Original Article

Formulation and Characterization of Chitosan Microparticulate System Using Central Composite Design for the Drug: Lafutidine

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ABSTRACT

Aim: To formulate a Micro particulate system using central composite design to remain in the stomach for prolonged time and used for Gastroretentive drug delivery. **Materials and Methods:** Gastroretentive Microspheres were prepared by Emulsion Solvent Evaporation. Micro particulate system were evaluated for micro meritic study, percentage yield, drug entrapment efficiency, *in-vitro* buoyancy, surface morphology, *in-vitro* drug release, *in-vivo* floating study and stability studies. **Results:** The micro meritic parameters of floating microspheres were found to be within the acceptable limits. The particle size of microspheres was found to be in the range 3.43–15.38 μm. The entrapment efficiency was found to be in the range of 72.02–95.02%. The floating microspheres were spherical in shape with distinct pores, slightly rough surface when observed under scanning electron microscopy. The percentage yield was found to be in the range of 68–89%. The *in-vitro* buoyancy was found to be in the range of 55.67–92.55% and a total buoyancy time of more than 10 h. The *in-vitro* dissolution studies showed a cumulative % release in the range of 77.67–95.41%. The optimized formulation F4 was floating in rat stomach for almost 8 h. All the formulations followed Korsemeyer- Peppas kinetics indicating drug release by non-fickian release mechanism. The stability studies showed that floating microspheres were stable at 40 ± 2°C. **Conclusion:** The optimized formulation showed good floating for 12 h in stomach of rat. The formulation was able to treat the alcohol induced ulcer and also found good stability.

Key words: Lafutidine, Chitosan, Central composite design, *In vitro* drug release, Microparticulate system.

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INTRODUCTION

The most common and suitable route for various drugs is oral route. This route usually considered as perfect drug delivery system because of these two main properties:

- Prolonged action with a single dose.
- Directly deliver the drug to the target.[1]

Floating drug delivery systems (FDDS)

Floating systems are low-density systems that have sufficiently buoyancy to float over the gastric content and remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time, which results in a increased gastric retention time and a better control of fluctuation in plasma drug concentration. After release of drug, the residual system is emptied from the stomach.[2] These problems have prompted researchers to design a drug delivery system which can stay in the stomach for prolonged and predictable period.[3] Attempts are being made to develop a drug delivery system which can provide therapeutically effective plasma drug concentration for a longer period, thereby reducing the dosing frequency and minimizing fluctuation in plasma drug concentration at steady state by delivering the drug in a controlled and

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reproducible manner.[4,5] Lafutidine is newly developed second generation histamine H2–receptor antagonist, having poor water solubility and short elimination half-life up to 3.0 hr, belonging to BCS class-II drugs. This drug is very much effective in the treatment of gastric ulcer, gastroesophageal reflux disease and pathological hyper secretory 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. Chitosan (obtained by alkaline deacetylation of chitin) is a swellable, natural linear bio poly amino saccharide. Chitin is a straight homopolymer composed of -(1,4)-linked N-acetylglucosamine units, while chitosan comprises of copolymers of glucosamine and N-acetyl-glucosamine.[6,7]

Advantages of chitosan:

- It forms film that reduces effect of gastrointestinal transit time.
- Hallow microcapsule tend to float on gastric fluid for about 12hrs.
- Release rate of drug followed zero order kinetics

MATERIALS AND METHODS

Drug (Lafutidine) has been obtained as a gift sample from Unichem Lab. and other excipients has been procured/purchased.

Identification of Formulation Variables and Responses: Fabrication of GRDF with Chitosan

The formulation variables were selected as (a) Drug: Chitosan ratio (b) Chitosan: Gelling agent ratio at three levels -1, 0 and +1.

The responses selected for this formulation will be (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 will be prepared (Batches CF1 to CF13) as given in Table 1.

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). 1 mL of this solution was pipette out in another volumetric flask and volume was made up to 10 mL (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.

Establishment of Calibration Plot

- 10 mg of Lafutidine was accurately weighed and transferred into a 10 mL volumetric flask containing approximately 5 mL of acetic acid. Flask was then gently shaken and volume was finally made up to 10 mL using the same solvent (stock solution "A")
- 1 mL of this solution was pipette out in another volumetric flask and volume was made up to 10 mL with 0.1N HCl in order to obtain the resulting solution of 100µg/mL (stock solution "B"). Finally by using stock solution "B", solutions of various concentrations such as 2, 4, 6, 8, 10 µg/mL were prepared. 0.1N HCl was taken as blank and absorbance of different dilutions were taken at 286 nm. The readings for the calibration curve are shown in Table 2 (within 0.1 N HCL), Table 3 (within phosphate buffer), Table 4 (within distilled water) and plots are shown in Figure 1 (with 0.1 N HCL), Figure 2 (within phosphate buffer) and Figure 3 (within distilled water).

Table 1: Coded factor levels of the formulation.

Formulation Code	Coded Factor Levels	
Sr. No.	X_1	X_2
CF1	-1	-1
CF2	-1	0
CF3	-1	+1
CF4	0	-1
CF5	0	0
CF6	0	+1
CF7	+1	-1
CF8	+1	0
CF9	+1	+1
CF10	0	0
CF11	0	0
CF12	0	0
CF13	0	0

Translation of coded levels in actual units			
Coded level	-1 (low)	0 (middle)	+1(high)
X_1 : Drug Chitosan Ratio	1:1	1;2	1:3
X_2 : Chitosan: Gelling Agent (TPP) Ratio	1:3	1:4	1:5

- Similarly, standard plots of pure Lafutidine were also constructed using phosphate buffer (pH 6.8) at 285 nm and distilled water at 276.5 nm.

Preparation of Microsphere with Chitosan: Gastroretentive Microspheres were prepared by Ionotropic Gelation Technique. Accurately weighed amount of drug (Table 5) was dispersed uniformly in 2% Acetic acid with stirring. To this dispersion, desired polymer (Chitosan) in different concentrations was mixed in suitable proportion and stirring is continued. The resulting solution was then added drop by drop into Light Liquid Paraffin containing suitable concentration of Span 60 and Magnesium Sterate. Then the solution was kept on Magnetic stirrer for 1 hr for the emulsification. Then Gelling agent (Sodium Triployphosphate) dissolves in water and added to the above prepared Emulsion. The solution was kept on Magnetic stirrer for 3 to 4 hr at 60 to 65' C. The formed microspheres were kept suspended in the solution for 1 day to improve their mechanical strength and then collected, washed with Petroleum ether. The formulated microspheres (Batch CF1-CF13) were then dried using vacuum oven at 40-45°C and stored in airtight containers.

RESULTS AND DISCUSSION

The microsphere blend was estimated for their flow properties. *Bulk density* and *Tapped density* were found between 0.515-0.580 gm/cm^3 and 0.571-0.651 gm/cm^3 respectively. Results are shown in Table 2. *Carr's index* indicating good flow, was found to be in the range of 5.21-14.73. *Hausner's ratio* values indicating low interparticle friction for all the formulations were found to be near about 1.1. *Angle of repose* was found between 20.07-26.80. 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 -1 characteristics peaks at 3278 cm due to -NH Stretch, 3094-2940 cm due to C-H Stretch, at 1620 cm due to C=C Stretch, 1261 cm at due to N-C Bending, 1211-1157cm due to C-O stretching, 1211-1157 cm at due to C-O Bending.

Micromeritics Studies of Prepared Microspheres: Following micromeritics parameters has been carried out.

a. Angle of repose: This is the angle between the horizontal plane and surface of a pile of microspheres blend. It was determined by using the funnel method. The perfectly weighed granule blend is being taken in the funnel.[7] The altitude of the funnel adjusted to the maximum cone height (h) and microspheresblend was poured through the funnel freely on to the surface. Then the radius of the heap (r) was measured and

Table 2: Calibration Plot of drug in 0.1 N HCL.

Sr. No.	Conc. (µg/mL)	Absorbance
1	2	0.1301
2	4	0.2512
3	6	0.3814
4	8	0.5132
5	10	0.6312

Table 3: Calibration Plot in Phosphate Buffer (pH 6.8).

Sr. No.	Conc. (µg/mL)	Absorbance
1	2	0.1101
2	4	0.2311
3	6	0.3441
4	8	0.4322
5	10	0.5330

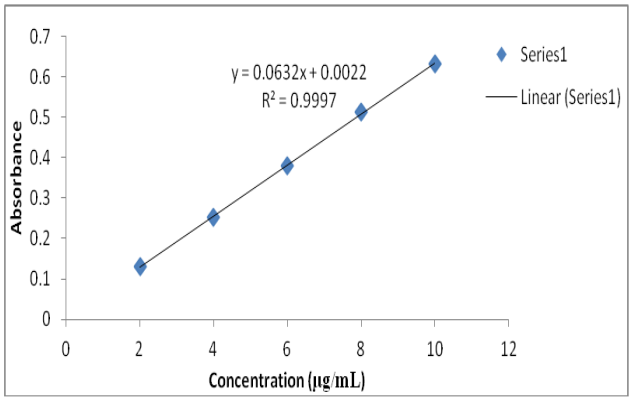

Figure 1: Calibration Plot of drug in 0.1 N HCL.

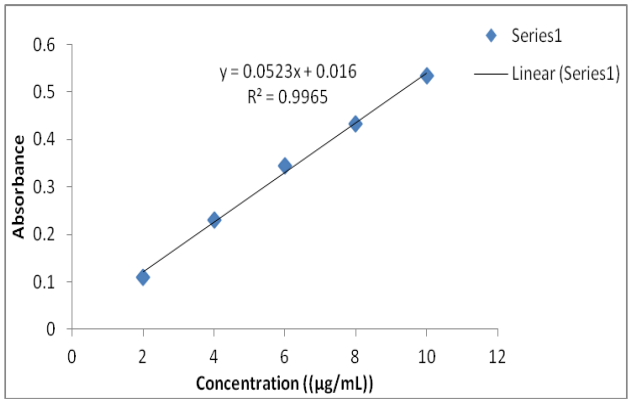

Figure 2: Calibration Plot of drug in Phosphate Buffer (pH 6.8).

angle of repose was calculated. The diameter of the microspheres cone will be measured and then the angle of repose.[8,9]

$$\tan\theta = h/r$$

b. Bulk density (BD) and Tapped density (TD): 2 g of granules blend was introduced to a measuring cylinder of 100 ml. The cylinder was tapped 100 times and the tapped volume of packing was recorded.[10,11]

BD and TB are calculated using the following formulae:

$$BD = \frac{\text{weight of the granule blend}}{\text{Untapped volume of the granules}}$$

$$TD = \frac{\text{weight of the granule blend}}{\text{tapped volume of the granules}}$$

c. Compressibility index: It was calculated by using the Carr's compressibility index as given in formula below here.[12,13]

$$\text{Carr's Index} = \frac{(TD-BD) \times 100}{TD}$$

Where, TD is tapped density and BD is bulk density.

d. Hausner's ratio: It is an index of ease of powder flow; calculated using the following formula.[14,15]

$$\text{hausner's Ratio} = \frac{TD}{BD}$$

Where, TD is tapped density and BD is bulk density.

All these calculated flow properties of different batch are given in Table 6. From the above pre compression results it was found that the granular blend has good flow.

SEM: The microscopy image of the optimized formulation is shown in Figure 4. The prepared microspheres were spherical in shape with slight distinct pores of the slightly rough surface of microspheres. Yellow squares represent the presence of microspheres. The samples for SEM were prepared by adhering the microparticleon a double adhesive tape stuck to an aluminum stub. The stubs were then coated with

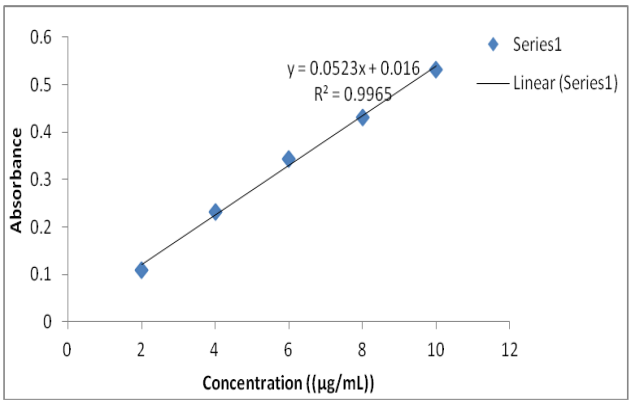

Figure 3: Calibration Plot of drug in Distilled Water.

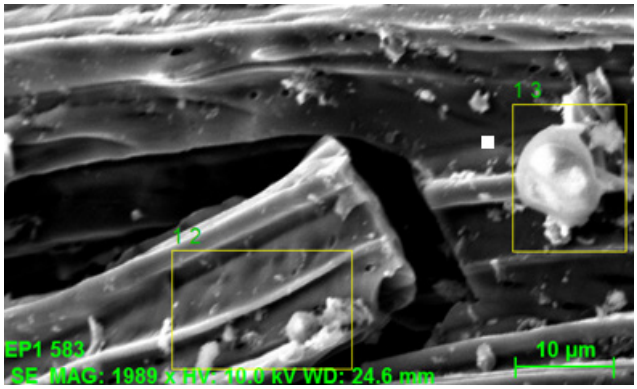

Figure 4: Scanning electron micrographs of floating microspheres.

Table 4: Calibration Plot in Distilled Water.

Sr. No.	Conc. (µg/mL)	Absorbance
1	2	0.1291
2	4	0.2412
3	6	0.3842
4	8	0.5121
5	10	0.6333

Table 5: Composition of formulations.

INGREDIENTS	CFI	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9	CF10	CF11	CF12	CF13
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. Sterate	750	750	750	750	750	750	750	750	750	750	750	750	750
Chitosan	125	100	83.33	250	200	166.66	375	300	250	200	200	200	200
Sodium TPP	375	400	416.66	750	800	833.33	1125	1200	1250	800	800	800	800
Sodium Bicarbonate	500	500	500	500	500	500	500	500	500	500	500	500	500

silver under an argon atmosphere using a high-vacuum evaporator (Polaron SEM coating system). The internal cavity of the microparticle 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: FTIR spectroscopy was carried out to study the compatibility of pure drug Lafutidine with the polymer chitosan used in the formulation of floating microspheres. All important functional group frequencies for Lafutidine showed no significant shifts in combination spectra indicating no interaction between Lafutidine and polymers (Figure 5). It shows that there was no significant change in the chemical integrity of the drug. The different functional groups are given in Table 7.

Determination of Melting Point: 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 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 6.

Differential Scanning Calorimetry (DSC):X-ray Diffraction Studies: X-ray diffraction analysis of pure Lafutidine (Figure 7) and the optimized formulation

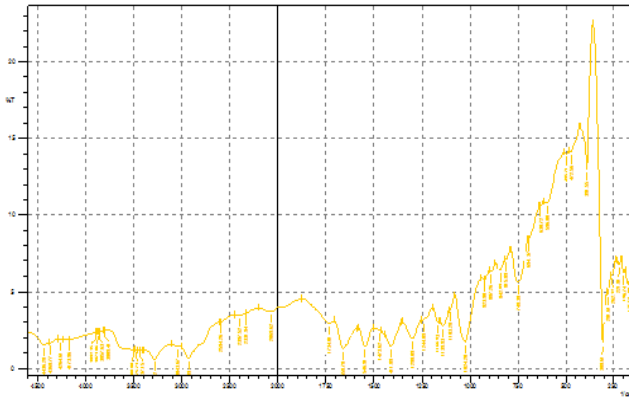

Figure 5: Fourier transform infrared (FTIR) spectroscopy of drug.

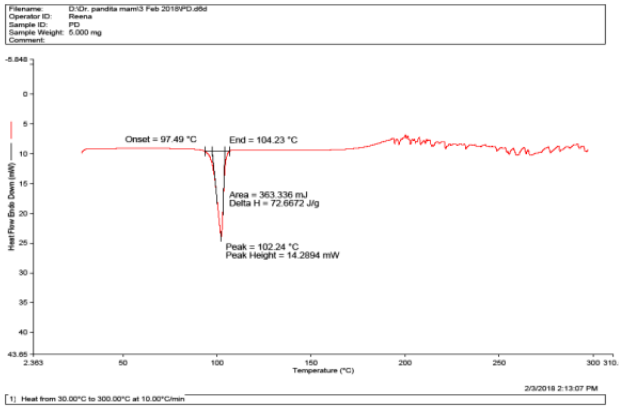

Figure 6: Differential Scanning Calorimetry (DSC).

Table 6: Pre Compression Studies of Different Batches.

Batch No.	Bulk Density (gm./cm³)	Tapped Density(gm./cm³)	Carr's Index (%)	Hausner's Ratio (H_R)	Angle of repose (Θ)
CF1	0.515	0.571	9.80	1.10	24.34
CF2	0.524	0.576	9.02	1.09	22.30
CF3	0.532	0.591	9.08	1.11	24.69
CF4	0.541	0.601	9.98	1.11	23.96
CF5	0.579	0.651	11.05	1.12	22.40
CF6	0.542	0.602	9.96	1.11	24.10
CF7	0.551	0.615	10.40	1.11	21.20
CF8	0.535	0.594	9.93	1.11	25.30
CF9	0.545	0.606	10.06	1.11	25.10
CF10	0.563	0.594	5.21	1.05	26.80
CF11	0.538	0.631	14.73	1.17	25.70
CF12	0.568	0.648	12.34	1.14	25.40
CF13	0.580	0.627	7.49	1.18	23.69

(Figure 8) was done by X-ray powder diffracto meter (PW 3040/ 60 Xpert PRO, Panlytical, Netherlands). The X-ray diffraction patterns were recorded using Cu Kα radiations (λ=1.5405980Å), 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.

Encapsulation Efficiency: For determination of encapsulation efficiency10 mg microspheres were crushed and dispersed into 25 ml phosphate buffer (pH 7.4). The prepared mixture was shaken for 24 h. After 24 h, 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.

Buoyancy Study: The floating ability of the prepared beads were evaluated in acidic buffer (pH 1.2). The floating ability of the beads is directly related to the amount of gas generating agent added, in order to make the beads to float onto the surface of the media.

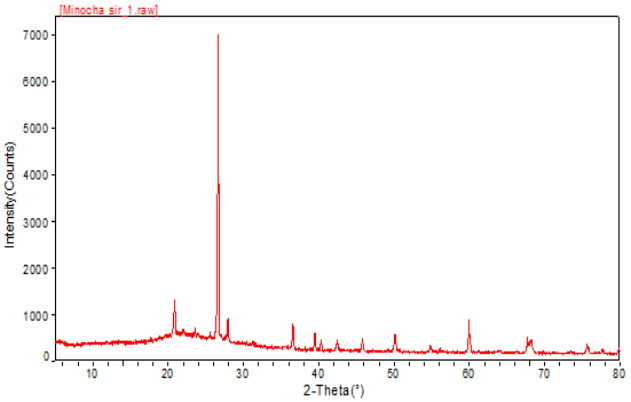

Figure 7: X-ray diffraction patterns of pure drug Lafutidine.

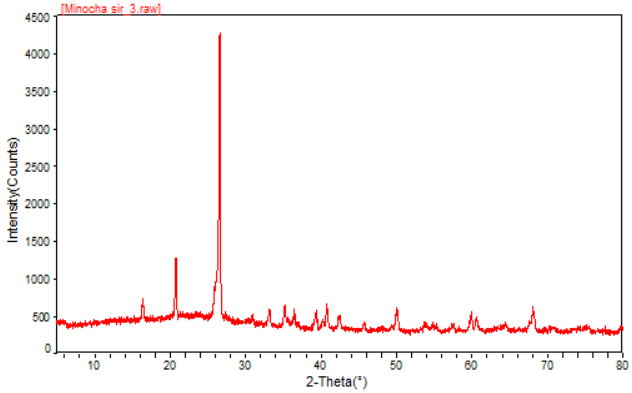

Figure 8: X-ray diffraction of drug-loaded floating microspheres.

Table 7: 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.	1620	C=C Stretch
4.	1586-1486	C=O Stretch
5.	1261	N-C Bending
6.	1211-1157	C-O Bending
7.	1032	S=O Bending

Table 8: Charaterization of microparticles.

Formulation code	Shape	Mean Particle Size	Yield	Buoyancy (%)	Encapsulation efficiency (%)
CF1	Spherical	11.62	72.63	90.28	91.02±3.74
CF2	Spherical	9.47	68.67	78.33	73.12±2.10
CF3	Spherical	10.23	76.45	77.56	85.22±1.73
CF4	Spherical	6.43	79.77	82.33	88.42±1.54
CF5	Spherical	3.43	89.27	92.55	95.02±3.75
CF6	Spherical	8.56	86.43	90.32	84.05±6.36
CF7	Spherical	8.29	76.89	55.67	79.32±2.77
CF8	Spherical	3.78	81.40	66.67	79.02±1.73
CF9	Spherical	11.89	81.49	67.98	86.02±2.33
CF10	Spherical	4.87	79.69	68.65	79.02±1.74
CF11	Spherical	12.66	80.33	77.55	84.02±3.79
CF12	Spherical	15.38	82.79	69.99	72.02±2.78
CF13	Spherical	5.88	81.10	81.55	83.02±1.77

Floating capacity of all the formulations ranged from 67.3% to 87% (Table 8). All the formulations showed a total floating time of for more than 10 h.

***In-vitro* Drug Release Study:** The drug release rate from different formulations (CF1– CF13) was determined using USP type II apparatus (TDT- 08L, Electro lab, Mumbai, 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. Micro particle 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 hr 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 9.

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 on % CDR to study the fitting and significance of model as given in Table 10. The model developed from multiple linear regression to estimate effect (Y) can be presented mathematically as:

$$Y = 84.44 - 1.24 X_1 - 1.38 X_2 + 1.60 X_1X_2 + 2.44 X_1^2 - 0.44 X_2^2$$

Where, Y is % CDR, X$_1$: Drug: Chitosan Ratio, X$_2$: Chitosan: Gelling Agent (TPP) Ratio

F-test was carried out to compare the regression mean square with the residual mean square. The ratio F = 4.38 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

Table 9: Total floating time and Percentage Cumulative Drug Releaseof Batches (CF1-CF13).

Batch No.	Total Floating Time (hr)	Cumulative drug release
CF1	> 12	79.42 ±2.13
CF2	> 11	82.54 ± 1.21
CF3	> 12	89.02 ± 2.32
CF4	> 12	82.21 ± 2.11
CF5	> 14	95.41 ± 1.57
CF6	> 13	91.92 ± 2.61
CF7	> 11	84.72 ± 1.32
CF8	> 12	77.67 ± 1.23
CF9	> 12	86.67 ± 1.87
CF10	> 11	82.92 ± 2.31
CF11	> 12	82.23 ± 2.88
CF12	> 13	81.71 ± 1.76
CF13	> 13	86.21 ± 2.08

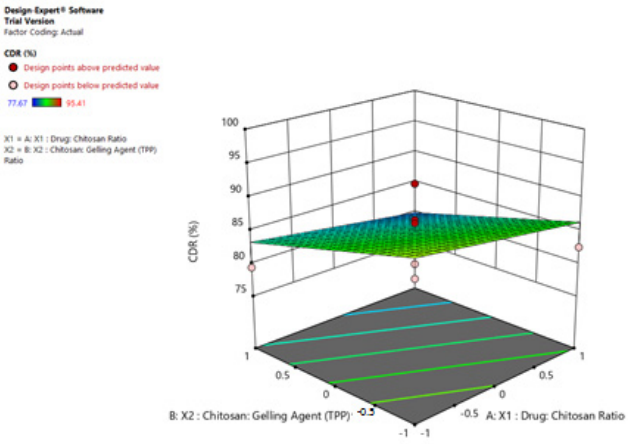

Figure 9: 3D Surface Model Graph.

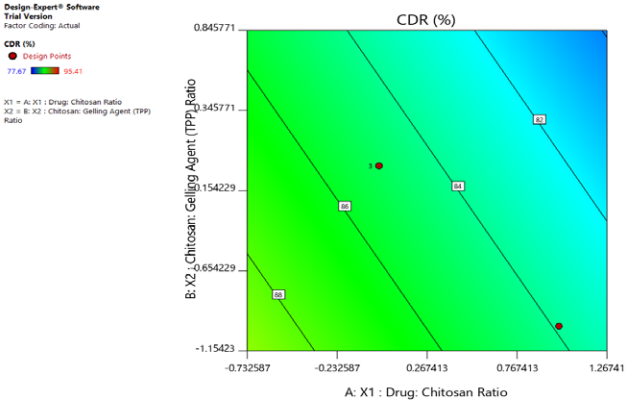

Figure 10: Contour Model Graph.

Table 10: ANOVA of the Regression (%CDR).

	Degree of freedom	Sum of squares	Mean square	F	F-significance
Total	18	193.46	-	-	-
Residual	11	39.66	3.97	-	-
Regression	9	162.80	16.68	4.29	0.0152*

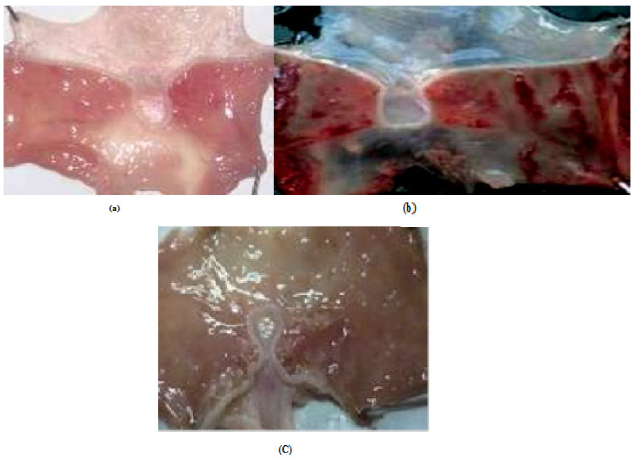

Figure 11: Evidence for the protective effect of Lafutidine microspheres in rats treated with ethanol, (a) Ulcerated control stomach (b) Optimized formulation treated stomach (c) Control group (treated with formulation without drug)

determine the desired %CDR. Figure 9 and Figure 10 display the 3D surface and contour plot of cumulative percent of drug release as a function of formulation variables.

Release kinetics: The release data was fitted to various kinetic models in order to determine the release constant and regression coefficient. The drug release profiles for formulations (CF1 to CF13) were best is best explained by the Korsemeyer Peppas model. In Korsemeyer Peppas model if the value of n (slope) = 0.5 indicates a Fickian diffusion mechanism, for 0.5<n>1.0, indicates anomalous (non-Fickian) and *n* =1 implies class 2 transport. 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. Thus the release profile of the optimized batch CF5, fitted best to the Korsemeyer Peppas model (0.9695). Based on the analysis parameters optimized batch was found CF5.

Antiulcer activity: In control group of animals, oral administration of absolute ethanol produced characteristic lesions in the glandular portion of rat stomach which appeared as elongated bands of thick, black and darkred lesions. In ethanol-induced ulcer model, oral administration of 95% ethanol in control group, produced characteristic lesions in stomach which emerged as elongated bands of broad red lesions. The *in-vivo* evaluation showed that significant protection ulcerative index 89.04% of optimized formulation of Lafutidine in comparison to control group (Figure 11).

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 CF5 showed good results with respect to the various evaluation parameters, so it was selected as the optimized formulation. The particle size increased with increase in polymer concentration. The drug entrapment efficiency was increased with increase in concentration of polymers. *In-vitro* buoyancy and the *in-vitro* drug release decreased with respect to increase in concentration of polymers. The optimized formulation showed good floating for 12 h in stomach of rat.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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:** Gastroretentive 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.

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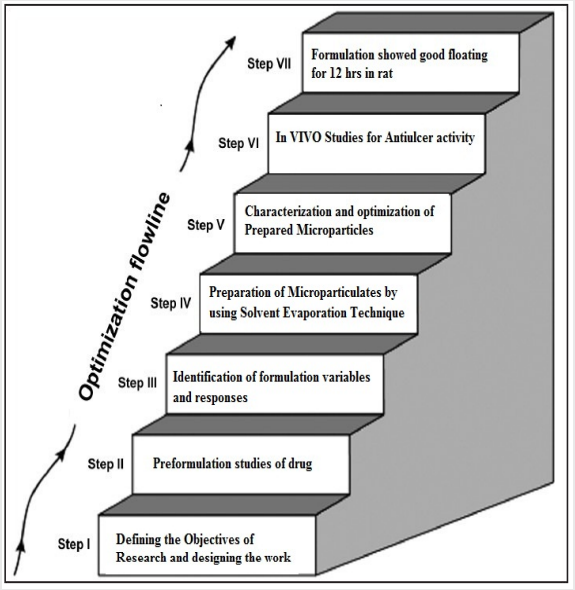
PICTORIAL ABSTRACT



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Sunil Kumar did his B.Pharmacy in 2006, LSCP, SPSA, M.Pharmacy (Pharmaceutics) in 2008 from Annamalai University, (T.N), Sumbmitting Doctorial Research work in Pharmaceutics (Ph.D), Uttarkhand Technical University, Dehradun. Presently working as Assistant Prof. or Head , Department of Pharmaceutics, Vanish Institute of Pharmaceutical Education and Research, Rohtak (HR). He is having more than 11 years teaching Experience. He guided 10 Research Project at PG level. He is having more than 15 publications in national and international journal. He attended more than 25 national and international conference, 02 FDP and Presented papers. He is having life membership of IPGA, IPA, HSPC etc. He had successfully organised the CPE Programm of Harjana state Pharmacy council as a coordinater in 2014 and 2019 at Rohtak.

SUMMARY

The Gastroretentive Micro particulate system had formulated using central composite design to stay in the stomach for prolonged time and worn for gastroretentive drug delivery. Gastroretentive Microspheres were prepared by using Emulsion Solvent Evaporation technique. Micro particulate system were assessed for micro meritic study, percentage yield, drug entrapment efficiency, *in-vitro* buoyancy, surface morphology, *in-vitro* drug release, *in-vivo* floating study and stability studies. The micro meritic parameters of floating microspheres were found to be within the acceptable limits. The particle size of microspheres was found to be in the range 3.43–15.38 μm. The entrapment efficiency was found to be in the range of 72.02–95.02%. The floating microspheres were spherical in shape with distinct pores, slightly rough surface when observed under scanning electron microscopy. The percentage yield was found to be in the range of 68–89%. The *in vitro* buoyancy was found to be in the range of 55.67–92.55% and a total buoyancy time of more than 10 h. The *in vitro* dissolution studies showed a cumulative % release in the range of 77.67–95.41%. All the formulations followed Korsemeyer- Peppas kinetics indicating drug release by non-fickian release mechanism. The stability studies showed that floating microspheres were stable at 40 ± 2°C. The optimized formulation showed good floating for 8 h in stomach of rat. The formulations were able to treat the alcohol induced ulcer.

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