Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

Formulation and Development of Raft-Forming Suspension of Famotidine as Gastro-Retentive Drug Delivery System

Satyawan Singh Dangi, Om Prakash Agrawal

Department of Pharmacy, Bhabha University, Jatkhedi, NH 12, Narmadapuram Rd, Jatkhedi, Bhopal, Madhya Pradesh 462026

(Received: 16 June 2025 Revised: 20 July 2025 Accepted: 07 August 2025)

KEYWORDS

Famotidine, raft-forming drug delivery systems, gastro-retentive drug delivery systems, bioavailability, gastric residence time, in-vitro diffusion studies, gastro-esophageal reflux disease

ABSTRACT:

Objective

This study investigated the raft-forming suspension of famotidine as an anti-reflux formulation to improve the oral bioavailability of narrow absorption window drugs by enhancing gastric residence time (GRT) and preventing gastro-esophageal reflux disease (GERD).

Method

Various combinations of raft-forming agents, such as Tragacanth gum (TG), guar gum (GG), and xanthan gum (XG), were evaluated alongside sodium alginate (SA) to develop an effective raft. Preformulation studies and preliminary screening were conducted to identify the most suitable raft-forming agent, and GG was chosen due to its mucilaginous properties. The formulation was optimized using a 32 full factorial design, with the quantities of GG and SA as independent factors and apparent viscosity and in-vitro drug release (%) as dependent factors. The in vivo floating behavior study was performed for optimized and stabilized formulation.

Results

Among the tested batches, F6 was selected as the optimized formulation. It exhibited desirable characteristics such as adequate raft weight for extended floating in gastric fluid, improved apparent viscosity, and a significant percentage of drug release at 12 h. A mathematical model was applied to the in-vitro data to gain insights into the drug release mechanism of the formulation. The stability of the suspension was assessed under accelerated conditions, and it demonstrated satisfactory stability. The formulation remains floating in the Rabbit stomach for more than 12 h.

Conclusion

It concludes that the developed formulation has enhanced bioavailability in the combination of GG and SA. The floating layer of the raft prevents acid reflux, and the famotidine is retained for an extended period of time in the gastric region, preventing excess acid secretion. The developed formulations are effective for stomach ulcers and GERD, with the effect of reducing acid secretion by H2 receptor antagonists.

INTRODUCTION

Gastro-retentive drug delivery systems (GRDDS) have demonstrated advantages over sustained-release formulations. They are particularly beneficial for drugs with a narrow absorption window or those that exhibit high absorption in the stomach but are prone to decomposition in the intestine.[1] GRDDS promotes prolonged retention of pharmaceutical formulations in the stomach, increasing drug solubility for poorly soluble drugs in the intestine, and enhancing absorption and bioavailability. GRDDS allows for higher drug concentrations in the gastric mucosa by releasing drugs locally in the gastrointestinal tract. This could help keep therapeutic drug levels in the systemic circulation.[2]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

Gastro-esophageal reflux disease (GERD) occurs when gastric contents or bile irritate the esophagus, causing discomfort and the reflux of acidic fluids from the stomach. Weakening or relaxation of the lower esophageal sphincter allows this acid reflux to occur, leading to painful symptoms and potential damage to the esophagus.[3] Smoking, hefty meals, late-night eating, trigger foods, alcohol, coffee, soda, and specific medications taken without consulting a doctor can all aggravate GERD. Symptoms include stomach pain, chest burning pain, dysphagia, persistent laryngitis or hoarseness, throat pain, new-onset asthma, night time coughing, an acidic taste in the throat, regurgitation of food and fluids, and a sensation of a lump in the throat. GERD arises from impaired lower esophageal sphincter function, resulting in acid reflux from the stomach. Currently, available treatments for GERD include antacids, which neutralize stomach acid, medications to reduce acid production such as histamine (H2) blockers (e.g., cimetidine, famotidine, and nizatidine), and proton pump inhibitors like pantoprazole, lansoprazole, and omeprazole.[4] These medications neutralize or prevent acid secretion, but they cannot prevent the reflux of stomach contents into the esophagus. In contrast, the raft-forming drug delivery system prevents the reflux of stomach contents and helps prevent GERD.

Raft development techniques have been effectively employed to prevent its occurrence.[5] Raft-forming drug delivery systems (RFDDS) represent an innovative oral controlled drug delivery approach. When these systems come in contact with gastric fluid, they gel and form a thick, porous layer on the stomach.[6] This relieves acid reflux disorder and slows steady drug release. RFDDS are liquid at ambient temperature but undergo gel formation due to cation-induced gelation and temperature-dependent properties. Raft formation can occur through physical mechanisms involving swelling, diffusion, ion cross-linking, and physiological stimulus based on pH and temperature. This unique mechanism allows the raft formulations to develop a floating layer in the upper part of the stomach, effectively preventing acid reflux while releasing the drug from the delivery system.[7–9]

Famotidine, classified as a BCS class II drug due to its low aqueous solubility and low intestinal permeability, faces challenges in achieving optimal bioavailability.[10] Only 40%–50% of the drug is absorbed in the upper gastrointestinal tract, with the remaining portion being either poorly available for absorption or completely unavailable.[11] To address this issue, raft-forming drug delivery systems (RFDDS) have been developed to enhance the gastric residence time (GRT) of drugs, thereby improving the bioavailability of famotidine.[12]

In RFDDS, sodium alginate is combined with natural mucilages like xanthan gum, guar gum, and tragacanth to form the rafts. Sodium bicarbonate acts as an effervescent mixture, while calcium bicarbonate and carbopol 974 enhance the strength of the rafts. Natural mucilages enhance the GRT of drugs and reduce stomach acidity, which is beneficial for famotidine due to its low bioavailability. Famotidine, an H2 receptor antagonist used for treating ulcers and GERD, exhibits only 40%–50% bioavailability.[13] Combining famotidine with antacids promotes absorption by the receptors in the parietal cell wall. GRDDS, employing rafting technology, helps retain the drug in the stomach for an extended period, enhancing its bioavailability.

MATERIALS AND METHODS

Famotidine obtained as gift sample from Steril Gene Life Sciences (P) Limited. All the other required excipients like sodium alginate (SA), xanthan gum (XG), guar gum (GG), carbopol, and tragacanth were purchased from Sigma Aldrich, Chennai.

Preformulation studies

Solubility study

To determine the solubility profile of famotidine, the shake flask method was employed. Initially, 100 mL of a solubilizing medium was transferred into a 250-ml conical flask, followed by the addition of an excess amount of famotidine. The experiment was conducted at a controlled temperature of 25°C. The conical flask, containing the solubilizing medium and famotidine, was placed on a rotary shaker operating at 200 RPM for a period of 24 h.

After the incubation period, a portion of the famotidine solution was solubilized in buffer solution. Using a UV-visible spectrophotometer, the absorbance of the solubilized famotidine was measured at a specific wavelength of 265 nm. This measurement allowed for

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

the estimation of the quantity of famotidine dissolved in the solubilizing medium, which was then recorded.[14]

To ensure accuracy and reliability, the solubility study was repeated three times using different buffer solutions with varying pH values, including pH 1.2, 4.2, 6.8, and 7.4. Each repetition allowed for the assessment of famotidine's solubility under distinct pH conditions.

Calibration curve for famotidine

Solution I: In a 100-ml volumetric flask, 100 mg of famotidine was solubilized with the required amount of 0.1 N HCl. The remaining volume was then filled with 0.1 N HCl, resulting in a concentration of 1 mg/mL or 1000 µg/ml.

Solution II: From Solution I, 10 mL was withdrawn and diluted with 0.1 N HCl in a 100-ml volumetric flask, producing a concentration of 100 µg/ml. Subsequently, aliquots of 0.2, 0.4, 0.6, 0.8, and 1 mL were withdrawn from this diluted solution and further diluted in 10 mL volumetric flasks with 0.1 N HCl. This resulted in concentrations of 2, 4, 6, 8, and 10 µg/ml, respectively.

Using a UV-visible double beam spectrophotometer, the absorbance of each diluted solution was measured at a wavelength of 265 nm.[15] This data was then utilized to construct the calibration curve for famotidine, allowing for accurate determination of its concentration in subsequent samples based on their absorbance values.

Drug and excipients compatibility studies

Drug-excipient compatibility was determined by analyzing the interaction between the FTIR spectra of famotidine and the FTIR spectra of the drug with excipients. Compatibility study by FTIR Shimadzu IR-Tracer 100 performed with the KBr pellet method. The testing samples were uniformly mixed with KBr crystals, and then they were compressed as a disc. The spectrum was taken by placing the disc on the FTIR spectrophotometer.[16]

Method of Preparation

Accurate weighing of the drug and excipients was performed. Solid substances including sodium bicarbonate, calcium carbonate, sodium alginate, and sodium chloride were finely triturated using a mortar and pestle and then passed through a No. 40 sieve. The quantities of each ingredient for preliminary batches were documented in Table 1. The required apparatus were dried in an oven at 60°C. Then sodium benzoate was dissolved in purified water with constant stirring. [1] The natural mucilages were hydrated by dispersing a portion of the vehicle. Carbopol 974p was dispersed in water, and sodium chloride was utilized to neutralize the pH. Tragacanth, xanthan gum, and guar gum were dispersed separately in glycerol. Sucralose was solubilized in water. The famotidine was dissolved in purified water. Aspartame and sodium saccharin were dissolved one by one in hot distilled water with continuous stirring to achieve a transparent solution. Menthol or mint flavoring agent was dissolved in propylene glycol with continuous stirring to obtain a clear solution. Sodium bicarbonate, calcium carbonate, sodium alginate, and sodium chloride were slowly mixed with the solution from polymer dispersion under continuous agitation. The dispersed drug was then added and vigorously agitated for 5 min. Natural mucilages such as tragacanth, guar gum, or xanthan gum were incorporated into the above suspension. Sweetener and flavor were added while continuously mixing. The final volume was adjusted with purified water. The process of raft development for the famotidine suspension is illustrated in Figure 1.

Table 1. Formulation of famotidine suspension by RFDDS

Ingredients (mg)	G1	G2	T3	T4	X5	X6	S7	S8
Famotidine	20	20	20	20	20	20	20	20
SA	500	250	500	250	500	250	500	250
GG	100	100	—	—	—	—	—	—
Tragacanth	—	—	100	100	—	—	—	—
XG	—	—	—	—	100	100	—	—

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

Carbopol 974 P (gel)	65	65	65	65	65	65	65	65
Sodium bi carbonate	200	200	200	200	200	200	200	200
Calcium carbonate	120	120	120	120	120	120	120	120
Sucralose	10	10	10	10	10	10	10	10
NaCl	1%	1%	1%	1%	1%	1%	1%	1%
Sodium benzoate	1	1	1	1	1	1	1	1
Menthol/mint flavor	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

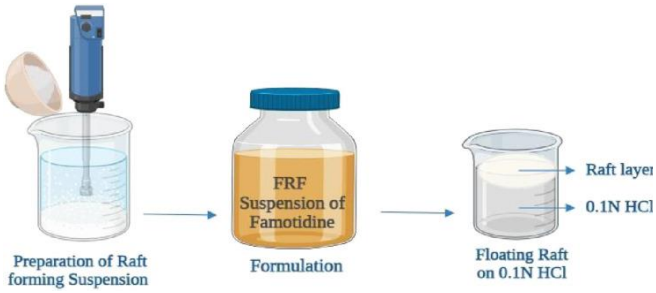

Figure 1. Process of raft development of famotidine suspension.

Preliminary studies

To enhance the raft weight, in-vitro gelation time, in-vitro dissolution studies, and ANC (acid-neutralizing capacity), preliminary studies were conducted. The aim was to select an appropriate natural gum, such as tragacanth, guar gum, and xanthan gum, in combination with sodium alginate. Eight batches were prepared and evaluated to determine their performance.

After analyzing the results of the preliminary studies, it was determined that the combination of guar gum and sodium alginate showed promising outcomes. Hence, this combination was chosen for further optimization using 32 full factorial designs. The goal of the optimization process was to enhance the desired characteristics of the raft-forming drug delivery system.

Optimization of a selected batch

To investigate the influence of independent variables on the formulation, a factorial design was chosen. The 32 full factorial design was selected, and the coding values of the independent variables were presented in Table 2. The key independent variables in this design were the ratios of guar gum with sodium alginate combinations, which had a significant impact on the final quality of the formulation.

Table 2. Coding of variable for 32 full factorial design.

Coding value	−1	0	1
Quantity of sodium alginate	230	250	270
Quantity of guar gum	85	100	115

The dependent variables for this study were the in-vitro dissolution study and in-vitro gelation time, which were crucial indicators of the formulation's performance. A three-level, two-factorial design (32) 17 was employed for the optimization study. This design allowed for the exploration of nine different combinations, as outlined in Table 3 (F1–F9). Through this optimization study, the aim was to determine the ideal combination of guar gum and sodium alginate that would yield the desired in-vitro dissolution characteristics and gelation time.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

Table 3. Optimization by three-level two-factorial design (batch G2).

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Famotidine	20	20	20	20	20	20	20	20	20
SA	230	230	230	250	250	250	270	270	270
Sodium bi carbonate	200	200	200	200	200	200	200	200	200
Calcium carbonate	120	120	120	120	120	120	120	120	120
GG	85	100	115	85	100	115	85	100	115
Carbopol 974 P (gel)	65	65	65	65	65	65	65	65	65
Sodium chloride	1%	1%	1%	1%	1%	1%	1%	1%	1%
Sucralose	10	10	10	10	10	10	10	10	10
Sodium benzoate	1	1	1	1	1	1	1	1	1
Menthol/mint flavor	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation of famotidine suspension

In-vitro gelation time

10 mL of formulation was added to a 250-ml beaker, which contains 100 mL of 0.1 N HCl, to determine in vitro gelation time. The time needed to form a raft on the solution and clear the lower part of the beaker is known as in-vitro gelation time.[18]

Floating time

10 mL of formulation was added to a 250-ml beaker, which contains 100 mL of 0.1 N HCl, to determine the floating time. This is described by the extensive time period during which the raft remains floating on the liquid.[19]

Raft weight

For this test, 100 mL of 0.1 N HCl was taken in a 250 mL beaker. In this, 10 mL of formulation was poured; raft lefts developed uniformly. After complete development of the raft, the beaker is kept to one side for 30 min, and any leftover liquid in the beaker is decanted carefully. The raft was collected from the beaker and transferred to the butter paper; excess liquid in the raft was removed by using a paper towel, and the raft dried for 2 h. Afterward, the dried raft weight was calculated and noted.[20]

Raft volume

The empty beaker was weighed after it had dried completely and written as W1. 100 mL of 0.1 N HCl (raft-developing liquid) was transferred into a beaker, marked for the level of liquid, then weighed and written as W2. In this beaker, 10 mL of formulation was added. Then allow it to develop into a raft and keep it aside for a few minutes. Afterward, leftover liquid was drained, and the raft was collected in a butter paper bag and dried with paper towels. Then, the raft was weighed and written as W3. Purified water was filled up to the mark made in the same beaker used for raft development while 100 mL of raft-developing liquid was added; in this dried raft, weight was taken and written as W4; with all the collected data, raft volume was estimated by the below formula [21]

$$\text{Raft Volume} = (W4 - W1) - (W2 - W1 - W3)$$

Raft strength

Sufficient strength is necessary to prevent the reflux of the stomach contents into the esophageal region. To assess this, 10 mL of the formulation was transferred into a 250 mL glass beaker containing 150 mL of pH 1.2 buffer. The raft was allowed to develop and kept aside for 30-min with an L-shaped wire probe which was immersed straight within the beaker. The strength of the

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

resulting raft was determined using the modified balance method. Water was added drop by drop to the pan, and the amount of water needed to break the raft was recorded. [22]

Raft resilience

The raft was formed in a 250 mL glass jar by adding a bilayer tablet to 150 mL of SGF pH 1·2 previously maintained at 37°C. The raft was allowed to develop for 30 min; the capped jar was positioned in a modified cube mixer, set to revolve at 20 rpm, to simulate gastric agitation. The raft was assessed visually for such a time that a raft could no longer be detected. A raft was distinct or dispersed into two or more hovering gels at least 15 mm dia. [23]

Acid neutralization capacity (ANC)

A tablet powder equivalent to unit dose was taken in a 250-ml beaker. Water was added to make a total volume of about 70 mL, heated to 37°C and stirred continuously by maintaining the temperature at 37°C. 30 mL of 1M hydrochloric acid (previously heated to 37°C) was added and mixture was maintained at 37°C for 15 min with continuous stirring. The excess acid was titrated with 1M sodium hydroxide to a pH of 3.5. The number of meq of acid consumed by the tablet tested was calculated by the following formula 24 :

Total mEq = (V HCl *N HCl) – (V NaOH *N NaOH)

Where, M HCl = molarity of hydrochloric acid

M NaOH = molarity of sodium hydroxide

V NaOH = volume of sodium hydroxide

Dissolution studies

The in-vitro drug release data was determined by the USP Type II dissolution apparatus. The paddle shaft was rotated at 25 rpm, and the chamber was maintained at 37°C. For this study, 900 mL of 0.1 N HCl was taken in a basket. 10 mL of the formulation was placed in the dissolution testing basket, and the raft was left to develop uniformly.[11] Then the paddle began to rotate at 25 rpm, and from the basket, 1 mL of solution was collected in 10 mL standard flasks at every 30 min interval, and the volume was filled up to the level with 0.1 N HCl. Replace the volume with 1 mL of 0.1 N HCl. Using a UV-visible double-beam spectrophotometer, the absorbance was analyzed at 265 nm to get the concentration by applying a calibration factor. [25,26]

In-vitro diffusion study

A Keshary–Chien-type diffusion cell was used for the release study. The cellophane membrane, or dialysis membrane, was immersed in phosphate buffer overnight. Later, the membrane was mounted between the donor and receptor compartments. Micro-bead placed inside the receptor compartment to maintain the hydrodynamics of the fluid at 400 rpm. The compartments were clamped together, and the temperature was maintained at 37°C. Receptor compartment filled with pH 7.4 phosphate buffer. 1 mL of samples was withdrawn at particular time intervals. The same volume was replaced with buffers to maintain sink conditions. The absorbance of samples was analyzed in a UV-visible spectrophotometer. [27–29]

In vivo floating behavior by X-ray imaging

The study was performed after obtaining approval from the Institutional Animal Ethics Committee (IAEC). The in vivo floating behavior of floating raft formulation was analyzed by X-ray imaging technique were performed in Albino rabbits. Barium sulphate-loaded floating raft formulation was administered under fasting, and compared with marketed formulation. The X-ray images of rabbits can indicate whether a selected formulation is capable of developing a raft in the stomach. Through these images the in vivo floating behaviour of guar gum can be determined.[30–32]

Results and Discussion

Preformulation studies

The solubility of the drug was determined using the shake flask method, and the results indicated that the drug exhibited solubility in pH 1.2 buffer, as presented in Table 4. The calibration curve for famotidine was constructed using 0.1 N HCl as the solvent. Statistical data for the calibration curve are summarized in Table 5, with a regression coefficient value of 0.996, indicating a strong correlation between the two axes. The equation Y = 0.0443x + 0.0014 represents the line equation derived from the calibration curve.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

Table 4. Solubility profile of famotidine at different pH.

S. No.	Buffer solution (pH)	Solvent (ml) used for dissolve 1g solute	Solubility Criteria
1	pH 1.2	28.62	Soluble
2	pH 4.2	43.8	Moderately soluble
3	pH 7.4	890.56	Slightly soluble
4	pH 6.8	1012.4	Very slightly soluble

Table 5. Statistical analysis of the calibration curve.

S. No.	Factors	Values
1	Slope	0.043
2	Y- intercept	0.043x + 0.014
3	R square	0.996

The profiles of the drug and excipients provided valuable insights for the formulation development. Compatibility testing between the drug and excipients involved evaluating their physical characteristics and potential chemical reactions. The FT-IR analysis revealed no significant interaction between the drugs and excipients, as depicted in Figures 2 and 3. This finding confirmed that the selected excipients were suitable for the development of the raft-forming suspension of famotidine.

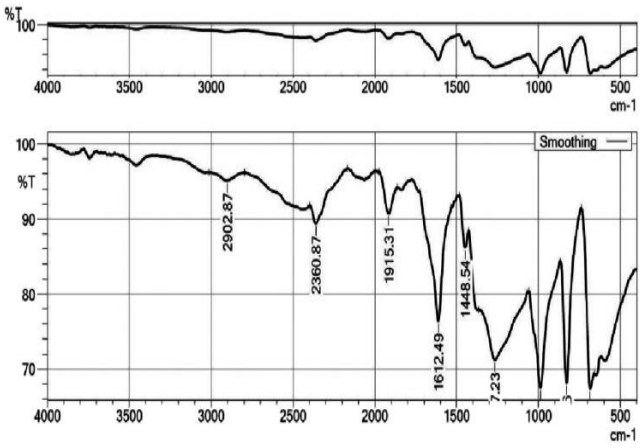

Figure 2. FTIR spectra of famotidine.

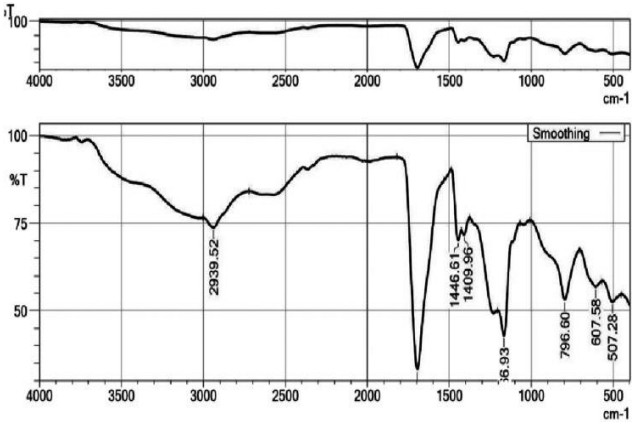

Figure 3. FT-IR spectra of formulation.

Surface morphology

The particle size of the optimized raft-forming suspension of famotidine is around 1 to 100 µm (Figure 4). The morphology of the raft-forming suspension was analyzed by SEM (Figure 5). The photograph was examined at higher resolution for the optimized formulation through a scanning electron microscope.

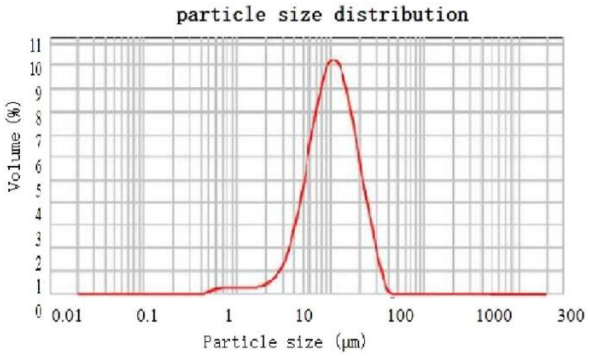

Figure 4. Particle size analysis.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

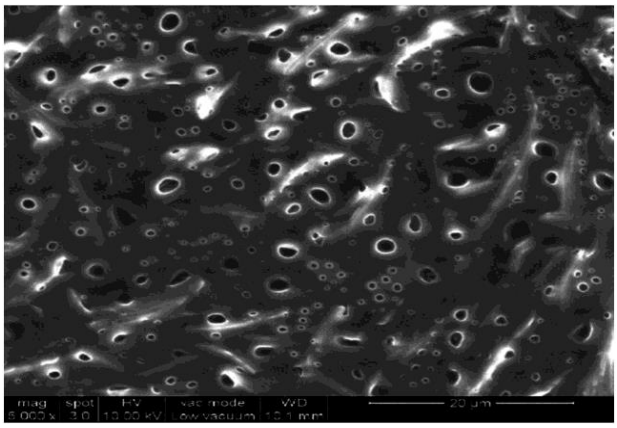

Figure 5. SEM image of formulation (F6).

Results of preliminary batches

Based on the preliminary studies, guar gum (G2) demonstrated superior performance in terms of floating lag time, raft weight, and ANC compared to other formulations listed in Table 6. The combination of guar gum with sodium alginate (GG-SA) exhibited better raft formation compared to sodium alginate alone and the combination of xanthan gum and tragacanth gum with sodium alginate. These other formulations were found to be ineffective in producing a suitable raft-forming suspension and had longer floating lag times. Therefore, GG-SA was selected for further optimization studies.

Table 6. Comparative results of preliminary studies in raft-forming suspension of famotidine.

Formulation	pH	Floating lag time (sec)	Floating time (hrs)	Raft weight (gm)	Raft volume (ml)	Viscosity in centipoises	ANC (mEq)
G1	8.22 ± 0.8	39 ± 0.3	>12	2.481 ± 0.4	2.781 ± 0.8	1290 ± 2	6.95 ± 0.3
G2	8.45 ± 0.4	30 ± 0.6	>12	2.899 ± 0.8	3.199 ± 0.5	1460 ± 5	7.15 ± 0.4
T3	7.61 ± 0.1	45 ± 0.2	>12	2.578 ± 0.4	2.878 ± 0.4	1280 ± 3	5.35 ± 0.8
T4	7.83 ± 0.6	52 ± 0.8	>12	2.672 ± 0.9	2.972 ± 0.8	1360 ± 2	5.55 ± 0.6
X5	7.99 ± 0.0	68 ± 0.5	>12	2.562 ± 0.7	2.862 ± 0.2	1340 ± 4	4.4 ± 0.3
X6	7.91 ± 0.1	64 ± 0.3	>12	2.391 ± 0.7	2.691 ± 0.3	1390 ± 2	4.65 ± 0.7
S7	7.92 ± 0.1	42 ± 0.5	>12	2.373 ± 0.8	2.57 ± 0.28	1320 ± 4	7.27 ± 0.5
S8	8.09 ± 0.3	40 ± 0.5	>12	2.299 ± 0.2	2.49 ± 0.31	1330 ± 1	7.25 ± 0.2

n = 3*.

Results of optimized batch

The optimized batch yielded favorable results across all evaluation parameters in raft development technology, as presented in Table 7. The combination of guar gum, sodium alginate, and carbopol 947 resulted in the formation of a uniform raft on 0.1 N HCl, while sodium

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

bicarbonate and calcium carbonate interacted with the polymer to form a porous floating layer within an average time of 21 ± 0.3 s.

Among the optimized formulations, F6 demonstrated better in-vitro drug release (91.40 ± 0.12) at 12 h and a higher ANC (7.44 ± 0.3) compared to other formulations. Thus, F6 showed a more significant impact on raft development, exhibiting suitable pH (8.41 ± 0.1), in-vitro gelation time, raft volume (3.29 ± 0.22), viscosity (1480 ± 3), ANC, and in-vitro drug release. The comparative study of percentage drug release for all optimized batches is illustrated in Figure 6. Additionally, the optimization results of the raft-forming suspension using sodium alginate and guar gum, including contour plots and response surface plots of ANC and in-vitro drug release (%), are depicted in Figure 7 (a)–(d). Model statistics for responses Y1 and Y2 (raft-forming suspension using sodium alginate and guar gum) are presented in Table 8.

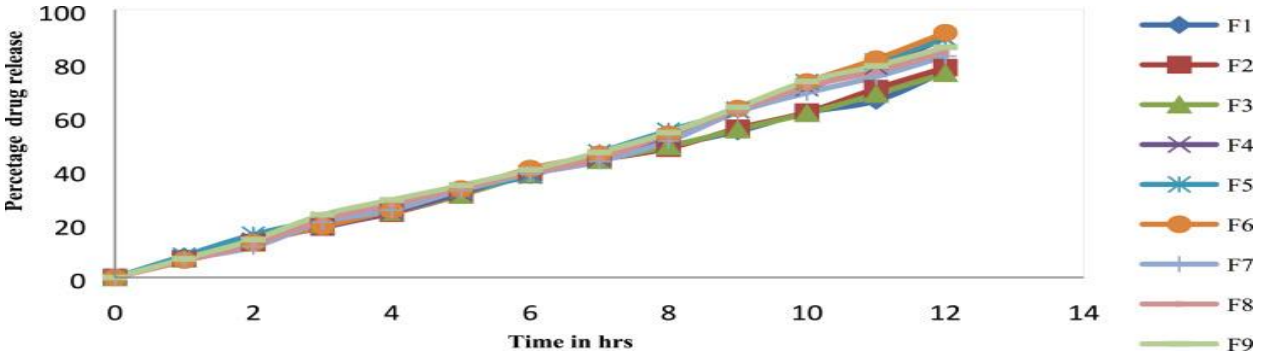

Figure 6. In-vitro percentage drug release of optimized batch.

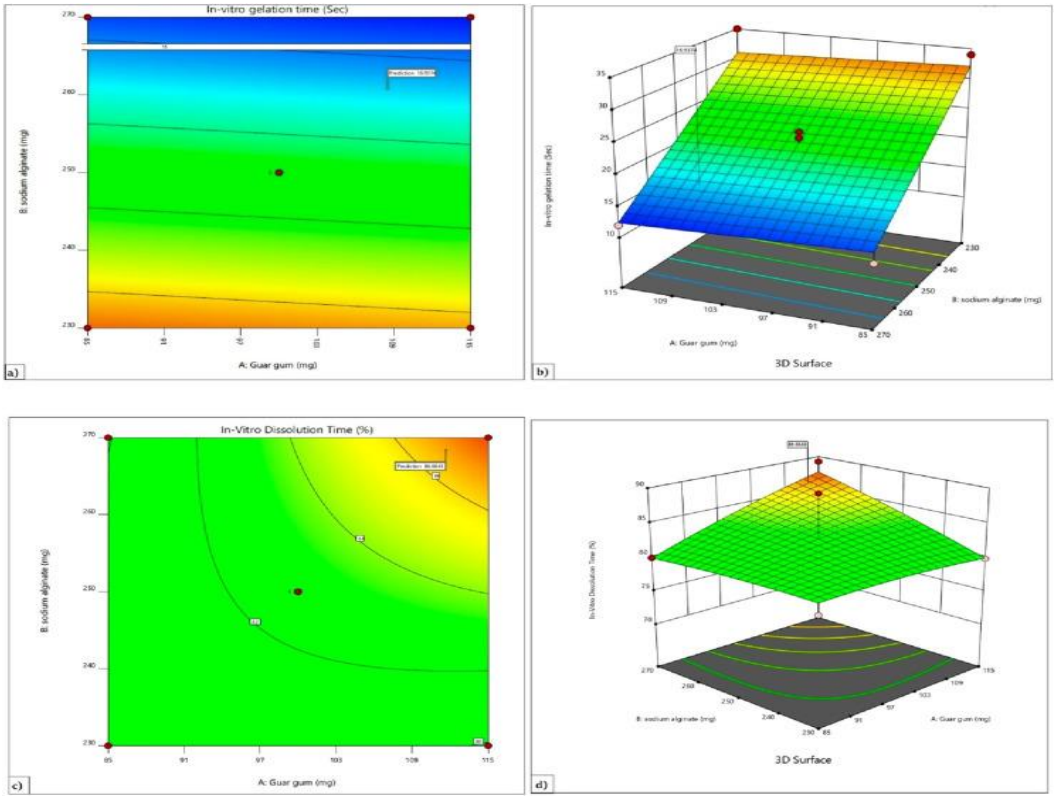

Figure 7. (a), (b), (c), and (d): Contour plot and response surface plot of ANC and in-vitro drug release (%) in raft-forming suspension using sodium alginate and guar gum.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

The regression equations for the raft-forming suspension using sodium alginate and guar gum were determined using the response surface method.

$Y1 = 22.29-0.6250*X1-9.25*X2$

$Y2 = 82.08 + 1.76*X1-0.9275*X2+2.08*X1*X2*-0.4932*X12 -0.3882*X22$

The mathematical models, including zero order, first order, Higuchi matrix, and Korsmeyer–Peppas model, were applied to the in-vitro dissolution data to analyze the drug release mechanism from the dosage form. Table 9 and Figure 8(a)–(d) present the results of this analysis. The R2 values obtained from the kinetic analysis indicate that the release of famotidine from the raft-forming drug delivery system follows zero-order kinetics.

Conclusion

In conclusion, a famotidine suspension formulated using a raft-forming drug delivery system with guar gum and sodium alginate as the raft-developing polymers has been successfully developed. The inclusion of calcium carbonate and sodium bicarbonate as acid-neutralizing agents further enhances the formulation. When the suspension comes into contact with 0.1 N HCl, the release of CO2 triggers the formation of a floating raft within a desirable floating lag time of 21 ± 0.3 to 45 ± 0.5 s. Optimization of the formulation was achieved using a three-level, two-factorial design, with the combination of guar gum and sodium alginate (GG-SA) demonstrating improved floating lag time, pH, raft volume, raft weight, and acid neutralization capacity. The optimized formulation was able to release the drug effectively for a sustained period of 12 h. Kinetic analysis revealed that the famotidine release from the raft-forming drug delivery system follows zero-order kinetics, indicating controlled and prolonged drug release. The FT-IR analysis confirmed no significant interaction between the drugs and excipients, ensuring formulation stability. The optimized formulation remained stable under accelerated conditions of temperature and humidity. The controlled release of famotidine from the GG-SA formulation exhibited a significant effect on the absorption window, leading to improved bioavailability by extending the gastric retention time of the drug in the stomach. The in-vitro drug diffusion results further support the enhanced drug release achieved with the F6 formulation. The in vivo floating behavior study confirms the floatability of raft in the stomach for more than 12 h. Overall, the development of a raft-forming suspension using GG-SA provides a promising approach for enhancing bioavailability and optimizing the treatment of gastro-esophageal reflux disease (GERD) and stomach ulcers.

References

1. Hanif M, Abbas G, Shah S, et al. (2020) Raft-forming system for pantoprazole and domperidone delivery: in vitro and in vivo study. Bioinspired, Biomimetic Nanobiomaterials 9(3): 137–146.
2. Patel R, Vaishnav G. (2020) Raft forming system - gastroretentive drug delivery system. International Journal of Advanced Engineering, Management and Science 6(12): 515–519.
3. Bhavsar DN. (2012) Advances in Grdds: raft forming system a review. J Drug Deliv Therapeut 2(5): 123–128.
4. Sai MG, Suraj Narayana M, Glory Margaret P, et al. (2021) Raft forming systems: a novel approach to gastric retention. IJPSN 14(5): 5594–5602.
5. Panda S, Madhusrota P, Sethi G. (2019) Raft forming system-A novel approach for improving gastric retention. J.Pharm.Sci&Res 11(12): 3761–3772.
6. Abou Youssef NAH, Kassem AA, El-Massik MAE, et al. (2015) Development of gastroretentive metronidazole floating raft system for targeting Helicobacter pylori. Int J Pharm 486(1–2): 297–305.
7. Gananarajan G, Pal R. (2021) Raft forming gastro retentive drug delivery system-a novel approach. JPPS 10(8): 650–659.
8. Joshi V, Awasthi R. (2021) Floating in-situ raft forming liquid gastroretentive drug delivery system containing poorly water-soluble drug. BFSA 44(2): 301–312.
9. Du Y, Zhai Y, Zhang J, et al. (2013) Development and evaluation of taste-masked dry suspension of cefuroxime axetil for enhancement of oral bioavailability. Asian J Pharm Sci 8(5): 287–294.
10. Manna S, Jayasri K, Annapurna KR, et al. (2016) Alginate based gastro-retentive raft

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

forming tablets for enhanced bioavailability of tinidazole. Int J Appl Pharm 9(1): 16–21.

11. Yaswantrao PA, Khanderao RJ, Manasi NN. (2015) A raft forming system: an novel approach for gastroretention. Int J Pure App Biosci 3(4): 78–192.
12. Choudhary PD, Pawar HA. (2014) Recently investigated natural gums and mucilages as pharmaceutical excipients: an overview. Journal of pharmaceutics 2014: 204849.
13. Hanif M, Shah S, Rasul A, et al. (2020) Enhancement of oral bioavailability of ibandronate through gastroretentive raft forming drug delivery system: in vitro and in vivo evaluation. Int J Nanomed 15(7): 4847–4858.
14. Hani U, Rahamathulla M, Osmani RAM, et al. (2022) Development and characterization of oral raft forming in situ gelling system of neratinib anticancer drug using 32 factorial design. Polymers 14(13): 2520.
15. Noel Preetham D, Sujana K, Sankar PDS. (2024) Development and validation of UV spectrophotometric method for the estimation of lisinopril in bulk and pharmaceutical formulation. Int J Pharmaceut Sci Rev Res 25(1): 257–259.
16. Sai VM, Guptha DV, Krishna BSM, et al. (2016) Stability indicating assay method development and validation of naratriptan hydrochloride by RP–HPLC. Res J Pharm Technol 9(8): 1177–1182. DOI: 10.5958/0974-360X.2016.00225.0.
17. Gusai T, Dhavalkumar M, Soniwala M, et al. (2020) Formulation and optimization of microsponge-loaded emulgel to improve the transdermal application of acyclovir—a DOE based approach. Drug delivery and translational research 11(5): 2009–2029.
18. S Al-Lami M. (2017) Formulation and evaluation of sustained and raft forming antacid tablet. Iraqi Journal of Pharmaceutical Sciences 26(1): 26–31.
19. Newton AMJ, Indana VL, Kumar J. (2015) Chronotherapeutic drug delivery of Tamarind gum, Chitosan and Okra gum controlled release colon targeted directly compressed Propranolol HCl matrix tablets and in-vitro evaluation. Int J Biol Macromol 79: 290–299.
20. Tareq A. (2016) Preparation and characterization of PVA-NaAlg interpenetrating polymer network (IPN) hydrogel for controlled delivery of carbidopa. Am Chem Sci J 17(1): 1–10.
21. Vrettos NN, Roberts CJ, Zhu Z. (2021) Gastroretentive technologies in tandem with controlled-release strategies: a potent answer to oral drug bioavailability and patient compliance implications. Pharmaceutics 13(10): 1591.
22. Meka VS, Nali SR, Songa AS, et al. (2012) Statistical optimization of a novel excipient (CMEC) based gastro retentive floating tablets of propranolol HCl and it's in vivo buoyancy characterization in healthy human volunteers. Daru: Journal of Faculty of Pharmacy, Tehran University of Medical Sciences 20: 21.
23. Al-Tabakha MM, Khan SA, Ashames A, et al. (2021) Synthesis, characterization and safety evaluation of sericin-based hydrogels for controlled delivery of acyclovir. Pharmaceuticals 14: 234.
24. Hassan H, Adam SK, Alias E, et al. (2021) Central composite design for formulation and optimization of solid lipid nanoparticles to enhance oral bioavailability of acyclovir. Molecules 26: 5432.
25. Abouelatta SM, Aboelwafa AA, El-Gazayerly ON. (2018) Gastroretentive raft liquid delivery system as a new approach to release extension for carrier-mediated drug. Drug Deliv 25: 1161–1174.
26. Bhavsar DN. (2012) Advances in grdds: raft forming system a review. J Drug Deliv Therapeut 2: 123–128.
27. Soni H, Patel VA. (2016) Preparation and evaluation of raft forming chewable tablets of ranitidine hydrochloride. Int J Pharmaceut Res Allied Sci 5: 290–296.
28. Dash S, Murthy PN, Nath L, et al. (2010) Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm 67: 217–223.
29. Raut SS, Shinde HA. (2018) In-situ raft forming system: a review. IJP 5(6): 337–349.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2271-2282 | ISSN:2251-6727

30. Megha S, Seema K, Agnimitra D. (2015) In-vitro and in-vivo evaluation of repaglinide loaded floating microspheres prepared from different viscosity grades of HPMC polymer. Saudi Pharmaceut J 23: 675–682.
31. Aseem K, Anil KS, Rohit D. (2021) A Review of gastro-retentive drug delivery systems for antidiabetics and its present status. RJPT 14(1): 538–546.
32. Rawat S, Sangali S, Gupta A. (2018) Formulation and evaluation of floating matrix tablets of acyclovir using 32 factorial design. Res J Pharm Dosage Forms Technol 10(1): 1–9.
33. Rahamathulla M, Saisivam S, Alshetaili A, et al. (2021) Design and evaluation of losartan potassium effervescent floating matrix tablets: in vivo X-ray imaging and pharmacokinetic studies in Albino rabbits. Polymers 13(20): 3476.