ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 11, Issue 8, 2018

Online - 2455-3891
Print - 0974-2441

Research Article

FORMULATION AND EVALUATION OF NOVEL *IN SITU* GEL OF LAFUTIDINE FOR GASTRORETENTIVE DRUG DELIVERY

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Received: 03 March 2018, Revised and Accepted: 20 April 2018

ABSTRACT

Objective: The aim of the present study was to formulate and evaluate the novel *in situ* gel of lafutidine for gastroretentive drug delivery

Methods: A gastroretentive *in situ* gel of lafutidine was formulated by pH-triggered ionic gelation method using different concentrations of gelling polymer such as sodium alginate, gellan gum, and xanthum gum. Prepared formulations were evaluated for viscosity, density, buoyancy lag time and buoyancy duration, and drug content. *In vitro* drug release studies of all formulations were also performed. *In vivo* fluorescence imaging study was conducted for optimized formulation and compared with control.

Results: The concentration of gelling agents and release retardant polymers significantly affected viscosity, floating behavior, and *in vitro* drug release of the formulations. The pH and drug content were found in the range of 6.72–7.20 and 88.74–95.33%, respectively. Floating lag time was <2 min; duration of floating was more than 12 h. Minimum and maximum *in vitro* drug release were found to be for formulation F9 (51.74%) and F1 (82.76%), respectively, at the end of 12 h. The drug was released from the all the formulations in a sustained manner. *In vivo* studies confirmed the gastroretention of the formulation in mice stomach for 8 h. Stability studies indicated that the there was no significant change in the visual appearance, floating behavior, and drug content.

Conclusion: The gastroretentive *in situ* gel system, prolonged the gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract.

Keywords: Lafutidine, Gastroretentive *in situ* gel, pH-triggered gelation.

 DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11i8.25582

INTRODUCTION

There has been a renewed interest in the academia as well as the industry toward the development of gastroretentive *in situ* gelling system. This is mainly due to the considerable advantages of the *in situ* gelling system such as ease of administration and reduced frequency of administration, which help to increase the patient compliance [1]. Gastroretentive *in situ* gelling system also known as stomach-specific systems have the ability to provide controlled drug delivery within the stomach with enhanced gastroretention. *In situ* gelling systems are liquid at room temperature but undergo gelation when in contact with body fluids or change in pH [2]. Since the gel formed from *in situ* gelling system is lighter than gastric fluids, it floats over the stomach contents or adhere to gastric mucosa due to the presence of bioadhesive nature of polymer and produce gastric retention of dosage form and increase gastric residence time resulting in prolonged drug delivery in the gastrointestinal tract [3,4]. The system makes use of polymers that undergo sol–gel phase transition owing to changes in specific physicochemical parameters. Different polymers which are used for the formation of *in situ* gel include gellan gum, alginic acid, xyloglucan, pectin, chitosan, polycaprolactone, polylactic acid, and poly(lactic-co-glycolide). The principle involved in the *in situ* gel formation is the pH-induced ionic gelation. The trisodium citrate incorporated into the formulation helps to maintain the formulation in liquid form until it reaches the stomach. Once the formulation reaches the stomach, in the presence of acidic environment Ca^{++} gets released and triggers the gelation of the formulation. The carbon dioxide that is released in the gastric pH helps to maintain the buoyancy of the *in situ* gel for an extended period [5,6].

Lafutidine is a novel second-generation histamine H_2-receptor antagonist. It is absorbed in the small intestine, reaches gastric cells through the systemic circulation, and then directly and rapidly binds to gastric cell histamine H_2 receptors, resulting in immediate inhibition of gastric acid secretion. Lafutidine is used in the treatment of gastric ulcers, duodenal ulcers, and gastric mucosal lesions associated with acute gastritis. Lafutidine has a receptor binding affinity which is 2-80 times higher than other representative H_2-receptor antagonists (e.g., famotidine, ranitidine, and cimetidine) [7].

However, lafutidine has a short biological half-life and low bioavailability, therefore, requires frequent dosing. Hence, gastroretentive drug delivery of lafutidine in the form of oral *in situ* gel will increase the residence time of the drug and also will release the drug for an extended period, thereby can reduce the frequency of dosing and also increase the bioavailability.

MATERIALS AND METHODS

Materials

Lafutidine was gifted by Zuventus Healthcare Ltd., xanthum gum, trisodium citrate, calcium carbonate, Tween 80, liquid paraffin, concentrated HCl, and sodium fluorescein were purchased from Loba Chemie, Mumbai, India. Sodium alginate and gellan gum were obtained from Himedia laboratories, Mumbai and Yarrow chem Products, Mumbai, India, respectively. Deionized water was purchased from BN laboratories Mangalore, India.

Methods

Preparation of the gastroretentive in situ gel

The required quantities of sodium alginate, gellan gum, xanthum gum, trisodium citrate, calcium carbonate, propylparaben, and methylparaben were weighed accurately along with the measured quantities of Tween

80 and liquid paraffin. Various concentrations of gelling polymer (sodium alginate or gellan gum) were dissolved in deionized water with weighed amount of trisodium citrate on a magnetic stirrer at 70°C. After the above solution has cooled down to 40°C calcium carbonate and release retardant polymer xanthum gum was added. In another beaker, required quantities of Tween 80 and liquid paraffin were added and kept for stirring in a magnetic stirrer. Water was then added drop by drop to form an emulsion followed by the addition of weighed amount of the drug with continuous stirring. The polymeric solution was then added to this drug solution followed by the addition of preservatives, i.e., methyl and propylparaben. Finally, the volume was adjusted with the deionized water, and the resultant solution was stirred well and stored in amber-colored bottles until further use [6].

Drug excipient compatibility studies

Fourier transform infrared (FTIR) spectroscopy was performed using a Shimadzu FTIR 8300 Spectrophotometer and from 4000 to 400/cm region, the spectrum was recorded. The drug was dispersed in KBr (200–400 mg) and made into disc form by compressing it with a pressure of 5 tons for 5 min in a hydraulic press and the spectrum was obtained. The spectra obtained for drug and optimized formulation was compared [8].

Characterization of *in situ* gel

Determination of the visual appearance

All the formulations were visually inspected for their appearance, clarity, and consistency.

Measurement of the pH

The pH for each of the formulations was measured using a calibrated pen pH meter. The readings were recorded three times for each of the formulation and the averages of the readings were considered [9].

In vitro gelation study

5 ml of the simulated gastric fluid (0.1N HCl, pH 1.2) in a 15ml test tube maintained at 37°C followed by the addition of 1 ml of the formulation using a pipette. The pipette was positioned facing the surface of the fluid in the test tube and slowly the formulation was released from the pipette. When the formulation came in contact with the gelation medium, it was quickly converted into a gel-like structure. Based on the stiffness of gel as well as the duration, for which the gel remains as such the *in vitro* gelling capacity was investigated [10].

The *in vitro* gelling capacity was mainly divided into three categories based on gelation time and time period the formed gel remains.

- (+): Gels in few second and disperse immediately
- (++): Immediate gelation does not disperse rapidly
- (+++): Gelation after few minutes remains for extended periods.

Determination of viscosity

Viscosities of the formulations are determined with the help of Brookfield's digital Viscometer (DV-II) +Pro using S21 spindle at 50 rpm and measurement was for done for 6 times with fresh samples being used each time and the average reading was taken.

In vitro buoyancy study

The studies were conducted in a USP Type II dissolution apparatus using simulated gastric fluid (0.1N HCl, pH) as the dissolution medium at 37±0.5°C. About 10 ml of the *in situ* gel formulation was placed in the dissolution medium. The time taken by the *in situ* gel formulation on the surface of the medium (floating lag time) and time period for which the formulation remained buoyant (duration of floating) was noted [11].

Determination of the drug content

5 ml of the formulation equivalent to 10 mg of the drug was added to 80 ml of 0.1N HCl, pH 1.2, and stirred for 1 h in a magnetic stirrer. After 1 h, the solution was filtered and diluted with 0.1 N HCl, pH 1.2. The drug concentration was then determined by ultraviolet (UV) visible spectrophotometer at 279 nm against a suitable blank solution [12].

Measurement of water uptake by the gel

To conduct this study, the *in situ* gel formed in 40 ml of 0.1N HCl, pH 1.2 has been used. From each of the formulation, the gel part was separated from the buffer and the excess buffer was blotted out with the help of Whatman filter paper. The gel was initially weighed and its weight was noted, followed by the addition of 10 ml distilled water to this gel. After every 30 min interval, water was decanted and weight of the gel was noted and difference between initial and final weight was calculated and recorded [13].

Measurement of density of gel

30 ml of the *in situ* formulation was poured into a beaker containing 50 ml of 0.1N HCl. 10 ml of the gel formed was taken in measuring cylinder and weight of the gel was measured. Using the weight as well as the volume of the gel, the density was calculated. This method was followed for all the formulations [14].

Measurement of gel strength

30 g of the gel was taken in a 50 ml beaker and a 50 g weight was placed on the center of the surface of the gel and allowed to penetrate through the gel. The time taken by the 50 g weight to penetrate 5 cm down through the gel was noted for all the formulations. The same method was followed for 6 times for each fresh formulation and average time was noted [15].

In vitro drug release study of the in situ gel formulation

The drug release of the formulations was determined using a USP dissolution apparatus (Type II) with a paddle stirrer at 50 rpm. This slow speed is necessary to avoid breaking of the gelled formulation. 500 ml of the simulated gastric fluid (0.1N HCl, pH1.2) was used as the dissolution medium and the temperature was maintained at 37±0.5°C. 10 ml of the formulation was introduced into the dissolution vessel without disturbing the dissolution medium resulting in the formation of *in situ* gel. At each time interval, 3 ml of the sample was withdrawn and replenished with fresh medium. The samples collected were filtered, suitably diluted, and analyzed at 279 nm using UV spectrophotometer [16].

Drug release kinetics study [17]

To study drug release kinetics of *in situ* gel formulation, data obtained from *in vitro* drug release studies were plotted in various kinetic models: Zero order (Equation: 1) as

cumulative percentage of drug released versus time, first order (Equation: 2) as log cumulative percentage of drug remaining versus time

$$\text{Zero-order equation } Q_t = Q_0 + K_0 t \quad (1)$$

$$\text{First-order equation } \log Q = \log Q_0 - K_1 t/2.303 \quad (2)$$

where Q_t is the percentage of drug release at time t and K_0 and K_1 are the coefficients of the equation.

Mechanism of drug release

Mechanism of drug release from drug-loaded SLN was evaluated by subjecting the data obtained from *in vitro* drug diffusion studies in Higuchi's model (Equation: 3) as cumulative percentage of drug released versus square root of time and Korsmeyer–Peppa's model (Equation: 4) as log cumulative percentage drug released versus log time.

$$\text{Higuchi equation, } Q = Kt_{1/2} \quad (3)$$

$$\text{Korsmeyer–Peppas model equation, } Mt/M\infty = Kt^n \quad (4)$$

where Mt/M∞ is a fraction of drug released at time t, K is the release rate constant, and n is the release exponent.

In vivo fluorescence imaging

Health mice of either sex were divided into two groups of three mice each. One group received the optimized formulation and another group was given a conventional non-gel solution and will be served as the control. Mice were fasted for 24 h before administration of the formulations but were allowed free access to water. 0.2–0.4 ml of the optimized formulation containing the appropriate amount of sodium fluorescein calculated based on the body weight was orally administered to the mice and fluorescence images were recorded at 535 nm at 1 h time intervals for 6–8 h [18].

Stability studies

The optimized formulation of *in situ* gel was placed in an amber color bottle with aluminum cap as a closure. It was tightly sealed. The stability study was carried out as per the ICH guideline, i.e., 5°C±3°C (refrigerator), room temperature of 25°C±2°C/60%±5% RH, and accelerated temperature 40±2°C/75%±5% RH for 1 month. Samples were withdrawn periodically (0, 15, and 50 days) and evaluated for visual appearance, drug content, pH as well as floating behavior [19].

RESULT AND DISCUSSION

FTIR and compatibility studies

No considerable changes in the IR peaks of the drug were observed in the optimized formulation when compared with pure drug as shown in Table 2, which indicate the absence of any chemical incompatibility between drug and excipients.

Characterization of the *in situ* gel formulations

Visual appearance

The visual appeal of the formulation is an important parameter as it has an impact on the patient compliance. All the formulations were subjected to visual appearance. The results are given in Table 3 and all the prepared formulations had off-white appearance. The formulations were free running and did not produce any gelation at room temperature.

pH measurements

The pH of all the formulation was found to be satisfactory in the range of 6.72–7.25 as depicted in Table 3. The pH of all the formulations was within the orally acceptable range. Therefore, it will not cause any irritation on administration of the formulations.

In vitro gelation study

The gelation study was conducted in 0.1N HCl, pH 1.2. Gelation characteristics of the formulations were assessed on an ordinal scale ranging between + and +++ as shown in Table 3. All the formulations on contact with the gelation medium had undergone sol-to-gel transition. In the presence of gel-forming polymers such as sodium alginate and gellan gum and also calcium carbonate and trisodium citrate. The *in situ* released calcium ion from calcium citrate complex gets entrapped in polymeric chains resulting in the cross-linking of polymer chains to form a gel matrix. Thus, stiff gels were formed with formulations containing high concentrations of sodium alginate, formulations containing combination of sodium alginate and gellan gum as well as sodium alginate along with xanthum gum.

Viscosity

The viscosity of all the *in situ* gelling formulations determined at 50 rpm at 25°C using Brookfield DV-II+Pro. The results of viscosity measurement of all the formulations are shown in Table 5. The order of viscosity of the formulations from F1 to F9 is F9 >F8 > F7 > F6 > F5 > F4 > F3 > F2 > F1. The increase in viscosity of the formulations that were observed with the increase in the concentration of polymer can be related to the increasing crosslinking of the polymer. Formulations containing xanthum gum have higher viscosities because of the viscosity enhancement property of xanthum gum. Formulations F8 and F9 were too viscous, making them difficult to pour from the container.

In vitro buoyancy study

The time taken by the formulation to emerge on the surface of the medium is the floating lag time and the time period for which the formulation constantly floated on the surface of the medium is known as floating duration. Buoyancy studies results are given in Table 4. When the formulation comes in contact with the acidic environment, gelation as well as cross-linking of the calcium ions takes place providing a gel barrier on the surface of formulation. The carbon dioxide released is entrapped in the gel matrix giving buoyancy to the formulation. Then the polymeric network further restricts the diffusion of carbon dioxide as well as drug release. The floating ability of the formulations mainly depends on concentration of the gelling polymer, carbon dioxide, and cation source. All the *in situ* gel formulations had a floating lag time of

Table 1: Composition of the *in situ* gelling formulations

Ingredients	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lafutidine (10 mg/5 ml)	200	200	200	200	200	200	200	200	200
Sodium alginate	1	1.5	2	1	1.5	2	1	1.5	2
Gellan gum				0.75	0.75	0.75			
Xanthum gum							0.25	0.25	0.25
Trisodium citrate	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Calcium carbonate	1	1	1	1	1	1	1	1	1
Tween 80	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Liquid paraffin	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Propylparaben	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09
Methylparaben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01

Table 2: Major IR peaks of lafutidine and optimized formulation

Samples	Composition	Major peak (wave numbers cm^{-1})
A	Pure lafutidine	3282.84,2933.73, 2791.00, 2752.42, 2357.01, 2791.00, 2752.42, 2357.01, 1654.92, 1608.63, 1550.77, 1346.31
B	Optimized formulation (F9)	3282.14, 2933.73, 2791.00, 2752.42, 2357.01, 1753.29, 1656.85, 1608.63, 1546.91, 1477.47, 1398.39, 1301.95

IR: Infrared

<2 min and all the formulations floated for more than 12 h. Therefore, the extended duration of floating was responsible for the sustained release of drug.

Drug content

Drug content is one of the important evaluation parameters for any type of dosage form. The percentage drug content of all the formulations was in the range of 88.74–95.90 indicating uniform distribution of drugs in all formulations as per monograph.

Water uptake by the gel

The amount of water associated with the drug delivery system plays an important role in determining the release of the drug from the polymer matrix. The drug release mainly involves the penetration of water into the matrix and simultaneous release of the drug through diffusion or dissolution. The percentage water uptake of all the formulations is given in Fig. 3. When compared with other formulations, F9 showed a better water uptake of 19.26%. The high water uptake may be because of the high swelling capacity of the polymer as the concentration of the polymer increases the water uptake by the gel also increases.

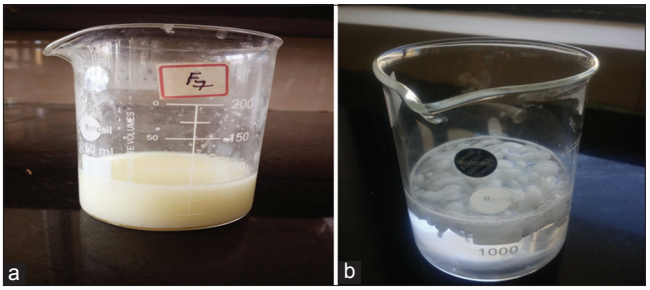

Fig. 1: (a) *In situ* gelling formulation of lafutidine (b) gastroretentive *in situ* gel of lafutidine

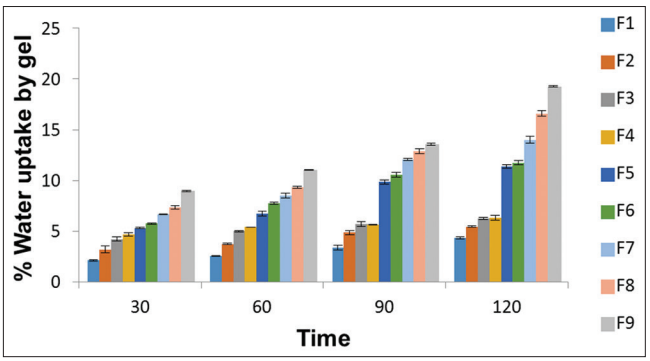

Fig. 2: Histogram of water uptake of *in situ* gel formulations at different time interval

Table 3: Appearance, pH and gelling capacity, and pourability of the *in situ* gel formulations

Formulation code	Appearance	pH	Gelling capacity	Pourability
F1	Off-white	6.72±0.06	+++	Easily pourable
F2	Off-white	7.25±0.09	+++	Easily pourable
F3	Off-white	6.78±0.04	+++	Easily pourable
F4	Off-white	6.83±0.02	+++	Easily pourable
F5	Off-white	6.88±0.07	+++	Easily pourable
F6	Off-white	6.73±0.04	+++	Easily pourable
F7	Off-white	6.96±0.05	+++	Easily Pourable
F8	Off-white	7.20±0.03	+++	Pourable
F9	Off-white	7.14±0.07	+++	Pourable

Measurement of density of the gel

Density is an important evaluation parameter as far as the buoyancy ability of the gastroretentive dosage form is concerned. For the formulation to float on the gastric contents, it should have a density less than or equal to that of the gastric contents (~1.004 gcm^{-3}). The density of all the formulations given in Table 5 has density less than the above-specified value. As a result, the floating of the gastroretentive *in situ* gel is promoted in the stomach.

Measurement of gel strength

All the formulations showed good gel strength which ranged from as low as 15.3 s for F1 to higher values of 65.6 for F9 formulations which have the combination of sodium alginate and gellan gum. Gel strength gives an indication about the tensile strength of the gelled mass. It demonstrates the ability of the gelled mass to withstand the peristaltic movement in *in vivo*. Table 5 gives the gel strength of all the formulations.

In vitro drug release study of the in situ gel formulation

The *in vitro* drug release studies, it was observed that as the concentration of gelling agent increase, release of drug from the gastroretentive *in situ* gel prepared decreases. Drug releasing pattern of different formulation contains a different concentration of gelling agent and drug release retardant polymers are given as follows: With sodium alginate: F1 > F2 > F3, with sodium alginate and gellan gum: F4 > F5 > F6 and with sodium alginate and xanthum gum: F7 > F8 > F9 as shown in Figs. 4-6. The percentage drug release from formulations containing different concentrations of sodium alginate at the end of 12 h was found to be 82.76%, 78.90%, and 76.24%, respectively, for F1, F2, and F3.

Similarly, percentage drug release from formulations containing different concentrations of sodium alginate and gellan gum at the end of 12 h was found to be 77.23%, 75.23%, and 71.47%, respectively, for F4, F5, and F6. The retarded release observed in formulations F4, F5, and F6 is because the gelation and aggregation of gellan gum occur through chemical bonding between calcium and carboxylic groups in the gellan chains. Calcium, being a hard electrophile, interacts with the carboxylate group of gellan gum electrostatically.

The percentage drug release from formulations containing different concentrations of sodium alginate and constant amount of xanthum gum at the end of 12h was found to be 58.23%, 55.24%, and 51.84% respectively for F7, F8, and F9.

As the concentration of sodium alginate, sodium alginate with gellan gum, and sodium alginate with xanthum gum increased, there was a decrease in the drug release. In the formulations F7, F8, and F9, there was a drastic decrease in the drug release due to the presence of xanthum gum which acts as a drug release retardant polymer as well as viscosity-enhancing agents. Xanthum gum hydrates rapidly without lumping and increases the viscosity. Even at low concentrations, xanthum gum imparts high viscosity. Due to high swelling nature of xanthum gum, it forms a thick gel structure which increased the diffusion path length of the drug as a result there is delayed release of the drug from the formulation. The result of this, the drug from formulation F7, F8, and F9 were shown sustained release pattern.

For kinetics study, release data of all *in situ* gel formulation were fitted to various kinetic models. All formulations followed first-order release kinetics with high linearity regression coefficient when compared to zero-order kinetic models. The mechanism of drug release from *in situ*

Table 4: Viscosity, floating lag time, floating duration, and percentage drug content of the *in situ* gel formulation

Formulation code	Viscosity (cps)	Floating lag time (s)	Floating duration (h)	Percentage drug content
F1	70.34±0.45	27±0.83	>12	95.10±0.03
F2	76.78±0.59	34±1.39	>12	92.18±0.07
F3	85.96±0.26	38±1.07	>12	88.74±0.05
F4	116.43±0.55	46±0.73	>12	93.53±0.09
F5	139.86±0.37	49±0.95	>12	90.29±0.05
F6	164.02±0.24	51±1.11	>12	92.35±0.03
F7	195.32±0.48	54±1.26	>12	95.33±0.06
F8	215.08±0.62	63±0.52	>12	91.47±0.09
F9	232.43±0.32	68±0.92	>12	90.68±0.08

Table 5: Density and gel strength of the *in situ* gel formulation

Formulation code	Density (g cm^3)	Gel strength (s)
F1	0.431±0.14	15.3±0.13
F2	0.456±0.09	19.7±0.15
F3	0.492±0.17	25.4±0.20
F4	0.517±0.18	28.5±0.14
F5	0.540±0.11	35.6±0.23
F6	0.553±0.15	42.3±0.08
F7	0.589±0.07	53.2±0.11
F8	0.610±0.09	59.2±0.07
F9	0.624±0.15	65.6±0.10

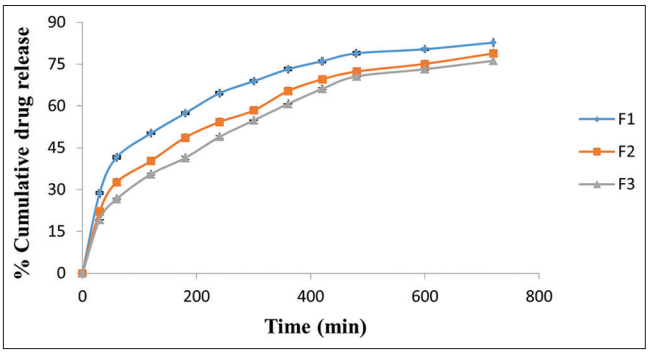

Fig. 3: Comparative in vitro drug release profile of formulations containing different concentrations of sodium alginate

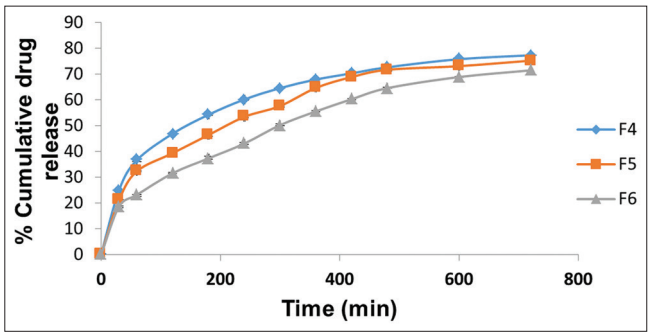

Fig. 4: Comparative *in vitro* drug release profile of formulations containing different concentrations of sodium alginate and gellan gum

gel formulation was studied by fitting the data into Higuchi's model and Korsmeyer–Peppas model. As per the drug release plot, Higuchi's model showed good linearity when compared with Korsmeyer–Peppas model, which shows that the drug release is governed by matrix diffusion process. It is dictated by the fact that gelling agent present in this swell upon imbibitions of water-created gelled matrix through which drug must diffuse.

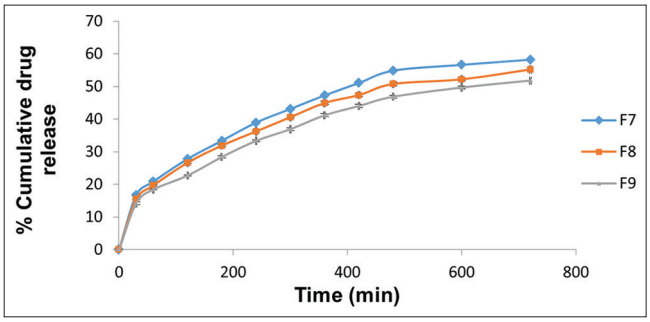

Fig. 5: *In vitro* drug release profile of *in situ* gel formulations containing different concentrations of sodium alginate and xanthum gum

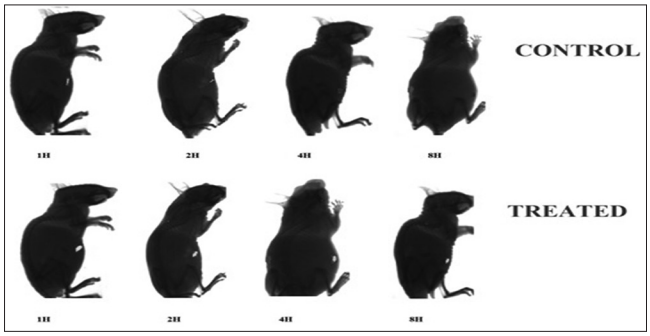

Fig. 6: *In vivo* fluorescence image of the control and gastroretentive *in situ* gel formulation

On the basis of all, the evaluated parameters of *in situ* gelling formulation and F7 were selected as the optimized formulation. Its easy pourability and viscosity, near to neutral pH, gel strength and sustained drug release. All other formulations displayed incompetency in one or more of the above parameters.

In vivo fluorescence imaging

In vivo studies in mice were carried out by orally administering optimized formulation containing sodium fluorescein and comparing with the control by taking fluorescence images of control as well as optimized formulation at predetermined time intervals. From the fluorescence image of the optimized formulation (F7) obtained, it was observed that the formulation remained in the mice stomach for more than 8 h. Thus, the successful gastroretention of the *in situ* gel formulation was demonstrated in the study.

Stability studies

The optimized formulation F7 was subjected for stability studies as per the ICH guidelines for 1 month. Stability study's results indicated that the there was no significant change in the visual appearance, floating behavior, and drug content as shown in Table 7.

Table 6: Kinetic parameter for *in vitro* drug release of *in situ* gel formulations

Kinetic model	F1	F2	F3	F4	F5	F6	F7	F8	F9
Zero order									
R^2	0.9217	0.96	0.9007	0.9627	0.102	0.9748	0.9747	0.9844	0.955
K	0.1025	0.1062	0.0975	0.1065	0.991	0.0803	0.0764	0.0723	0.1008
First order									
R^2	0.9863	0.9941	0.9669	0.9938	0.9985	0.9929	0.992	0.9958	0.9998
K	0.0011	0.001	0.0009	0.001	0.0008	0.0006	0.0005	0.0005	0.0008
Higuchi									
R^2	0.9871	0.9884	0.9842	0.9891	0.9938	0.9954	0.9965	0.9941	0.9938
K	2.7324	2.8631	2.6398	2.8326	2.7985	2.1785	2.0592	1.9723	2.8226
Korsmeyer–Peppas Model									
R^2	0.9647	0.9573	0.9622	0.9829	0.9911	0.9938	0.9925	0.9916	0.9972
K	0.3411	0.0294	0.3647	0.4158	0.4591	0.4248	0.4282	0.4369	0.4454
N	0.8859	0.7546	0.8956	0.7352	0.5615	0.5771	0.5442	0.4864	0.6276

Table 7: Results of stability studies of the *in situ* gel formulation

Condition	Days	Appearance	% drug content	Gelling capacity	Floating lag time (s)
5±3°C	0	Off-white	95.28±0.9	+++	54.10±0.87
	15	Off-white	95.10+0.3	+++	55.21±0.72
	30	Off-white	94.54±0.5	+++	55.48±0.94
25±2°C/60±5% RH	0	Off-white	95.22±0.3	+++	53.95±0.82
	15	Off-white	94.78±0.5	+++	52.22±0.75
	30	Off-white	93.89±0.4	+++	51.37±0.90
40±2°C/75±5% RH	0	Off-white	95.02±0.2	+++	54.08±0.88
	15	Creamish white	93.64±0.7	+++	52.44±0.85
	30	Creamish white	91.95±0.3	+++	50.39±0.80

CONCLUSION

The present study has been a successful attempt to formulate gastroretentive *in situ* gel of lafutidine, an orally administrated anti-ulcer drug with a view to improving its oral bioavailability and provide sustained release of the drug. The developed formulations met all prerequisites to become gastroretentive *in situ* gel system that gelled and floated instantaneously in the pH conditions of the stomach. Hence, it can be concluded that stomach specific *in situ* forming gel of lafutidine can be an effective formulation that shows improved efficacy, prolonged release, patient compliance, and cost-effective over conventional formulation.

ACKNOWLEDGMENTS

The authors are thankful to Himalayan parenteral and formulations Pvt., Ltd., and Zuventus Healthcare for providing the gift samples of lafutidine. The authors are also thankful to Nitte Gulabi Shetty Memorial Institute of Pharmaceutical Sciences, Mangalore, for providing the necessary facilities to carry out the research work.

AUTHORS CONTRIBUTION

Sindhoor S M performed all formulation and characterizations of the studies. Amala Maxwell help him in various laboratory procedures. Dr. SnehPriya guided and supervised the study.

CONFLICT OF INTERESTS

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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