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Original Article

FORMULATION DEVELOPMENT AND CHARACTERIZATION OF LAFUTIDINE RAFT SYSTEM

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ABSTRACT

Objective: The present research work is focused to develop in situ raft gel of lafutidine. Sodium alginate is one of the critical components for the development in situ raft system.

Methods: The formulation was prepared using hydrophilic polymers such as ethyl cellulose, HPMC K4M, and chitosan. The formulations were subjected to evaluation characteristics such as pH, *in vitro* gelling time, viscosity, density, gel strength, drug-polymer compatibility studies, drug content floating lag time, swelling index, and *in vitro* release studies.

Results: The pH of all the prepared batches was found in the range of 5.7 to 7.6. All the prepared formulations showed viscosity in the range of 264 to 320 cps, with gelling time from 4-7 s. For F1-F15 batches Floating lag time was found to be in the range of 9-24 sec. Densities of all formulations stomach specific in situ gels were in the range of 0.4 to 0.8 gm/cm3. The highest swelling index was observed in F15 with 14.16% Highest gel strength is exhibited by F15; all the formulations were in the range of 95.46–99.95, indicating the uniform distribution of the drug. Formulation F15 containing chitosan in combination with ethyl cellulose gave the highest drug release of 99.78% and also showed sustained and controlled release for up to 24h.

Conclusion: F15 shows an R2 value of 0.999. As its value is nearer to the '1' it is confirmed as it follows the Zero order release with an 'n' value is 1.5021 for the optimized formulation (F15) i.e., the n value indicates super case II transport and is considered as optimized formulation.

Keywords: In situ gel, Lafutidine, Raft, Floating, Controlled release

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INTRODUCTION

Delivering a drug through the oral route has become more challenging as several alternate advanced systems are available. But bioavailability issue of drugs administered orally has still to be improved. Gastro retentive is one such approach to delivering the drug. In the gastro retentive system, the formulation is allowed to remain in the gastric region for the desired time and the formulation is fabricated to release the drug in a controlled manner to achieve the objective. Raft-forming systems are preparations that on contact with acidic pH undergo gelation to produce a thick layer that floats on gastric content [1, 2].

Lafutidine is a second-generation histaminic receptor antagonist which prevents acid secretion due to histamine release [3]. Histamine-related acid secretion. Mainly occurs in the nighttime. The imidazole derivatives such as omeprazole are the first-line treatment for diseases related due excessive secretion of acid, but unfortunately, these drugs cannot prevent nocturnal acid secretion. Lafutidine, not only prevents gastric acid secretion during the night but also during the day time (postprandial). The unfavourable physicochemical properties of lafutidine, such as low solubility, resulted in poor bioavailability. The drug has a pKa value of 3.8 and comes under class II of the BCS classification. The drug has an absorption window in the upper part GIT and an elimination half-life of 1-2 h, which makes the drug a suitable candidate for preparing the gastro retentive system [3, 4]. Sodium alginate is one of the hydrophilic polymers which has the unique property of undergoing gelation in contact with acidic pH. The formed gel has a density less than that of gastric juice. By adding and altering the combination of hydrophilic polymers, the solubility of the drug can be increased. In the present work, an attempt is made to develop in situ raft system of lafutidine to increase its bioavailability. The combined effort of retaining the drug in the gastric region and controlling the release of the drug made to attain the objective.

MATERIALS AND METHODS

Materials

Lafutidine was obtained as a gift sample from Hetero drugs Ltd, Hyderabad; ethyl cellulose, HPMC K4M, chitosan, sodium alginate, calcium chloride calcium carbonate, tri-sodium citrate, methyl, and propylparaben were purchased from Gattefosse, Mumbai. All other materials and solvents used were of pharmaceutical grade. Marketed product: Laciloc 10 mg tablet. Marketed product: Laciloc 10 mg tablet.

Methodology

Preformulation evaluation

Preformulation study is the first step in the preparation of any formulation. The Preformulation study confirms the formulation under consideration is will me*et al.* l the specifications to carry out such a study.

Organoleptic properties

The drug under consideration is examined for physical appearance to confirm its physical stability

Melting point

The melting point helps to investigate the purity of the drug. The study was carried out using a "melting point apparatus" with the help of a capillary tube. The obtained results were confirmed as a standard reference.

UV-visible spectroscopy

UV spectroscopic method was used to identify lafutidine [5, 6]. Standard solutions of lafutidine were prepared by diluting a known amount of the drug in 0.1N HCl (10, 20, 30, 40, 50, and 60µg/ml). The solutions were subjected to UV spectroscopic scanning to identify λ max of lafutidine. The spectrum was recorded at the 200-400 nm range.

Calibration curve

A calibration curve of lafutidine was constructed by taking concentrations of the drug (10, 20, 30, 40, 50, and 60µg/ml) versus the corresponding absorbance.

Differential scanning calorimetry

Thermal analysis of the lafutidine sample was carried out using a differential scanning calorimeter (DSC) [7]. To carry out the study, the sample was placed in an aluminum pan and heated at a rate of 10 °C/min over a range 30-300 °C under a nitrogen environment. The DSC spectrum will help to identify the sample purity.

Fourier transformer infra-red spectroscopy

To conduct Fourier Transformer Infra-Red (FTIR) study, 5 mg of the drug sample is mixed with 500 mg KBr (IR grade) in an agate mortar pestle to get a uniform mixture. This mixture is then pressed in a disc by applying 10-ton pressure using a hydraulic press. The disc was then subjected to FTIR scanning over a wave number range of 4000-400 cm^{-1}. The spectrum was then studied to identify various functional groups to identify the drug [8].

Selection of polymers

The literature survey was carried out to identify various polymers to prepare formulation. From the survey, it was found that sodium alginate (SA) is one of the key components to prepare in situ raft system. Along with SA, other polymers were added to achieve the desired objective. Sodium bicarbonate was used as a gas-generating agent.

Method of preparation of *in situ* raft system

Lafutidine and other ingredients were passed through sieve numbers 60 and 40, respectively. Prepare aqueous solutions of ethyl cellulose, HPMC K4M, and chitosan. Prepare homogeneous dispersion by adding the drug gradually into the above-prepared solution by using a magnetic stirrer operated at 150 RPM. Add sodium alginate to purified water containing sodium methyl and sodium propylparaben by heating at 60 °C to obtain SA solution [9] as mentioned in table 1.

Table 1: Formulation composition of lafutidine *in situ* gel

Composition	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Lafutidine (mg)	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Ethyl cellulose (%)	0.5		-	1	1.5	-	-	-	-	0.5	0.75	-	-	0.5	0.75
HPMC K4M (%)	-	0.5		-	-	1	1.5	-	-	0.5	0.75	0.5	0.75	-	-
Chitosan	-	-	0.5	-	-	-	-	1	1.5	-	-	0.5	0.75	0.5	0.75
Sodium alginate (%)	0.5	1	1.5	1	1.5	1	1.5	1	1.5	1	1.5	1	1.5	1	1.5
Calcium chloride (%)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Sodium bicarbonate (%)	0.5	1	2	0.5	1	2	0.5	1	2	0.5	1	2	0.5	1	2
$CaCO_3$ (%)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Tri-Sodium citrate (%)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Methyl and propyl paraben (9:1) (%)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Flavoring agent	Qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
Water	Volume make up to 100 ml														

Evaluation of lafutidine *in situ* raft system

The prepared in situ raft formulations were examined for various evaluation parameters.

Physical appearance

The prepared formulations (F1-F15) were subjected to physical evaluation to observe their physical integrity [10].

pH of the *in situ* gel solution

The hydrogen ion concentration (pH) of the formulations was evaluated using a digital pH meter (previously calibrated) at 37 °C. To analyze the results, evaluation was done in triplicate [10].

Viscosity

The resistant flow property (viscosity) of *In situ* gel formulations was determined at room temperature using a Brookfield viscometer type DV-II+PRO (LV1 Spindle) [11].

***In vitro* gelling time**

To measure *in vitro* gelling time of prepared formulations, 10 ml of the formulation was added to 10 ml 0.1N HCl in a measuring cylinder. The time taken for the gel to form was noted down [10].

***In vitro* floating duration**

In vitro floating duration was measured by taking a sufficient amount of (10 ml) of prepared formulation in a Petri plate or watch glass. The Petri plate was placed (without much disturbance) in dissolution apparatus (USP type II) containing 900 ml of 0.1N HCl as dissolution medium. The paddle speed was set at 50 RPM. The duration for which the formed gel was able to float was noted as floating time [10].

Floating lag time

The floating lag time (FLT) is known as the time taken for the formed raft or gel to reach the surface of the dissolution medium. The time taken for this should be less as possible to avoid gastric clearance due to peristaltic movement [10].

Measurement of density

Take a 50 ml volume of 0.1N HCl in a measuring beaker and add 30 ml in situ formulated gel. The amount of gel formed was transferred to the measuring cylinder and weight is measured by using the volume and weight of the gel; the density is calculated using the formula [11].

$$\text{Density} = \text{mass/volume}$$

Swelling index

The swelling index is done to determine the swelling nature of the in-situ formulated gel. It is done for all the formulations following the same method. Take 5 ml of each preparation into a Petri dish and slowly pour 40 ml of 0.1NHCl with pH 1.2. Then remove all the 0.1NHCl from the gel; even the traces are wiped using a paper towel. Now, consider the initial weight of the gel as Wo, to this add 10 ml of distilled water and allow it to rest for 30 min and decanted; now again weigh the gel and consider as final weight Wt. This procedure is repeatedly done for a period of 5 h and calculate the differences. % weight gain is calculated using the formula [11].

$$\%\ \text{swelling index} = \frac{\text{initail weight (W0)} - \text{final weight(Wt)}}{\text{intial weight (W0)}} \times 100$$

Measurement of gel strength

50 g weight was taken and placed on the surface of the 30g gel, making it centric, where penetration occurs through the gel. The whole process is done in a 50 ml beaker. The time taken to penetrate 5 cm down through the gel by 50g weight was recorded for all the formulations.

Drug content

Drug content of the formulation was measured by taking 5 ml of formulation into 50 ml of dissolution media 0.1N HCl (pH 1.2)

maintained on a magnetic stirrer at 37 °C for 1 h. on contact with 0.1N HCL; the formulation undergo gelation to form gel. The formed gel along with the solution was subjected to sonication for 10 min and filtered through whatman filter paper. The absorbance of solution was measured using uv spectrometer at 279 nm using 0.1N HCL as blank and drug content was calculated [10].

***In vitro* drug release study of lafutidine in situ gel formulation**

A paddle-type apparatus i.e. Type II USP dissolution apparatus was used to conduct the study. 900 ml of 0.1N HCl (pH 1.2) was used as a dissolution medium maintained at 37 °C. 10 ml of the formulation was introduced into dissolution medium and allowed for gelation to convert it in to gel. After the formation of gel at predetermined time, 10 ml of the dissolution sample was withdrawn and restored with fresh dissolution media to maintain proper sink condition [12]. The sample was diluted was analysed using UV spectrometer at 279 nm.

Release order kinetics

To obtain the best-fit model, the data which is obtained from diffusion kinetic studies of the optimised formulation was reasonably studies. The least slope value and highest R^2 value is achieved using this model [12, 13].

Drug polymer compatibility

Differential scanning calorimetry

Pure drug i.e. Lafutidine was analysed using Differential scanning calorimetry; correspondingly, the physical mixture and the physical form of raft systems were also analysed and reported to evaluate any passivity of drug-excipient interaction [14].

Fourier transform infrared spectroscopy

Fourier Transform Infrared Spectroscopy (FTIR) study was conducted to investigate any possible interaction of the drug with polymers used in the formulation preparation. IR spectra for pure lafutidine and with polymer were taken. FTIR spectra was run with the pellets prepared by KBr pellet method of pure drug, and with excipients, were recorded over a range of 4000-400 cm^{-1} [14].

Stability studies

It is carried out as per using ICH guidelines where the optimised formulation is packed in a well-closed stoppered glass container. It is conducted for a period of 1 mo maintained at 45 °C/75% RH. The following parameters were thoroughly studied i.e. floating duration, viscosity, gelling time, floating lag time, pH, dissolution studies, and drug content of lafutidine stomach specific in situ gel solution.

RESULTS AND DISCUSSION

Melting point

The melting point of lafutidine was to be the range 98-99 °C, which confirms its identity and purity.

UV visible spectroscopy

The lafutidine show its absorbance peak at 279 nm in 0.1N HCl from the concentration of Beer's law ranging from 10-50 µg/ml.

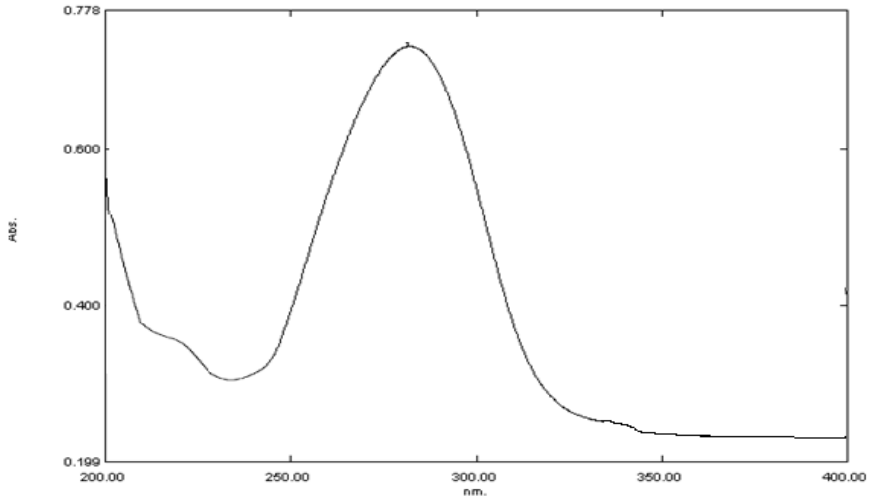

Fig. 1: UV spectrum of pure lafutidine

Table 2: The values are presented

S. No.	Concentration (µg/ml)	Absorbance (nm) mean+SD
1	10	0.145±0.001
2	20	0.292±0.001
3	30	0.497±0.001
4	40	0.65±0.002
5	50	0.793±0.001

The values are presented as mean n=3+SD

Calibration curve of lafutidine

The calibration curve of lafutidine show linearity over concentration range 10-50 µg/ml with a regression coefficient (R^2) value 0.9959

FTIR study of lafutidine

The major peaks for pure lafutidine were seen as below.3025.84 for–NH stretching, 2570.84, and 2006.52 for–CH (alkyl) stretching, 1814.40 and 1647.04–C=N stretching, 1526.42 and 1409.71 for-C=O stretching, 986.02 and 907.23 for SO stretching which confirms the important functional group lafutidine.

DCS study of pure lafutidine

The thermogram of pure lafutidine shows a characteristic sharp peak at 98.9 °C which corresponds to it melting point transition temperature.

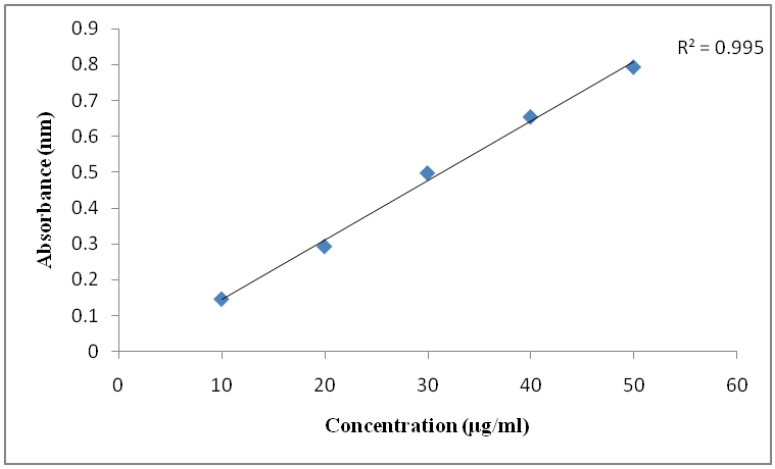

Fig. 2: Calibration curve of lafutidine using UV spectroscopy

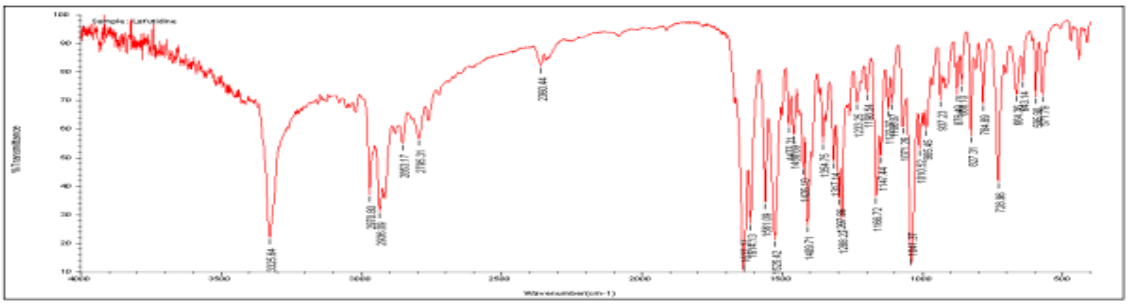

Fig. 3: FTIR spectrum of pure lafutidine

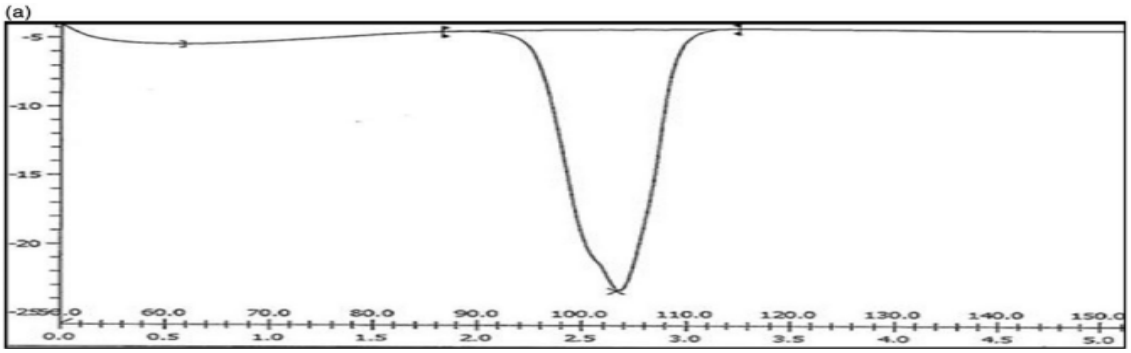

Fig. 4: DCS spectrum of pure lafutidine

Physical appearance

All the formulations (F1-F15) were observed to have a creamish-white color with smooth uniform consistency.

pH of *in situ* sol

The pH of all the formulations (F1-F15) were observed in the range of the pH of all prepared batches was found in the range of 5.7 to 7.7 (table 3).

Viscosity

All the preparations (F1-F15) have a viscosity in between 264 to 320 cps. From the above viscosity value, it can be concluded the preparations are easy pourable in nature, which leads to easy administration of dosage form. From the viscosity measurement, it has been observed that increasing concentrations of polymers enhanced the viscosity of preparations.

***In vitro* gelling time**

The *in vitro* gelling time of all the formulations (F1-F15) was found to be 4-7s. The results indicate immediate gelation of preparation upon contact with 0.1N HCl (table 3).

Floating lag time

For F1-F15 batches Floating lag time were observed to be in the range of 9-24 sec. on entering in 0.1 N HCl and show floating for 24h (table 3).

Density

Densities of all formulations (F1-F15) after undergoing gelation were observed in the range of 0.4 to 0.8 gm/cm^3 shown in table. From the results, it can be concluded the formulations can floats on gastric content and hence meets the criteria of gastric floating (table 4).

Table 3: pH. Viscosity, gelling time, floating lag time and floating duration of Lafutidine in situ gel RAFT system

Formulation code	pH*	Viscosity in cps*	Gelling time* (sec)	Floating lag time* (sec)	*In vitro* floating duration in h
F1	5.7±0.31	264.5±0.54	7±0.52	24±0.46	>4
F2	6.4±0.35	274.27±1.49	6±1.62	20±2.56	>8
F3	6.7±1.82	285.27±0.82	4±0.49	20±1.56	>8
F4	5.9±1.09	272.36±1.05	7±1.46	21±1.38	>16
F5	6.6±1.65	285.51±0.27	6±1.87	19±0.32	>20
F6	7.7±0.92	292.16±0.61	5±0.47	17±0.67	>16
F7	7.6±0.12	296.63±1.93	7±0.42	18±1.58	>12
F8	6.8±0.65	295.15±1.67	6±0.71	17±1.20	>16
F9	6.9±1.83	301.23±0.71	4±1.49	15±1.95	>12
F10	5.8±1.42	279.48±1.42	7±1.01	18±2.08	>12
F11	6.3±1.75	287.26±1.64	6±0.39	16±1.45	>20
F12	7.2±0.73	299.32±1.32	5±0.34	14±1.39	>20
F13	7.4±0.29	304.66±0.84	7±1.39	17±0.85	>24
F14	7.6±0.43	309.61±0.32	5±0.55	13±0.34	>24
F15	6.8±0.15	319.2±0.43	4±0.13	9±0.56	>24

*Above parameters are presented as Average±Standard Deviation; (n=3)

Swelling index

The swelling index of all the formulations (F1-F15) were in the range 7.3 to 14.16. This is due to an increase in concentration of polymers, which undergo hydration in the presence of a dissolution medium and also cause solvent imbibition into the gel network (table 4).

Measurement of gel strength

All the formulations ((F1-F15) have exhibited their gel strength in the range of 6.13-10.75 N/m^2, the highest exhibited by F15 (table 4). This is due to the fact of increasing polymer concentrations, which results in rigid three-dimensional network formation with double helical cross-linking with adjacent polymer chains.

Drug content

The drug content percentage of formulations (F1-F15) were in the charge 95.46-99.95 (table 4), which indicates that the distribution of the drug is uniform in all the formulations as per the monograph.

Table 4: Density, swelling index, gel strength determination and drug content of Lafutidine in situ gel RAFT system

Formulation code	Density (g/cm^3)	Swelling index (%)	Gel strength determination (N/m^2)	Drug content* (%)
F1	0.74±0.22	7.31±0.22	6.13±0.32	95.46±0.15
F2	0.715±1.33	7.36±0.82	6.48±0.93	96.46±0.62
F3	0.773±1.85	7.62±0.75	6.97±1.45	96.26±0.37
F4	0.658±0.53	7.92±1.24	7.38±0.92	96.47±0.26
F5	0.615±0.94	8.24±1.87	7.61±1.84	97.48±0.62
F6	0.685±1.04	8.54±1.96	7.29±1.23	97.26±0.73
F7	0.626±1.48	8.67±1.24	7.85±0.62	96.50±0.85
F8	0.547±1.92	9.25±0.38	7.32±0.83	97.17±0.27
F9	0.527±0.20	9.57±0.63	7.58±1.22	98.23±0.57
F10	0.514±0.34	9.73±0.54	8.13±1.45	97.49±0.16
F11	0.558±0.46	10.98±1.48	8.84±0.83	98.36±0.14
F12	0.496±0.72	11.47±1.05	9.15±1.52	98.33±0.58
F13	0.462±091	12.37±0.23	9.48±0.72	98.21±0.75
F14	0.426±0.83	13.93±1.09	10.42±0.52	98.89±0.39
F15	0.415±0.32	14.16±0.19	10.75±0.72	99.95±0.72

*Above parameters are presented as average±standard deviation; (n=3)

***In vitro* dissolution studies**

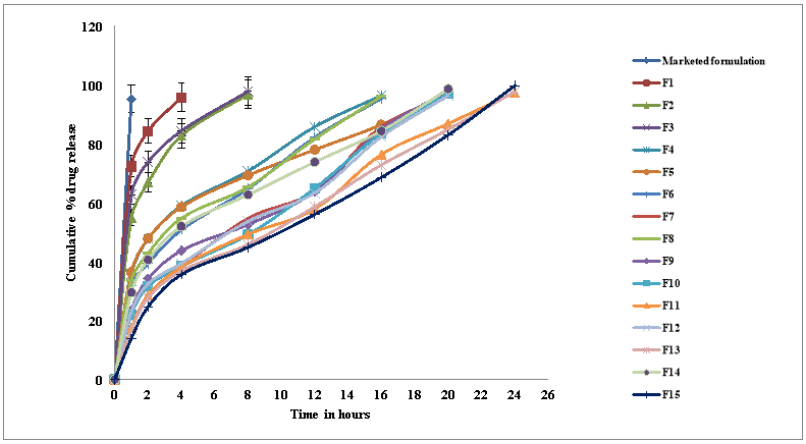

Fig. 5: Cumulative percentage drug release of lafutidine *in situ* gel RAFT formulations (F1-F15) and marketed product

Table 5: Cumulative percentage drug release of Lafutidine *in situ* gel RAFT formulations (F1-F15) and marketed product

Time (h)	Marketed formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	95.28±0.71	72.34 ±0.63	54.89 ±1.83	62.74 ±1.52	35.9 ±1.29	36.43 ±0.72	31.95 ±1.38	22.45 ±0.58	33.65 ±1.28	23.65 ±0.93	21.98 ±1.48	17.50 ±0.52	23.13 ±1.72	16.87 ±0.37	29.54 ±0.28	13.98 ±1.37
2	-	84.34 ±1.38	66.87 ±3.28	73.85 ±0.27	47.78 ±1.38	47.89 ±0.81	39.43 ±1.19	31.74 ±0.25	42.82 ±1.86	34.23 ±0.52	31.65 ±0.74	28.54 ±1.25	32.54 ±1.79	27.76 ±1.39	40.67 ±1.38	24.72 ±0.72
4	-	95.76 ±3.29	82.76 ±0.29	84.41 ±1.39	58.99 ±1.24	58.55 ±1.29	50.82 ±1.08	38.56 ±2.84	54.74 ±1.62	43.76 ±0.51	38.43 ±2.47	38.24 ±1,67	39.42 ±0.47	36.87 ±0.84	51.99 ±0.62	35.67 ±0.61
8	-	-	96.87 ±1.68	97.83 ±2.57	70.78 ±1.68	69.32 ±0.67	64.76 ±2.49	54.76 ±3.27	65.38 ±0.62	52.65 ±0.17	49.21 ±1.38	49.32 ±2.47	53.72 ±0.18	45.88 ±2.84	62.74 ±1.29	44.87 ±0.95
12	-	-	-	-	85.8± 2.93	78.01 ±1.25	82.27 ±0.58	63.84 ±1.20	81.64 ±1.47	63.76 ±1.39	64.97 ±0.36	57.86 ±0.38	63.34 ±0.19	58.65 ±1.03	73.85 ±0.57	56.07 ±0.25
16	-	-	-	-	96.45 ±1.84	86.52 ±0.28	95.43 ±1.35	85.86 ±2.48	96.16 ±0.37	84.97 ±1.86	83.65 ±0.56	76.43 ±0.72	82.43 ±0.47	72.87 ±0.38	84.41 ±0.27	68.64 ±1.04
20	-	-	-	-	-	97.04 ±0.59	-	96.56 ±0.41	-	97.83 ±2.57	97.03 ±1.29	86.86 ±1.38	96.35 ±2.18	84.87 ±0.81	98.63 ±1.39	82.99 ±0.83
24	-	-	-	-	-	-	-	-	-	-	-	97.53	-	97.77	-	99.78 ±0.51

The values are presented as mean (n=3)+standard deviation.

The Cumulative % drug releases of the various prepared formulations were compared with that of gastroretentive microspheres [15] and in situ gel prepared using other combination of polymers [9] shown in (table 4 and fig. 2). In all the formulations as sodium alginate concentration increased the release was increased and sustained but sodium alginate alone was not sufficient to produce the drug release as that observed in F1, F2, and F3 which sustained drug release to only 4-8 h where only minimal quantities of polymers (ethyl cellulose, HPMC K4M and chitosan) 0.5% was used. In gastro retentive lafutidine microsphere, the drug release range was found to be between 57-87% [15], whereas in situ formulations were able to control the drug release 51.7-82.76%. So, in order to get the desired drug release combination of gelling polymer sodium alginate and other matrix-forming polymers (ethyl cellulose, HPMC K4M, and chitosan) were used in high concentrations in the study from F4-F15. The use of polymer and preferably a combination of polymers gave the better control release up to 24 h and also sodium bicarbonate concentration enhanced the buoyancy nature of the formulation following the polymer concentration and increase in concentration up to 2.5% increased floating time up to 24 h. (82.76 by the end of 12h Formulation F15 containing chitosan in combination with ethyl cellulose gave the highest drug release of 99.78% and also showed sustained and controlled release up to 24h.

Release order kinetics

The various dissolution order kinetics, such as zero order, first order, Higuchi, and Korsmeyer-Peppas models were taken under consideration to fit dissolution data. From the data, it has been confirmed that the release kinetics follows zero-order with R2 value of 0.999. The mechanism of drug release was found to follow Korsmeyer-Peppas with n value 1.5021, which indicates that dissolution follows case-II transport.

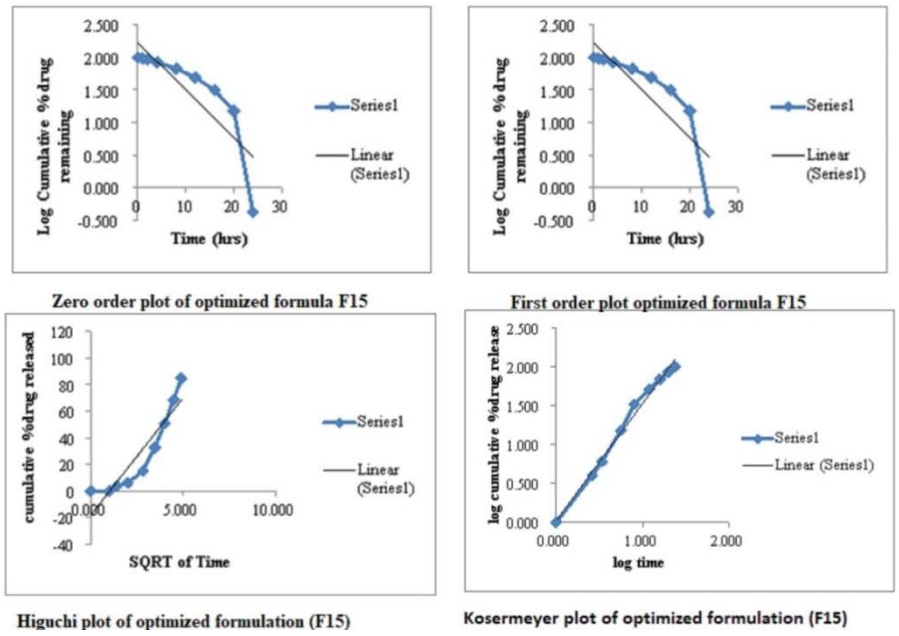

Fig. 6: Drug release kinetics of optimized formulation

Table 6: Release order kinetics for Lafutidine optimized formulation (F15) and marketed formulation

Formulation code	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyer-Peppas R^2	Korsmeyer-Peppas n value
F15	0.999	0.7144	0.8564	0.998	1.5021
Marketed	0.8051	0.9616	0.9669	0.674	0.8996

In vitro release order kinetics of optimized formulation (F15)

Differential scanning calorimetry

The melting point transition peak for pure lafutidine has shown endothermic peak at 99.8 °C.

The physical mixture of lafutidine along with its excipients also exhibits the melting point transition peak at 99.8 °C, which has confirmed that there were no compatibility issues among the drug and excipients used.

Fourier transform infrared spectroscopy

The major peaks of optimized formulation (F15) were seen at 3023.71 foe–NH stretching, 2963.45 and 2838.30-CH (alkyl) stretching, 1857.52 C=O stretching, 1657–CO-NH stretching 1487.92, 1170.10–CH bending, 1002.23–CH (aromatic) stretching, 722.21, 1657–C=O stretching. The spectrum has retained the peaks for the functional group, which indicate there were no interaction drug with used polymers.

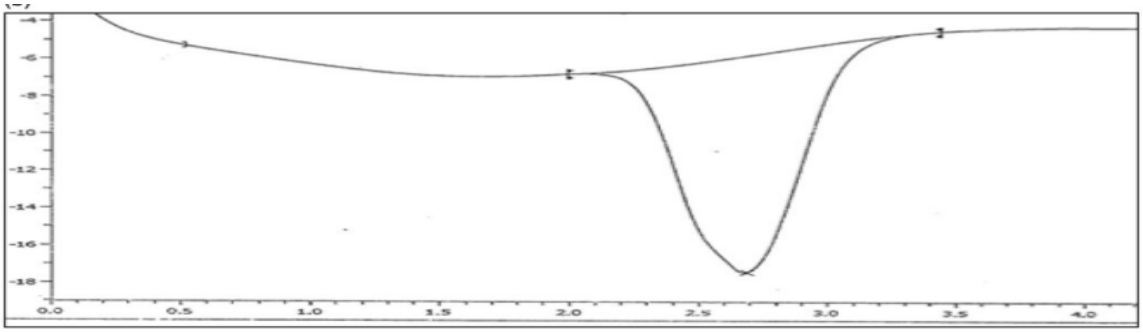

Fig. 7: DSC spectrum of optimized formulation (F15)

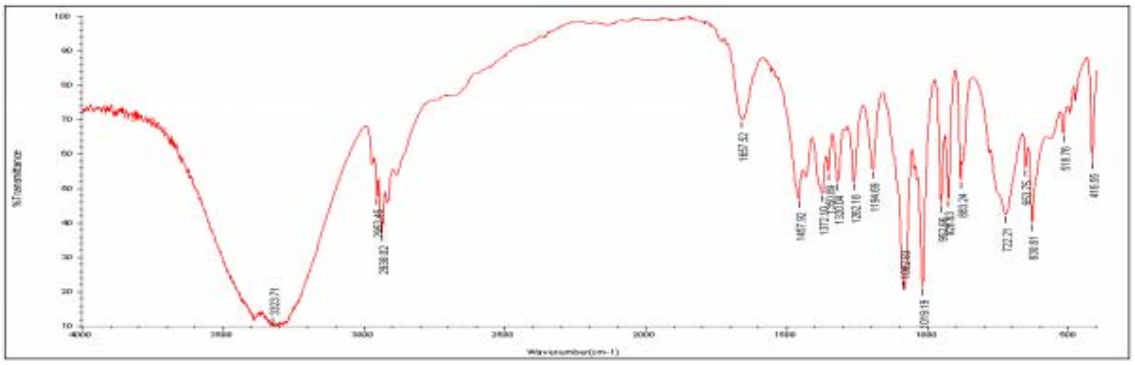

Fig. 8: FTIR spectrum of optimized formulation (F15)

STABILITY STUDY

The stability evaluations such as duration, viscosity, gelling time, floating lag time, pH, dissolution studies, and drug content were under permissible limits, ensuring the stability of preparation in rigorous conditions.

CONCLUSION

The in situ raft-forming gel of lafutidine was successfully prepared using hydrophilic polymers such as ethyl cellulose, HPMC K4M, sodium alginate, and chitosan. Because of polymer combinations in their respective concentrations was considered as suitable for attaining gastric retention for the required time. The prepared formulations exhibited the required evaluation characteristic. The optimized formulation (F15) was able to release 99.78% of drug in 24 h. From drug release kinetics, it was confirmed that it follows zero order and case II transport.

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AUTHORS CONTRIBUTIONS

All the authors have equal contributions to carry out the study

CONFLICT OF INTERESTS

The authors declares there is no conflict of interest

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