375	375	375	375
Sodium Bicarbonate	750	750	750	750	750	750	750	750	750	750	750	750	750

Table 3: Solubility Studies.		
Sr. No	**Media**	**Solubility (mg/ml)**
1	0.1 N HCL(pH1.2)	0.955
2	Phosphate Buffer (pH6.8)	0.710
3	Distilled water	0.846

d. Angle of Repose: Angle of repose is used to determine the flow property of microspheres lower the angle of repose, the better the flow properties.[15,16]

$$\text{Tan } \theta = h/r$$

Where θ = angle of repose, h = height of pile, r = radius of the base of the pile

e. Solubility Studies: An excess quantity of the microspheres was mixed separately with 5 mL of each solvent (i.e. 0.1N HCl, Phosphate buffer (pH 6.8) and distilled water (as given in Table 3) in conical flask and shaken on constant shaker for 24 hr at room temperature. These solution after equilibrium was filtered and absorbance were measured against saturated solution of Lafutidine in respective solvents at 286 nm by using U.V. spectrophotometer.

Encapsulation Efficiency

Accurately weighed (10 mg) microspheres were crushed and dispersed into 25 ml phosphate buffer (pH 7.4) for determination of encapsulation efficiency. The prepared mixture was shaken for 24 hr. After 24 hr, the solution was filtered, and the filtrate was analyzed for the drug content by a UV spectrophotometer at 227 nm after suitable dilution. The percentage encapsulation was calculated as follows: Encapsulation efficiency % ð Þ¼

$$Da = Dt \text{ ½ } \_\_100$$

Where, Da is the actual amount of drug present in the prepared microspheres and Dt is the theoretical amount of drug added in the preparation of microspheres.

Buoyancy Study

Fifty milligrams of prepared microsphere was placed in 100 ml simulated gastric fluid (SGF, pH 1.2) containing 0.02% Tween 20. The mixture was stirred at 100 rpm on a magnetic stirrer. After 8 hr, the supernatant SGF was filtered through a micro porous filter paper (0.2 μm) to separate floating microsphere. The settled microsphere were collected separately. Both floating and settled microsphere were dried at 40°C. The fractions of microsphere were weighed, and the buoyancy was determined by the following formula:

Percentage buoyancy ¼ Wf=Wf þWs ½ 100

Where Wf and Ws are the weights of floating and settled microsphere, respectively. The characterization parameters are given in Table 4.

In-vitro Drug Release Study

The drug release rate from different formulations (EF1– EF13) was determined using USP type II apparatus (TDT- 08L, Electrolab, Mumbai, and India). Dissolution medium (SGF, pH 1.2, 500 ml) containing 0.02% Tween 20 filled in the dissolution vessel, and the temperature was maintained at 37± 0.5°C. Microsphere equivalent to 50 mg of lafutidine were placed in the dissolution vessel, and the paddle was rotated at 50 rpm. Aliquots were withdrawn every 15 min in the first hour and then every hour till the 4th hour followed by the 6th and 8th hr till 12 hr and then cumulative drug release was calculated and Samples were then analyzed by a UV spectrophotometer at 228 nm. The study was conducted in triplicate as given in Table 5.

After evaluation the optimized batch was selected and preceded for the further evaluation.

Scanning Electron Microscopy

The morphology of the microsphere was studied by scanning electron microscopy (SEM) as shown in Figure 1. By adhering the microsphere on a double adhesive tape stuck to an aluminium stub the samples for SEM were prepared. Using a high-vacuum evaporator (Polaron SEM coating system) the stubs were then coated with silver under an argon atmosphere. The internal cavity of the microsphere was examined by cutting into two sections diametrically with a sharp surgical steel blade. The coated sample was then randomly scanned, and photomicrographs were taken with a scanning electron microscope (EVO-50, ZEISS; UK).

Fourier transform infrared (FTIR) spectroscopy

The IR spectra of Lafutidine showed characteristics peaks at 3278 cm due to -NH Stretch, 3094-2940 cm due to C-H Stretch, at 1641 cm due to C=C Stretch, 1263 cm at due to N-C Bending, 1222-1139 cm due to C-O stretching. Although the drug was obtained as gift sample but again in order to confirm its identity, FTIR spectroscopy method was utilized. The band position are given in Table 6 and the spectra is shown in Figure 2.

Determination of Melting Point/DSC

Capillary tube was fused from one side and then filled with the drug (Lafutidine) from another side. After that it was inserted into the melting point apparatus. Temperature was noted at which solid drug converts into liquid form by visual observation and same

Table 4: Characterization of microspheres.

Formulation code	Shape	Mean Particle Size	Yield	Buoyancy (%)	Encapsulation efficiency (%)
EF1	Spherical	10.62	77.63	91.28	90.02±3.74
EF2	Spherical	9.47	78.67	80.33	83.12±2.10
EF3	Spherical	10.23	66.45	76.56	75.22±1.73
EF4	Spherical	10.43	69.77	86.33	78.42±1.54
EF5	Spherical	8.43	80.27	82.55	80.02±3.75
EF6	Spherical	8.56	87.43	92.32	94.05±2.36
EF7	Spherical	4.29	76.89	45.67	69.32±2.77
EF8	Spherical	3.78	81.40	56.67	89.02±1.73
EF9	Spherical	7.89	82.49	67.98	76.02±2.33
EF10	Spherical	4.87	79.69	78.65	79.02±1.74
EF11	Spherical	9.66	84.33	78.55	84.02±3.79
EF12	Spherical	6.38	85.79	69.99	82.02±2.78
EF13	Spherical	5.88	83.10	80.55	83.02±1.77

Table 5: Total floating time and Percentage Cumulative Drug Release of Batches (EF1-EF13).

Batch No.	Total Floating Time (hr)	Cumulative drug release
EF1	> 12	81.42±2.13
EF2	> 12	92.54±1.21
EF3	> 13	79.02±2.32
EF4	> 12	80.21±2.11
EF5	> 12	85.41±1.57
EF6	> 12	96.92±2.61
EF7	> 13	84.72±1.32
EF8	> 12	87.67±1.23
EF9	> 12	86.67±1.87
EF10	> 12	87.92±2.31
EF11	> 12	82.23±2.88
EF12	> 14	81.71±1.76
EF13	> 13	83.21±2.08

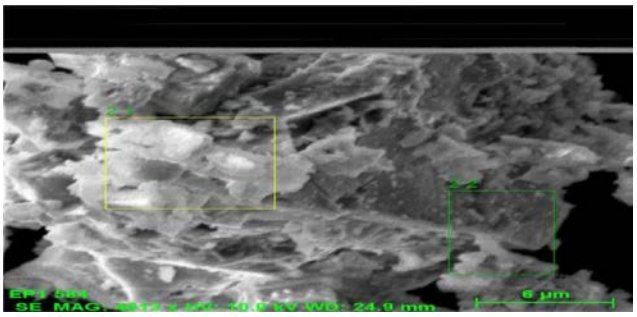


Figure 1: Scanning electron micrographs of floating microspheres.

Table 6: Band position and functional groups.

Sr.No.	Band position (cm^{-1})	Functional Group Assignment
1.	3278	-NH Stretch
2.	3094-2940	C-H Stretch
3.	1641	C=C Stretch
4.	1583-1456	C=O Stretch
5.	1263	N-C Bending
6.	1222-1139	C-O Bending
7.	1024	S=O Bending

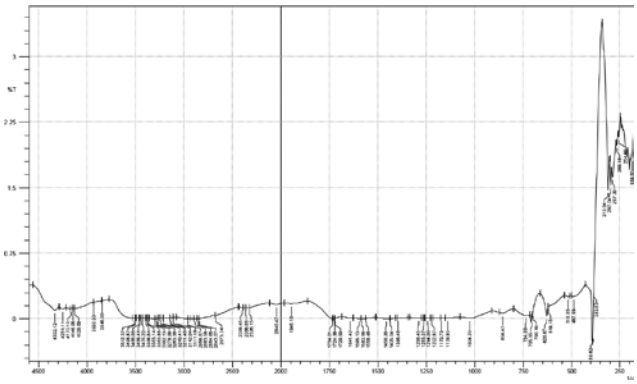


Figure 2: Fourier transform infrared (FTIR) spectroscopy of drug.

procedure was repeated thrice. The average range of melting point of the drug is found 102°C. Although it is calculated by Differential Scanning Calorimetry (DSC) also as shown in Figure 3.

X-ray Diffraction Studies

X-ray diffraction analysis of pure Lafuditine and the optimized formulation as shown in Figures 4 and 5

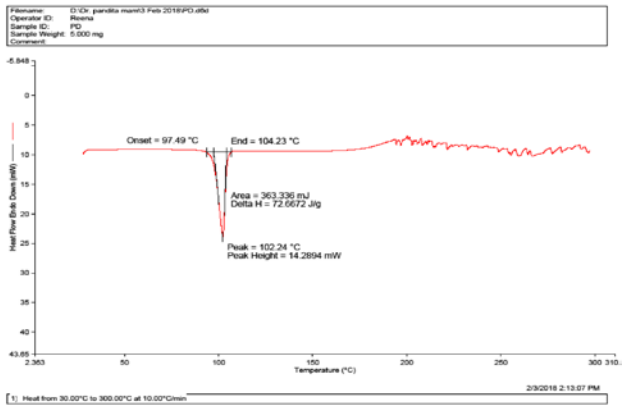


Figure 3: Differential Scanning Calorimetry (DSC).

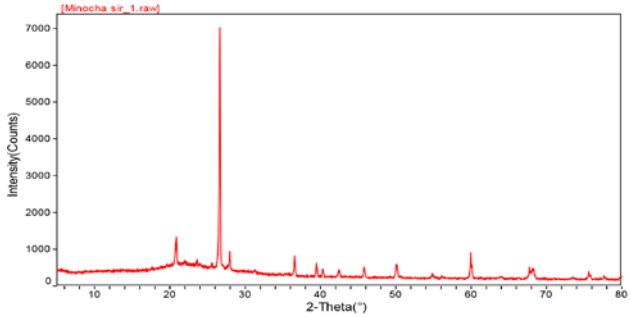


Figure 4: X-ray diffraction patterns of pure drug Lafutidine.

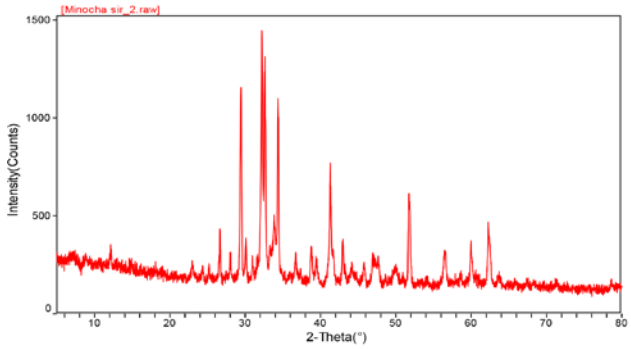


Figure 5: X-ray diffraction of drug-loaded floating microspheres.

respectively, was done by X-ray powder diffractometer (PW 3040/ 60 Xpert PRO, Panlytical, Netherlands). The X-ray diffraction patterns were recorded using Cu Kα radiations (λ=1.5405980), a current of 30 ma, and a voltage of40 kv. The samples were analyzed over 10–40 2θ range with a scan step size of 0.02 and 0.50 s per step.

Table 7: ANOVA of the Regression (%CDR).

	Degree of freedom	Sum of squares	Mean square	F	F-significance
Total	19	191.46	-	-	-
Residual	10	38.66	3.87	-	-
Regression	9	152.80	16.98	4.39	0.0151*

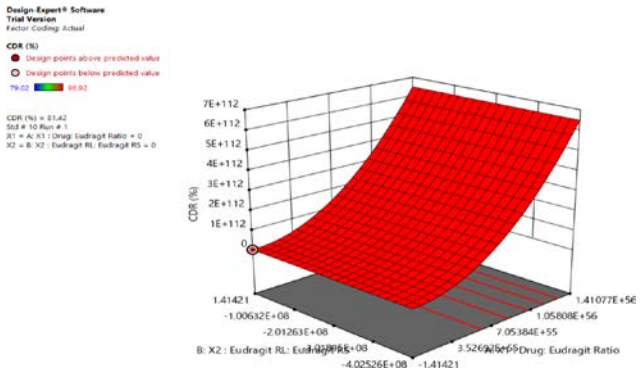


Figure 6: 3D Surface Model Graph.

ANOVA on percentage cumulative drug release from various formulations: Polymer decreases the drug release in formulation with increase in concentration while sodium bicarbonate increases drug release in formulation. % CDR increases with the increase in concentration of polymer. ANOVA was applied (given in Table 7) on %CDR to study the fitting and significance of model. The model developed from multiple linear regression to estimate effect (Y) can be presented mathematically as:

$$Y = 83.44 - 1.14\ X_1 - 1.28X_2 + 1.60\ X_1 X_2 + 1.44\ X_1^2 - 0.44\ X_2^2$$

Where, Y is % CDR, X_1: Drug: Eudragit Ratio, X_2: Eudragit RL: Eudragit RS[1]

ANOVA was applied using on the % cumulative drug release to study the fitting and significations of model in Table 5. *F*-test was carried out to compare the regression mean square with the residual mean square. The ratio F = 4.39 shows regression to be significant. The estimated model, therefore, may be used as response surface for the %CDR as shown by three-dimensional surface model graph and contour plots employing *Design Expert* software (Version 8.0.7.1, Stat-Ease Inc., Minneapolis, MN). The developed model can further be utilized to determine the desired %CDR. Figures 6 and 7 display the 3D surface and contour plot of cumulative

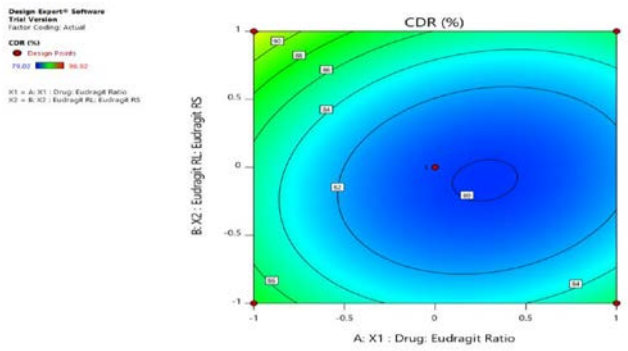


Figure 7: Contour Model Graph.

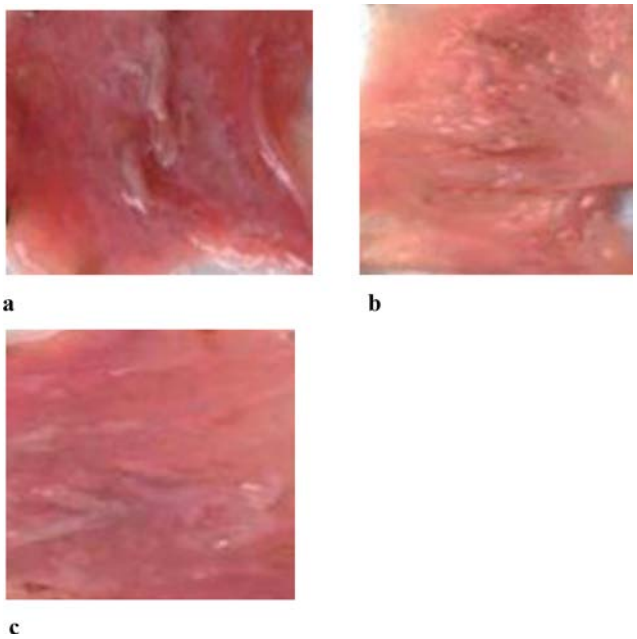


Figure 8: Evidence for the protective effect of Lafutidine microspheres in rats treated with ethanol, (a) control group showing normal gastric integrity (b) Lafutidine solution–treated group (100 mg/kg) (c) Lafutidine loaded microspheres–treated group.

percent of drug release as a function of formulation variables. Formulation EF6 showed good results such as maximum drug release after evaluation of various parameters, so the optimized formulation was selected as EF6.

Release kinetics: The release profile of the optimized batch EF6, fitted best to the Korsemeyer Peppas model (0.9695). In the present study, as per the Korsemeyer Peppas model the value of n (slope) was calculated 0.596, which is a characteristic of non-Fickian drug diffusion mechanism.

Anti-ulcer activity

95% ethanol was administered orally in control group in ethanol-induced ulcer model and it produced specific lesions in stomach which emerged as extended bands red lesions. For normal saline-treated group the *in-vivo* evaluation showed that UI values were 0.64±0.08, for Lafutidine solution 0.49±0.11 and for Lafutidine microspheres it found 0.14±0.08. As compared to free drug treated group microspheres-treated group showed significant ulcer protection (Figure 8).

Stability study: There was no significant change observed in the buoyancy %, entrapment efficiency and *in-vitro* drug release as conducted at an interval of 10 days after 2 months at 40 ± 2°C.

CONCLUSION

Formulation EF6 showed good results after evaluation of various parameters, so as the optimized formulation EF6 was selected. The particle size varies as the polymer concentration changes. With increase in concentration of polymers the drug entrapment efficiency was also increased. With respect to increase in concentration of polymers *in-vitro* buoyancy and the *in-vitro* drug release decreased. The optimized formulation showed good floating for 10 hr in stomach of rat. This prolonged local residence time may lead to effective management of *H. pylori*-induced peptic ulcer.

ACKNOWLEDGEMENT

The authors are highly thankful to the Late Prof. (Dr) S.K.Singh Dept. Of Pharmaceutical Sciences, GJUS&T, Hissar, Haryana for providing essential facilities and guidance to accomplish this research study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

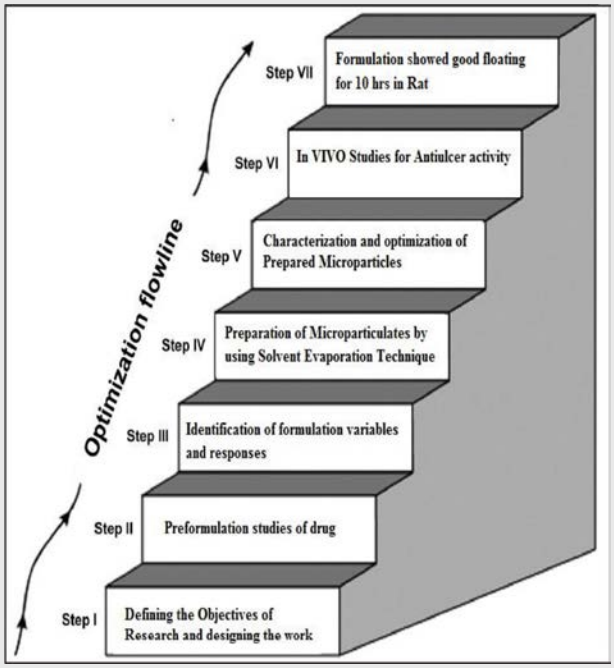
ABBREVIATIONS

ANOVA: Analysis of variance; **BCS:** Biopharmaceutical classification system; **BD:** Bulk density; **CDR:** Cumulative drug release; **CF:** Chitosan formulation; **cm:** Centimeter; **Conc.:** Concentration; **DSC:** Differential scanning calorimetry; **FDDS:** Floating drug delivery system; **FTIR:** Fourier-transform infrared; **gm:** Gram; µg: Micro gram; **GRDF:** Gastro retentive drug formulation; **HCL:** Hydrochloric acid; **IR:** Infrared; **Lab.:** Laboratory; **mg:** Milligram; **Min.:** Minute; **ml:** Milliliter; **nm:** Nanometer; **SEM:** Scanning electron microscope; **TD:** Tapped density; **TPP:** Tripolyphosphate; **USP:** United states pharmacopeia; **UV:** Ultraviolet.

REFERENCES

1. Sundar VD, Divya P, Suneendra G, Dhanaraju MD. Design development and evaluation of gastro retentive floating microspheres of atazanavir sulfate. Int J Pharm Sci Res. 2018;9(11):4642-50.
2. Kumari B. Recent development in floating drug delivery system: A review. Asian J Pharm Pharmacol. 2018;4(2):131-9. doi: 10.31024/ajpp.2018.4.2.6.
3. Garg R, Gupta GD. Progress in controlled gastroretentive delivery systems. Trop J Pharm Res. 2008;7(3):1055-66. doi: 10.4314/tjpr.v7i3.14691.
4. Kumar S, Nagpal K, Singh SK, Mishra DN. Improved bioavailability through floating microspheres of lovastatin. Daru. 2011;19(1):57-64. PMID 22615640.
5. Rimawi IB, Muqedi RH, Kanaze FI. Development of gabapentin expandable gastroretentive controlled drug delivery system. Sci Rep. 2019;9(1):11675. doi: 10.1038/s41598-019-48260-8, PMID 31406203.
6. Cekin AH, Taskoparan M, Duman A, Sezer C, Cekin Y, Yolcular BO, *et al*. The Role of Helicobacter pylori and NSAIDs in the Pathogenesis of Uncomplicated Duodenal Ulcer. Gastroenterol Res Pract. 2012;2012:189373. doi: 10.1155/2012/189373. PMID 23049545.
7. Gayathridevi M, Adlin JN, Tamizh M. Floating microsphere: A review. Int J Res Pharm Chem. 2016;6:501-10.
8. Sai Rama Rao C, K S, V K, N S. Development and *in-vitro* Evaluation of cefpodoxime proxetil gastro-retentive floating tablets. IJAPSR;1(1):31-41. doi: 10.21477/ijapsr.v1i1.9606.
9. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: Overview and special case of *Helicobacter pylori*. J Control Release. 2006;111(1-2):1-18. doi: 10.1016/j.jconrel.2005.10.031, PMID 16403588.
10. Gadad AP, Naik SS, Dandagi PM, Bolmal UB. Formulation and evaluation of gastroretentivefloatingmicrospheres of lafutidine. J Pharm Res. 2016;50(3):S76-81.
11. Selgrad M, Malfertheiner P. New strategies for *Helicobacter pylori* eradication. Curr Opin Pharmacol. 2008;8(5):593-7. doi: 10.1016/j.coph.2008.04.010, PMID 18555746.
12. Kumari B, Pandey P, Dureja H. Formulation and characterization of gastroretentive floating tablets of atorvastatin calcium using central composite design. J Pharm Res. 2017;16(3):247-56. doi: 10.18579/jpcrkc/2017/16/3/118782.
13. Saini S, Kumar S, Choudhary M, Nitesh BV. Microspheres as controlled drug delivery system: An updated review. Int J Pharm Sci Res. 2018;9(5):1760-8.
14. Felix SY. Formulation and in-and evaluation of floating microballoons of stavudine. Univers J Pharm Res. 2016;1:13-9.
15. Porwal A, Dwivedi H, Pathak K. Decades of research in drug targeting using gastroretentive drug delivery systems for antihypertensive therapy. Braz J Pharm Sci. 2017;53(3):1-15. doi: 10.1590/s2175-97902017000300173.
16. Anucharishma G, Hemalatha K, Swapna K. Raft forming drug delivery systems: Are view. Chronicles Pharm Sci. 2017;1:135-48.

PICTORIAL ABSTRACT



SUMMARY

The floating Microspheres had prepared to stay in the stomach for prolonged period of time for the gastroretentive drug delivery of the lafutidine. The floating Microspheres were formulated after identifying the formulation variables using central composite design and then prepared by using Emulsion Solvent Evaporation technique. The prepared microspheres were characterized for micromeritic studies, percentage yield, drug entrapment efficiency, *in-vitro* buoyancy, surface morphology, *in-vitro* drug release, and *in-vivo* floating study and stability studies. The micromeritic parameters of floating microspheres were found to be within the acceptable limits. The particle size of prepared floating microspheres was found to be in the range 3.78-10.62 μm. The entrapment efficiency of microspheres was found to be in the range of 69.32–94.05%. The described shape of microspheres was spherical with slightly rough surface when characterized under scanning electron microscopy. The percentage yield of Microspheres was found 66-85%. The buoyancy (*in vitro*) was found to be in the range of 42.68-95.75% and a total buoyancy time of more than 10 hr. The *in vitro* cumulative % release was determined by dissolution studies and found in the range of 79.02-96.92%. The stability studies were also performed for the floating microspheres, it was found stable at 40 ± 2°C. The optimized formulation EF6 showed floating time for 10 hr in stomach of rat. The prepared microspheres were ability to treat the alcohol induced ulcer.

Cite this article: Kumar S, Tiwari A, Goyal N. Floating Microspheres of Lafutidine: Formulation, Optimization, Characterization, *in-vitro* and *in-vivo* Floatability Studies using Eudragit Grades. Indian J of Pharmaceutical Education and Research. 2022;56(3):681-8.