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RESEARCH ARTICLE

Design and Evaluation of Gastroretentive Matrix Tablets Incorporating Famotidine using Naturally Sourced Polymers

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Abstract

Background: Famotidine has been widely utilized as a therapeutic intervention in the management of peptic ulcers for a number of years. Famotidine (FM) functions as a histamine H2-receptor antagonist, and it is prescribed for the treatment of various types of ulcers as well as hypersecretory disorders. This medication is employed both for active treatment and for long-term maintenance therapy. Despite its relatively short biological half-life (2.5-4h). **Aim:** this study aimed to enhance its therapeutic efficacy by formulating FM into gastro-retentive matrix tablets using natural polymers. **Methods:** A total of 15 gastro-retentive matrix tablets were prepared using the direct compression method. **Results:** The formulated tablets exhibited a thickness ranging from 4.1±0.31 to 4.4±0.20 mm, slightly higher than those utilizing synthetic polymers. Tablet hardness fell within the array of 3.7±0.12 to 4.0±0.14 kg/cm^2, ensuring good mechanical resistance. Friability, ranging from 0.20±0.22 to 0.50±0.24%, remained below 1%, indicating favourable tablet durability. Weight variation adhered to specified limits, and drug content ranged from 19.06±0.36 to 19.09±0.21 mg, meeting acceptable criteria. Swelling index studies demonstrated a concentration-dependent increase in swelling, with xanthan gum exhibiting the highest index (160 %) and guar gum the lowest (60 %). Gastro-retentive matrix tablets F1-F15 released 97.00 % to 71.67 % of the drug over 12 hours, showcasing prolonged release characteristics. **Conclusion:** *In-vitro* release studies affirmed sustained buoyancy for over 12 hours, reflecting the effectiveness of the formulations. Fourier Transform Infrared Spectroscopy (FTIR) showed no interactions between the drug and polymers, confirming the formulation's stability. DSC thermogram revealed the thermal stability of the drug within the formulated tablets, signifying its suitability for therapeutic use without undergoing any interactions.

Major Findings: The chosen gastro-retentive matrix tablet F4 showed stability in terms of drug content, weight fluctuation, friability, and *in-vitro* release profiles.

Keywords: Gastro-retentive Matrix Tablets, *In Vitro* Buoyancy, Natural Polymers, Peptic Ulcer

1. Introduction

The best suitable and favoured method of medication transfer to the systemic circulation is oral. Pharmaceutical companies are increasingly interested in oral controlled-release drug delivery because of its simplicity in dosing, better patient compliance, and flexible formulations. Medications with short half-lives and good gastrointestinal absorption are quickly eliminated from circulation, requiring frequent dosing. Oral sustained-release formulations gradually release the drug in the gastrointestinal tract, maintaining

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systemic concentration by providing a continuous supply after administration[1]. To create a site-specific orally delivered controlled release dosage form, medication administration should lengthen stomach residence duration. Prolonged stomach retention enhances bio-availability, medication release duration, waste reduction, and drug solubility in high pH environments[2]. Prolonged Gastric Retention Time (GRT) may benefit upper small intestine local action, such as peptic ulcer therapy.

Extending the time drugs remain in the stomach enables targeted release in the upper gastrointestinal tract, enhancing local or systemic effects. This approach improves the effectiveness of short half-life medications, increases bioavailability, reduces side effects, optimizes dosing schedules, and enhances drug solubility in high pH environments, ultimately improving patient compliance[3,4]. In recent decades, various Gastro-Retentive Drug Delivery (GRDD) methods have been developed, including high-density (sinking) systems that remain in the stomach and low-density (floating) systemsthat induce gastric fluid buoyancy, stomach mucosa-bioadhesive systems, unfoldable, extendable, or swellable mechanisms that restrict stomach pyloric sphincter dose form emptying, extremely porous hydrogel, magnetic, *etc*[5-11].

The stomach consists of the fundus, body, and antrum. The fundus is closest to the origin, while the body stores undigested substances. The pylorus mixes the contents and helps empty the stomach by pumping them out[12].

The stomach is an enlarged digestive tract between the oesophagus and small intestine. When empty, it contracts, causing the mucosa and submucosa to fold into rugae. The stomach has four main types of secretory epithelial cells that form gastric pits and glands. Mucous cells produce an alkaline fluid. Parietal cells make hydrochloric acid. Chief cells create pepsin, which is a protein-digesting enzyme. G cells release the hormone gastrin. The physiology of stomach represented in Figure 1.

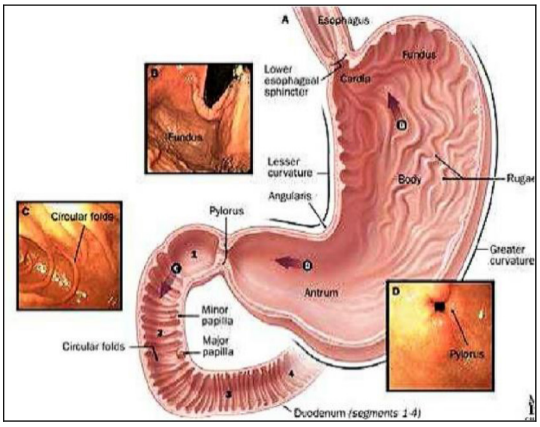


Figure 1. Physiology of stomach.

Both fasting and eating empty the stomach. During fasting, the stomach and intestines undergo electrical events every 2-3 h. The inter-digestive Mylo-electric Cycle (MMC) has four phases.

Phase I (Basal Phase): Lasts 40-60 minutes with infrequent contractions.

Phase II (Preburst Phase): With intermittent action potentials and contractions it lasts 40-60 min.

Phase III (Burst Phase): Involves powerful, regular contractions for 4-6 minutes.

Phase IV: Lasts between 0 and 5 minutes and occurs between phases III and I of two consecutive cycles[13].

Using H2-receptor antagonist's identical famotidine or ranitidine with antacids for oral gastric disorders improves localized medication delivery to parietal cell wall receptors. This targeted delivery approach increases medication bioavailability at the stomach wall receptor location and reduces acid secretion. This idea may improve systemic and localized famotidine

Table 1. Materials used

S. No	Materials	Supplier
1	Famotidine	Hetero labs ltd., Hyderabad
2	Guar gum	S.D Fine chemical pvt. Ltd, Mumbai
3	Xantham gum	S.D Fine chemical pvt. Ltd, Mumbai
4	Pectin	S.D Fine chemical pvt. Ltd, Mumbai
5	Tamarind seed powder	Finar chemical. Ahmedabad
6	Isbgol husk	Hi media laboroteries pvt ltd. Mumbai
7	Sodium bicarbonate	Helios pharmaceuticals. Gujarat
8	Talc	S.D Fine chemical pvt. Ltd, Mumbai
9	Citric acid	S.D Fine chemical pvt. Ltd, Mumbai
10	Beeswax	S.D Fine chemical pvt. Ltd, Mumbai
11	Magnesium sterate	Loba chemie pvt. Ltd, Mumbai
12	Hydrochloric acid	S.D Fine chemical pvt. Ltd, Mumbai
13	Lactose	S.D Fine chemical pvt. Ltd, Mumbai

administration, reducing stomach acid output. In this study, direct compression was used to make floating famotidine tablets and gastro-retentive matrix tablets with various natural polymers and gas-forming agents sodium bicarbonate and citric acid[14,15].

2. Materials and Methods

A free sample of famotidine came from Hetero Labs Limited-Hydera S.D Fine Chemicals Pvt Ltd., Mumbai supplied guar, xanthan, and pectin. Finar Chemicals, Ahmedabad, Gujarat, supplied tamarind seed powder. Glaxo Smith Klien Ltd, Mumbai supplied sodium bicarbonate. S.D. Fine Chemicals Pvt Ltd., Mumbai supplied lactose, magnesium stearate, and talc. All other compounds were analytical. The materials used for the current study represented in the Table 1.

2.1 Preparation of Famotidine Controlled-release Tablets

For matrix tablets containing Famotidine and other constituents, direct compression was cast-off. As a pill buffer, lactose makes components simpler to crumble and flow. Bubbles from sodium bicarbonate helped the dose form float. When pills contact an acidic dissolving liquid contained in the matrix, CO_2 is released. Famotidine gastro-retentive matrix tablets were prepared by crushing with a 12-mm flat-faced punch and mixing natural polymers like guar gum, xanthan gum, pectin, and tamarind seed powder. The active ingredients and polymers were combined with diluents and sodium bicarbonate, then kneaded with melted white beeswax into a soft mass. After sieving, the granules were dried, mixed with magnesium stearate and talc as flow promoters, and then compressed into matrix tablets[16-18] composition represented in Table 2.

2.2 Pre-compression Evaluation

2.2.1 Angle of Repose

To calculate the angle of repose (θ), the fixed funnel approach was used and the formula was Tan θ = h/r. Where θ is the angle of repose, h is the cone height, and r is the base radius. A funnel with its bottom tip 2.5 cm above the surface measured the angle of repose on a platform. Flat graph paper was placed. Powder mix fell freely on graph paper *via* the funnel (6.9 cm diameter) until the heap tip (8 mm diameter) reached the funnel. Angle of repose was estimated using heap radius. Free-flowing material has a repose angle below 30°. Tests were done three times[19-21].

$$Angle\ of\ repose: \mathrm{Tan}^{-1}(h/r) \qquad \text{Equation (1)}$$

2.2.2 Bulk Density

A funnel was used to transfer the correctly weighed powder to the graduated cylinder (50 ml) to calculate bulk density. The unsettled volume was read after properly leveling the powder without compacting. Volume was measured and bulk density (g/cm^3) was

Table 2. Composition of gastro-retentive matrix tablets of famotidine

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Famotidine	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Guar gum	150	200	250	-	-	-	-	-	-	-	-	-	75	-	-
Xantham gum	-	-	-	150	200	250	-	-	-	-	-	-	75	75	-
Pectin	-	-	-	-	-	-	150	200	250	-	-	-	-	75	75
Tamarind seed powder	-	-	-	-	-	-	-	-	-	150	200	250	-	-	75
Isbgol husk	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90
Sodium bicarbonate	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Citric acid	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18
Lactose	100	50	0	100	50	0	100	50	0	100	50	0	100	100	100
Magnesium sterate	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Bees Wax	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total Weight (mg)	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**

calculated from sample weight to volume. The test was repeated three times and noted the mean values[22,23].

$$Bulk\ density = \frac{Weight\ of\ Powder}{Bulk\ Volume.} \quad \text{Equation (2)}$$

2.2.3 Tapped Density

The sample was placed in a 50 ml graduated cylinder. The cylinder was controlled and lowered by its own weight using a mechanical tapping density tester. After 100-cylinder taps, volume was measured[21-23]. This formula calculated tap density in g/cm^3:

$$Tapped\ density = \frac{Weight\ of\ Powder}{Tapped\ Volume} \quad \text{Equation (3)}$$

2.2.4 Carrs Index

Powder flow was measured using Carr's index. Sample blend compressibility was calculated using apparent bulk density and tapped densities using the following formula. Tests were done three times[24,25].

$$\%Comressibility = \frac{Tapped\ Volume - Bulk\ density}{Tapped\ Volume} \times 100 \quad \text{Equation (4)}$$

2.2.5 Hausners Ratio

Hausners ratio indicates powder flow ability and is larger than 1.25 suggests poor flow ability. The equation below calculated Hausners ratio. Tests were done three times[26-28].

$$Hausner's\ ratio = \frac{Tapped\ Volume}{Bulk\ density} \quad \text{Equation (5)}$$

2.3 Evaluation of Gastro-retentive Matrix Tablets

2.3.1 Post Compression Evaluation

All tablets underwent a thorough evaluation to assess several key characteristics, including general appearance, thickness, hardness, physical properties, mechanical strength, and drug release allpost compression parameters represented in Tables 5 and 6[29-30].

2.3.1.1 Appearance

The tablets were examined visually for their shape, colour, and texture.

2.3.1.2 Thickness

Measurements of tablet thickness and diameter were obtained using Vernier calipers, with average values calculated from three separate tests for accuracy.

2.3.1.3 Hardness

The hardness of the tablets was assessed using a Monsanto hardness tester, with results expressed in kg/cm^2. Each tablet was subjected to three individual tests to ensure reliability[31-33].

2.3.2 Friability

Friction and shocks may chip, cap, or shatter tablets; therefore, the test assessed their impact. Tablet friability was tested using Roche friabilator. The friabilator was run for 100 rotations with 10 correctly weighed pills. Tablets were cleaned and weighed[34].

$$\%F = \left(W_0 - \frac{w}{} W_0 \right) \times 100 \quad \text{Equation (6)}$$

Where, W_0 and W are the weight of the tablets before after the test respectively. The test was done in triplicate. The tablets that loose less than 1% weight were considered to be compliant.

2.3.3 Weight Variation

To evaluate weight variability, a Shimadzu digital analytical balance was employed to measure the mass of 20 tablets. The system calculated the mean weight of the tablets, and the individual weights were subsequently compared to this average to assess deviations[35]. The limits for weight uniformity were represented in Table 3.

$$\%Deviation = \frac{Individual\ weight - Average\ weight}{Average\ weight} \times 100 \quad \text{Equation (7)}$$

2.3.4 Drug Content

Two weighed tablets were pulverized in a glass mortar. A 100 ml volumetric flask contained 20 mg famotidine

Table 3. Limits for weight uniformity

Average Weight	%Difference
≤130mg	±10
>130 mg but < 324mg	±7.5
≥324mg	±5

dissolved in 5 ml methanol, shaken for 10 min. The sample was diluted with 0.1N HCl to 100 ml. The filtered solution's drug content was measured at 266 nm using a UV-spectrophotometer, with three tests performed to calculate mean values[36,37].

2.3.5 Swelling Index

Swelling occurs when tablet matrices absorb fluids, increasing weight and volume. Tablets measured swelling as % weight gain. One tablet was weighed and put in a 200 ml 0.1 N HCl beaker for each formulation batch. After each interval, the pill was withdrawn from beaker and weighed up to 12 h[38-40]. Swelling index was computed using Equation 9.

$$\%Swelling\ Index = (Wt - Wo)/Wo * 100 \quad \text{Equation (8)}$$

Where, Wt = Weight of tablet at time t, Wo = Weight of tablet before placing in the beaker.

2.3.6 Floating Buoyancy Lag Time and Total Floating Time

The Floating Lag Time (FLT), Buoyancy Lag Time (BLT), is the time taken for a tablet to rise to the surface of a medium. The Total Floating Time (TFT) is how long the tablet stays on the surface. This study examined tablet buoyancy in 900 ml of 0.1 N hydrochloric acid (HCl) at pH 1.2, using a USP type II dissolution device at 37° C ± 0.5° C, with the floating duration visually monitored[41-44].

2.3.7 In-vitro Drug Release Studies

The matrix tablet medication release pattern was determined by *in-vitro* dissolving research. Famotidine gastro-retentive matrix tablets were dissolved using 8-station USP Type II dissolving test equipment. Dissolution tests were conducted in 900 ml 0.1 N HCl at 37 ± 0.5° C. Paddle speed was 100 rpm. Samples were taken every 1 h. An equivalent amount of new medium replaced a 5 ml sample aliquot at each time interval. The UV spectrophotometer analysed appropriately diluted samples at 266nm[45,46]. We computed drug release from each formulation using the mean of three experiments.

2.3.8 Kinetic Study

To analyse the release mechanism, several models were examined:

$$\text{Zero order: } Qt = Q_0 + K_0 t \quad \text{Equation (9)}$$

The amount of drug released at time t (Qt) is constant, determined by the apparent dissolving rate constant (Ko) and the original concentration (Qo), indicative of a steady release rate.

$$\text{First order: } InQt = InQo + K_1 t \quad \text{Equation (10)}$$

The release rate is proportional to the amount remaining in the dosage form, defined by the first order release constant (K_1).

$$Higuchi:\ Qt = K_H \sqrt{t} \quad \text{Equation (11)}$$

The drug release is described by the Higuchi release rate constant (KH), which is a common method for pharmaceutical materials.

$$Korsmeyer\ Peppas: \frac{Qt}{Q\infty} = K_k t^n \quad \text{Equation (12)}$$

Kk is a constant reflecting the drug dosage form's shape and structure, while n is the release exponent indicating the drug release type. For n values: 0.45 indicates Fickian (Case I) release, >0.45 and <0.89 indicates non-Fickian (Anomalous) release, 0.89 indicates Case II (Zero order) release, and >0.89 signifies super Case II release. Case II transport involves polymer breakdown due to chain relaxation, while Case III transport features simultaneous diffusion and dissolution-controlled release[47-49].

2.3.9 FTIR

FTIR analysis was performed on the pure medication and selected formulations (F4, F6, F9, and F12) to determine excipient compatibility. Samples were produced on KBr-press. Samples were scanned from 4000-400cm^{-1} using Fourier transformer infrared spectrophotometer[50-53].

2.3.10 Differential Scanning Calorimetry

A Shimadzu DSC-60 (Kyoto, Japan) was used for differential scanning Calorimetry. Pure medication and optimized gastro-retentive matrix tablet famotidine F4 DSC Thermogram were obtained. Blank and sample DSC aluminium cells were utilized. Using 2-3 mg sample for analysis. Thermogram was recorded from 20° C to 420° C at 20° C/min under nitrogen purge at 20ml/min[54].

2.3.11 Stability Studies

ICH recommended stability studies assessed medication and formulation stability. The optimized formulation F4 was stored in an aluminium pack at 25±2°C/60±5%RH and 40±2°C/75±5% RH for three months in the stability chamber. Drug content, floating or buoyancy test, and *in-vitro* dissolution rate were measured after three months of storage[55-58].

3. Results

3.1 Derived Properties of Prepared Formulations

All the micromeritic properties results are represented in table 4. The prepared formulations angle repose values in a range of 23°.69-29°.16, compressibility index values in a range of 4.44-14.28 and Hausners ratio values in a range of 1.04-1.28. All the prepared formulations showing excellent flow properties.

3.2 Post Compression Parameters for the Prepared Formulations

Post compression parameters for the prepared formulations represented in Table 5 all the values are within the limits as per IP 96. The thickness values are in a range of 4.1-4.5, hardness values in a range of 3.7-4.2, all the prepared formulations showing less than 1% friability and % weight variation also in a range of 1.54-3.48. Post compression evaluations like drug content for prepared formulations in a range of 19.6-19.9 and % swelling index were high (85.59) in F12 formulation represented in Table 6. Xanthan gum had the highest swelling index. For the different polymers, the order of swelling was Xanthan gum>Pectin>Tamarind seed powder >Guar gum.

3.3 Buoyancy Lag-time and Total Floating Time for the Prepared Formulations

Buoyancy lag-time for the prepared formulations in a range of 4-25 sec and total floating time is greater than equal to 12 hours for all the prepared formulations represented in Table 7. At a dose of 5% sodium bicarbonate, the buoyancy lag time was always less than 60 seconds for all formulations.

3.4 *In-vitro* Release Profiles of Prepared Formulations

All the prepared formulations F1-F15 tested for drug release upto 12 hours and shown in Figure 2.

Table 4. Micromeritic properties

Formulation	AR*(θ)	BD*(g/cm^3)	TD*(g/cm^3)	CI*(%)	HR*
Pure Drug	26.40 ± 0.80	0.33 ± 0.10	0.36 ± 0.56	8.33±0.04	1.09 ± 0.9
F1	29.16 ± 0.07	0.36 ± 0.12	0.39 ± 0.11	7.69 ± 0.08	1.08 ± 0.5
F2	25.79 ± 0.07	0.42 ± 0.11	0.46 ± 0.07	8.69 ± 0.06	1.09 ± 0.4
F3	27.19 ± 0.08	0.45 ± 0.92	0.48 ± 0.09	6.25 ± 0.04	1.06 ± 0.6
F4	25.13 ± 0.06	0.42 ± 0.14	0.45 ± 0.06	6.66 ± 0.06	1.07 ± 0.8
F5	28.71 ± 0.05	0.42 ± 0.11	0.50 ± 0.04	7.55 ± 0.07	1.19 ± 0.6
F6	27.61 ± 0.04	0.35 ± 0.08	0.45 ± 0.08	12.22 ± 0.03	1.28 ± 0.4
F7	28.42 ± 0.09	0.42 ± 0.15	0.48 ± 0.12	12.55 ± 0.06	1.14 ± 0.9
F8	24.14 ± 0.010	0.36 ± 0.11	0.42 ± 0.13	14.28 ± 0.07	1.16 ± 0.7
F9	25.78 ± 0.012	0.45 ± 0.13	0.48 ± 0.14	6.25 ± 0.08	1.06 ± 0.8
F10	23.69 ± 0.013	0.35 ± 0.16	0.38 ± 0.12	7.89 ± 0.011	1.08 ± 0.4
F11	29.09 ± 0.011	0.43 ± 0.08	0.45 ± 0.06	4.44 ± 0.013	1.04 ± 0.1
F12	26.09 ± 0.014	0.34 ± 0.09	0.36 ± 0.13	5.55 ± 0.014	1.05 ± 0.9
F13	21.63 ± 0.015	0.36 ± 0.12	0.43 ± 0.14	13.27 ± 0.015	1.19 ± 0.14
F14	26.64 ± 0.014	0.35± 0.14	0.46± 0.15	8.36 ± 0.013	1.22 ± 0.11
F15	25.60± 0.016	0.33 ± 0.15	0.39 ± 0.013	10.6 ± 0.015	1.18 ± 0.13

*Mean±SD

Table 5. Post compression evaluations

F. Code	Thickness (mm)** [n=10]	Diameter (mm)** [n=10]	Hardness Test (kg/cm^2)* [n=5]	Friability (%)** [n=10]	Weight Variation (%)*** [n=20]
F1	4.1 ± 0.33	10 ± 0.18	3.9 ± 0.22	0.26 ± 0.21	3.33 ± 0.12
F2	4.2 ± 0.31	10 ± 0.11	4.0 ± 0.15	0.42 ± 0.27	2.99 ± 0.17
F3	4.3 ± 0.22	10 ± 0.13	4.0 ± 0.12	0.15 ± 0.31	2.87 ± 0.13
F4	4.3 ± 0.22	10 ± 0.20	4.0 ± 0.18	0.20 ± 0.12	2.55 ± 0.44
F5	4.4 ± 0.14	10 ± 0.16	3.8 ± 0.22	0.42 ± 0.22	3.33 ± 0.48
F6	4.5 ± 0.25	10 ± 0.15	4.0 ± 0.05	0.25 ± 0.16	2.37 ± 0.53
F7	4.3 ± 0.29	10 ± 0.12	4.0 ± 0.17	0.06 ± 0.34	2.12 ± 0.31
F8	4.2 ± 0.12	10 ± 0.14	4.2 ± 0.19	0.42 ± 0.13	3.13 ± 0.28
F9	4.4 ± 0.32	10 ± 0.25	4.0 ± 0.17	0.20 ± 0.34	2.50 ± 0.24
F10	4.1 ± 0.13	10 ± 0.12	3.7 ± 0.13	0.66 ± 0.23	3.65 ± 0.12
F11	4.2 ± 0.21	10 ± 0.11	4.0 ± 0.13	0.33 ± 0.32	2.99 ± 0.15
F12	4.4 ± 0.24	10 ± 0.13	4.0 ± 0.12	0.20 ± 0.14	2.75 ± 0.18
F13	4.4 ± 0.23	10 ± 0.11	4.0 ± 0.13	0.20 ± 0.12	3.48 ± 0.16
F14	4.2 ± 0.33	10 ± 0.14	4.1 ± 0.12	0.48 ± 0.22	1.54 ± 0.12
F15	4.3 ± 0.31	10 ± 0.15	4.0 ± 0.14	0.20 ± 0.43	2.50 ± 0.22

*Mean±SD

Table 6. Post compression evaluation

F. Code	Drug Content (mg)*	Swelling Index*(%)
F1	19.8±0.36	78.12 ± 0.61
F2	19.7±0.23	79.98 ± 0.52
F3	19.9±0.25	82.65 ± 0.76
F4	19.6±0.11	77.72 ± 0.23
F5	19.7±0.41	79.45 ± 0.43
F6	19.8±0.24	81.23 ± 0.67
F7	19.6±0.26	71.39 ± 0.76
F8	19.7±0.22	75.43 ± 0.13
F9	19.7±0.28	77.59 ± 0.15
F10	19.8±0.23	78.71 ± 0.98
F11	19.6±0.25	81.62 ± 0.67
F12	19.9±0.22	85.59 ± 0.68
F13	19.7±0.32	75.41 ± 0.86
F14	19.8±0.15	76.78 ± 0.54
F15	19.7±0.18	74.65 ± 0.56

*Mean± SD

Table 7. Buoyancy lag-time and total floating time

F. Code	Buoyancy Lag Time (sec)*	Total Floating Time (h)*
F1	16±0.5	≥12
F2	13±0.4	≥12
F3	5±0.6	≥12
F4	8±0.9	≥12
F5	6±0.8	≥12
F6	11±0.5	≥12
F7	10±0.3	≥12
F8	12±0.6	≥12
F9	11±0.5	≥12
F10	20±0.2	≥12
F11	18±0.8	≥12
F12	25±0.6	≥12
F13	7±0.7	≥12
F14	4±0.3	≥12
F15	12±0.5	≥12

*Average of 3 determinations

Gastro-retentive matrix tablet F4, which was made with xanthan gum, showed controlled drug release of about 97.00% over 12 hours and was chosen as the best tablet. The type of polymer used affected the drug release from famotidine pills in a lab setting. The largest release was seen with Xanthan gum, while the lowest release was seen with tamarind seed powder. The improved gastro-retentive matrix tablet F4 had better controlled

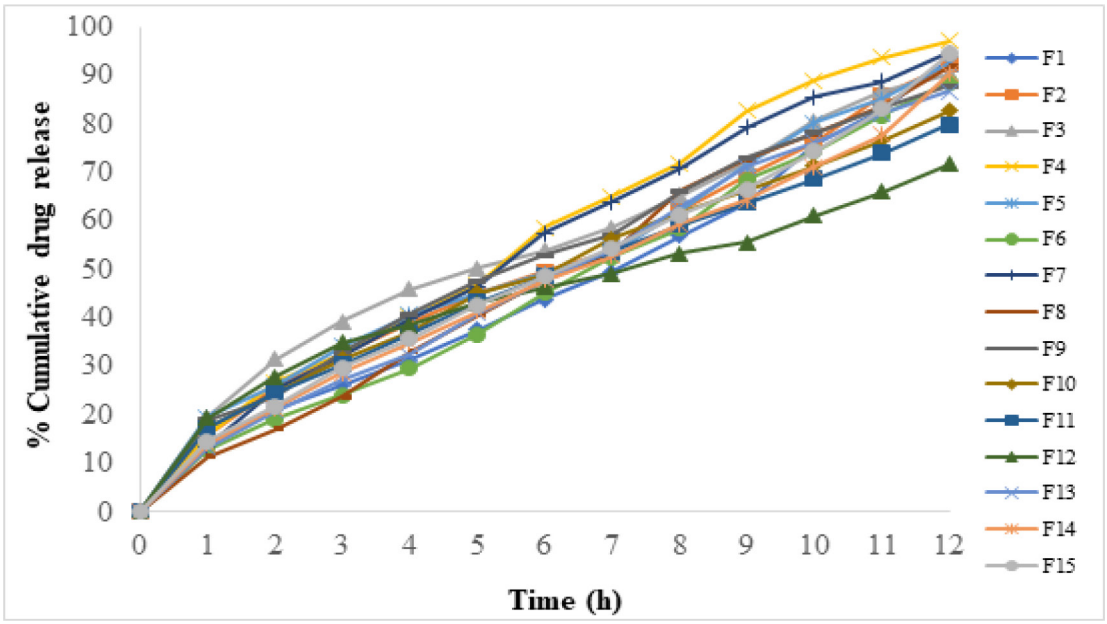


Figure 2. *In-vitro* release profile (F1 to F15).

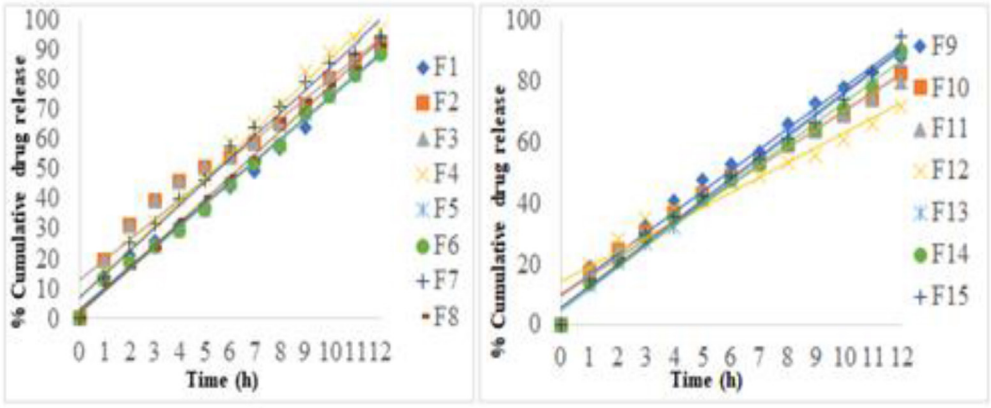


Figure 3. Zero order plots of gastro-retentive matrix tablets of famotidine (F1-F8) & (F9-F15)

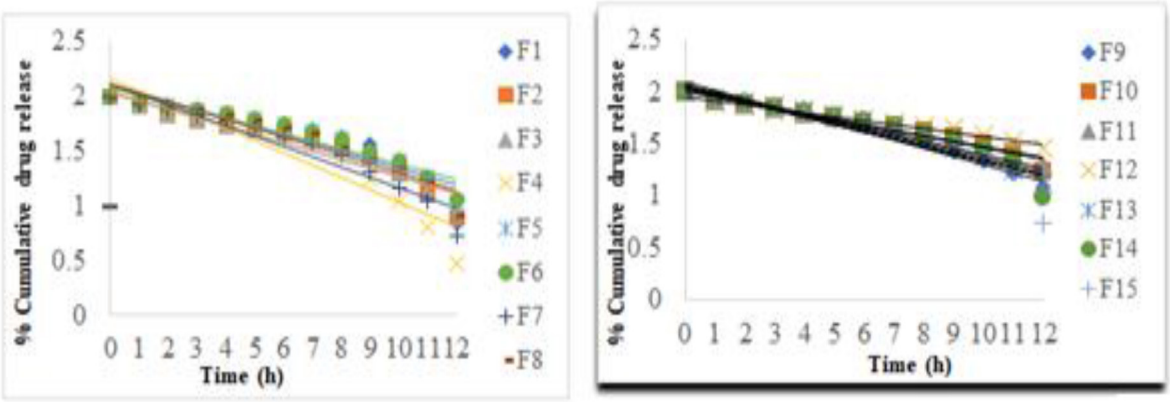


Figure 4. First order plots of gastro-retentive matrix tablets of famotidine (F1-F8) & (F9-F15)

drug release than the commercial product (film-coated tablet FAMOCID-20 by Sun Pharma - Goa). It released 97.00% over 12 hours, while the commercial product released 99.97% in 12 minutes.

3.5 Kinetic Profile of Famotidine Gastro-retentive Matrix Tablets

To analyse the drug release mechanism, several models like zero, first, higuchi and korsmeyer peppas regression coefficient and diffusion constant were determined and graphs were represented in Figure 3-6.

3.6 Drug Excipients Compatibility Studies

FTIR analysis was performed on the pure medication and selected formulations (F4, F6, F9, and F12) to determine excipient compatibility.

3.7 DSC

The thermal behaviour of pure famotidine and optimized formulation F4 represented in Figure 7 and 8.

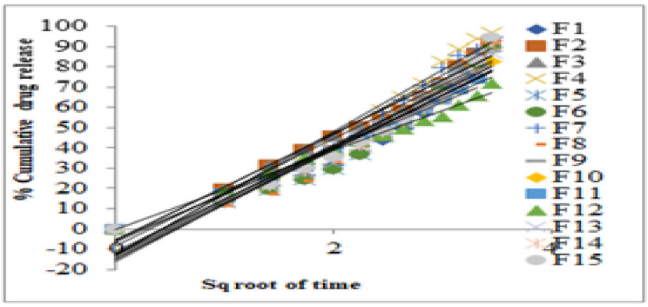


Figure 5. Higuchi plots of gastro-retentive matrix tablets of famotidine (F1-F15)

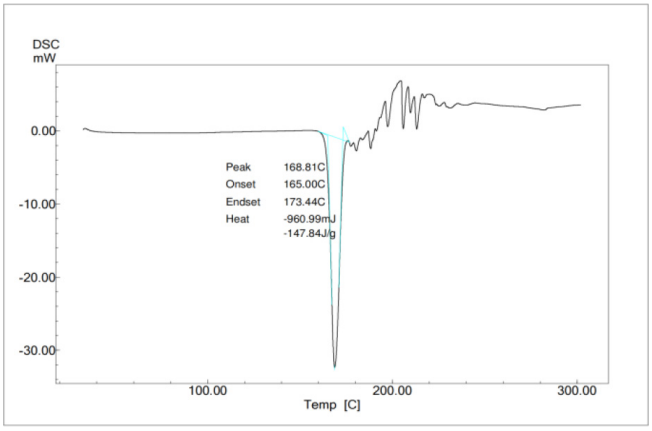


Figure 7. DSC thermogram of famotidine.

3.8 Stability Studies

The optimized formulation F4 shows good stability condition for a period of 3 months at different temperature and humidity conditions shown the data in Table 8.

4. Discussion

Pre-formulation studies on the drug famotidine align well with the established literature limits. Natural polymers, including Guar gum, Xanthan gum, Pectin, and Tamarind seed powder, exhibited favourable outcomes as rate-controlling polymers. Pre-compressional studies revealed favourable micromeritic properties of the powder blends. The adopted method consistently produced uniform and reproducible gastro-retentive tablets of famotidine utilizing all the selected natural polymers. Famotidine gastro-retentive matrix tablets were successfully developed through the direct compression method. The prepared

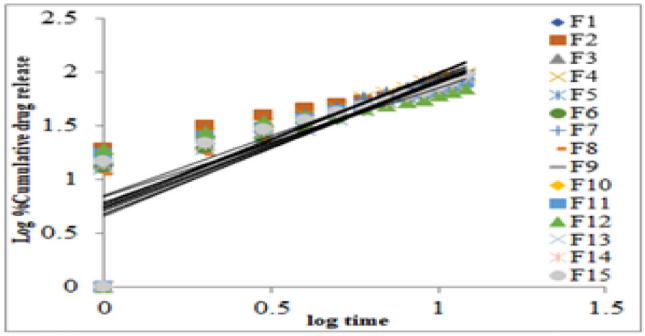


Figure 6. Korsmeyer-Peppas plots of gastro-retentive matrix tablets of famotidine (F1-F15)

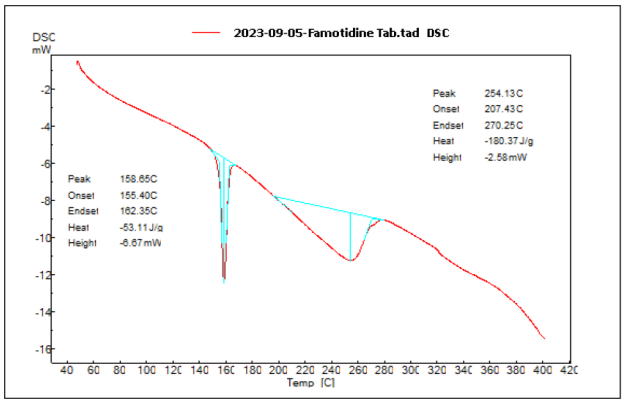


Figure 8. DSC thermogram of optimized F4 (Xanthan gum) famotidine GR matrix tablet.

Table 8. Optimized GR matrix tablet of Famotidine (F4) after a period of three months

Time (h)	Fresh F4*	F4* at 25±2 ^{0}C/ 60±5%RH	F4* at 40±2 ^{0}C/ 75±5%RH
0	0.000	0.000	0.000
1	15.717	14.616	13.157
2	26.705	24.810	23.605
3	32.587	31.520	30.487
4	40.272	38.270	37.172
5	46.802	45.801	44.702
6	58.650	57.646	56.550
7	65.037	64.034	63.137
8	71.892	70.792	69.792
9	82.744	81.7644	80.644
10	88.959	87.859	86.859
11	93.651	92.650	91.551
12	97.004	96.204	95.104

*Average of three determinations.

formulations angle repose values in a range of 23°.69-29°.16, compressibility index values in a range of 4.44-14.28 and Hausners ratio values in a range of 1.04-1.28. All the prepared formulations showing excellent flow properties.

The thickness values are in a range of 4.1-4.5, hardness values in a range of 3.7-4.2, all the prepared formulations showing less than 1% friability and % weight variation also in a range of 1.54-3.48. Post compression evaluations like drug content for prepared formulations in a range of 19.6-19.9 and % swelling index were high (85.59) in F12 formulation.

Xanthan gum had the highest swelling index. For the different polymers, the order of swelling was Xanthan gum>Pectin>Tamarind seed powder >Guar gum. At a dose of 5% sodium bicarbonate, the buoyancy lag time was always less than 60 seconds for all formulas. Gastro-retentive matrix tablet F4, which was made with xanthan gum, showed controlled drug release of about 97.00% over 12 hours and was chosen as the best tablet. The type of polymer used affected the drug release from famotidine pills in a lab setting. The largest release was seen with Xanthan gum, while the lowest release was seen with tamarind seed powder. The improved gastro-retentive matrix tablet F4 had better controlled drug release than the commercial product (film-coated tablet FAMOCID-20 by Sun Pharma - Goa). It released 97.00% over 12 hours, while the commercial product released 99.97% in 12 minutes.

5. Conclusion

The drug release process was administered by diffusion-controlled zero-order kinetics. The medication and the polymers utilized did not interact chemically, according to FT-IR and DSC analyses. During the stability period, the chosen gastro-retentive matrix tablet F4 showed stability in terms of drug content, weight fluctuation, friability, and *in-vitro* release profiles. The direct compression technique and natural polymers were used to successfully manufacture famotidine gastro-retentive matrix tablets with better dissolving profiles. These findings are encouraging and call for more in-vivo testing utilizing suitable animals.

6. Author Contribution

Conceptualization and study design: Janga Ramesh Babu; Preparation and evaluation: Janga Ramesh Babu, S. Vidyadhara and A. Sambasivarao; Writing and drafting: Janga Ramesh Babu, S. Vidyadhara, A. Sambasivarao and M. Niranjan Babu. All authors have read and agreed to the published version of the manuscript.

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