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Formulation and Evaluation of Famotidine Gastroretentive Floating Tablet by Using Biopolymer

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ABSTRACT

HPMC K4M, HPMC K15M, and HPMC K100M polymers are used in this study to make floating tablets of famotidine hydrochloride. Drug Delivery systems that are floating in the stomach have a lower bulk density than gastric fluids, therefore they stay buoyant in the stomach for a lengthy period of time without impacting gastric emptying rate. In the treatment of gastroesophageal reflex disease (GERD) and peptic ulcer (PUD). Famotidine is a histamine H2 receptor antagonist (GERD). Famotidine is an excellent option for a floating drug delivery system because of its short half-life, brief time in the stomach, and repeated doses. Melt-granulation technique was used to make famotidine floating tablets using HPMC K4M, HPMC K15M, and HPMC K100M. In vitro buoyancy, drug polymer compatibility (IR Research), weight fluctuation, hardness, friability, thickness, drug content and invitro dissolution experiments were all performed on the floating tablets. Using in vitro buoyancy and dissolvability experiments, we were able to establish that the micromeritic characteristic were excellent. HPMC K100M-based formulation F4 has an excellent in vitro buoyancy lag time and floating time, and in vitro dissolution investigations demonstrate a 96.78 percent release for 12 hours. As a result of the findings of this research, it can be concluded that famotidine floating tablets provide the potential for longest- term drug delivery and a consequent reduction in dosage frequency.

Keywords: Gastroretentive floating tablet, Famotidine, Formulation and Evaluation, Biopolymer

INTRODUCTION

The term "gastro retentive medication delivery system" refers to dosage forms that may kept in the stomach (GRDDS). When a medicine has an absorption window, a continuous release of the drug before it reaches the absorption site improves the controlled delivery [1].

Because of their simplicity of administration, patient compliance, and formulation flexibility, CR dosageforms (DFs) have been created throughout the last three decades [2]. Because of the varying rates of stomach emptying and motility, this method faces a number of physiological challenges, including a lack of capacity to restrict and precisely place the controlled drug delivery system in the targeted GIT area [3]. Because the stomach and upper intestine have such a short gastric emptying time (GET), drugs might be released incompletely from the drug delivery system, reducing their effectiveness in the body [4]. "This can happen in humans because of the GET, which is typically 2-3 hours in the main absorption zone. A range of critical medications, including those with a small absorption window in the GI tract or with stability issues, may benefit from precise control over drug delivery system (DDS) placement [5].

Based on these factors, a novel gastro-retentive oral controlled-release dosage form was created. For example, a DF such as this might prolong the duration the medicine spends in the stomach after consumption, facilitating its transport to the intestines and, ultimately, the bloodstream. When a medicine is administered in a gastro retentive dose form, it may remain in the digestive tract for an extended period of time [6]. Increased bioavailability, less waste formation, and improved solubilization of medications that are less soluble in a high pH environment are all benefits of prolonged stomach retention. Medications may be delivered straight to the stomach or small intestine using this method [7].

MATERIALS AND METHODS

Famotidine drug was purchased from molecules India Pvt. Ltd. Other Chemicals such as HPMC K4M, HPMC K15M, HPMC K100M were procured from Sooriyan pharmaceuticals., Chennai. Carbopol 934 was obtained from Fine Chem, industries. Bees wax was purchased from Fine Chem, industries. Pectin was purchased from Yarrow Chem, Maharashtra. Other chemical reagents Sodium bicarbonate, Talc, Lactose, and Magnesium Stearate were obtained from Fine Chem, industries, Standard chemicals and Advance labs respectively.

Preparation of Floating tablet.

All of the materials were weighed precisely. Famotidine, HPMC K4, HPMC K15, andHPMC K100 were all sieved using a No. 80 mesh screen. White bees wax was melted in a china dish." To the molten material, add the medicine Famotidine and stir until completely dissolved. Next, combine HPMC polymer, sodium bicarbonate, and lactose in a bowl [8]. After waiting for the material to reach room temperature, china dish was scraped off on it. In order to separate the incoherent particles, sieve number 20 was used. Magnesium stearate and talc were added to the resultant granules. The lubricated granules were compressed using a typical concave punch in a 10-station. rotating Proton small press machine, ensuring that the desired tablet weight of 200 mg was maintained throughout the process. Friability, dissolving, and assay tests were performed after compression weight variationswere made Table 1.

Table 1: Formulation of Famotidine tablets

INGREDIENTS (in mg)	FORMULATION BATCHES							
	F1	F2	F3	F4	F5	F6	F7	F8
Famotidine	40	40	40	40	40	40	40	40
HPMC K4M	-	30	-	-	30	30	-	30
Pectin	-	-	30	-	30	-	30	30
HPMC K100M	-	-	-	30	-	30	30	30
NaHCO3	20	20	20	20	20	20	20	20
Bees wax	30	30	30	30	30	30	30	30
Lactose	98	68	68	68	38	38	38	8
Magnesium sterate	6	6	6	6	6	6	6	6
Talc	6	6	6	6	6	6	6	6
Average weight	200	200	200	200	200	200	200	200

EVALUATION OF FORMULATED TABLETS OF FAMOTIDINE"

The following list of official and informal criteria was used to evaluate all sustained-release tablet formulations.

1. Weight Variation

Each batch had twenty pills sampled at random and weighed separately. In order to determine the mean and standard deviation of tablet weight, twenty tablets were weighed.To pass the weight variation test, the batch must have no more than two tablets with weights that differ from the average weight by more than twice the percentage stated in a none [9].

"% deviation= tablet weight-average weight × 100

For tablets to be widely accepted by consumers and for there to be consistent quality amongst different tablets, thickness control is crucial. Digital Vernier calipers were used to measure to exacting tolerances. The tablet us thickness, which is directly proportional to its hardness, may serve as a primary regulating variable [10].

Digital Vernier calipers were used to measure the thickness of six tablets taken at randomfrom each batch.

2. Hardness

It is a priority to achieve optimal compactness for transportation, coating, and packing, as well as a desirable form and layout [11]. A hardness tester was used to get accurate results. Six pills from each batch were put through the Pfizer hardness testing [12]. The amount of force necessary to crack the tablet is measured in kilograms per square centimeter (Kg/cm2).

Observation

The pills in each batch had a hardness that varied between 6 and 16Kg/cm2.

3. Friability

The Roche friabilator was used to crush 20 tablets at a time at 25 revolutions per minute for 4 minutes. After the revolution, the tablets were reweighed and their new weights were recorded. The following formula was used to determine the degree of friability [13]:

$$\%F = \{1-(W_t /W)\} \times 100$$

"Where, %F = friability in percentage

W = initial weight of tablets after revolution"

Observation

All batches of the formulation were tested and determined to be within the IP-mandated range of 0.1 to 0.6.

4. Buoyancy Lag Time

It is measured to evaluate how long it takes the dosage form to rise to the surface of the dissolving media. All of these may be assessed in one go during a dissolution test [14].

The findings were tabulated for ease of reference.

5. Floating Time

The buoyancy test is often done in 37 degrees Celsius of Simulated Gastric Fluid (SGF). The floating time is the period of time during which the dose form remains afloat on the dissolving medium [15].

6. Dissolution study

Preparation of buffer

Fill a 1000 ml volumetric flask with distilled water until the content reads 1000 ml, thenadd 8.5 ml of HCL [16].

"Requirements

Medium: 0.1N HCl Volume: 900 ml Apparatus: USP II (paddle) RPM: 100Time: upto 12 hrs Temperature: 370 c + 0.50c λmax : 266 nm"

The disintegration vessels contained 900 ml of 0.1 N HCl and were kept at 37 °C 0.5 °C; at the designated time, the vital measure of test was removed and replaced with a similar measure of 0.1 N HCl (to keep up with sink condition); the absorbance was then taken, and the level of delivery was determined [17].

"% purity = absorbance × 900 × dilution × 100 Slope × 1000 × label claim"

7. **Assay**

Twenty tablets of famotidine, corresponding to 20 milligrams, should be crushed and weighed before being dissolved in 0.1N HCl and the remaining amount brought up to 100 milliliters. Take 10 ml out of it, and add 0.1 N HCl to get the volume up to 100 ml. Take an absorbance reading at 266 nm with a UV spectrophotometer [18].

8. Kinetics of drug release

The in vitro disintegration profiles of all four groups were then each fitted to one of four different models-the Zero request model, the first request model, the Higuchi model, and the Koresmeyer-Peppas model-to determine the motor displaying of drug discharge. Using a regression analysis, we were able to derive R2 values for the linear trends shown in the preceding graph [19].

"Zero-order kinetic model – Cumulative % drug released Vs time.

First- order kinetic model – log cumulative % drug remaining Vs time.

Higuchi model - Cumulative % drug released Vs square root of time. Korsmeyer-Peppas model - log cumulative % drug released Vs log time.

Zero-order kinetics

Zero order release would be predicted by the following equation:

$A_t = A_o - K_o t$

A_t- Drug release at time 't' A_o- Initial drug concentration

K_o- Zero-order rate constant (hr^{-1})

When the data plotted as cumulative % drug release Vs time and the plot is linear, then thedata obeys zero-order equal to Ko [20].

First order kinetics

First order release would be predicted by the following equation:

[Log C = log Co – Kt / 2.303]C- Amount of drug remained at time 't'

Co- Initial drug concentration

K- First-order rate constant (hr^{-1})

It can be shown that the release follows first order kinetics since a straight line is formed when plotting the data as the log cumulative percent remaining vs. time. Multiplying the slope values by 2.303 yields the constant K [21].

Higuchi's Model

By adapting the traditional diffusion equation proposed by Higuchi, we may be able to account for the diffusional release of pharmaceuticals from matrix devices.

"Q= [D€/t (2A-εCS) CSt] ½

Q- Amount of drug released at time 't'

D- Diffusion coefficient of the drug in the matrix A- Total amount of drug in unit volume of matrixCS- The solubility of drug in the matrix

€ - Porosity of the matrixt - Tortuosity

t- Time at which amount of drug released"

When plotting the total percentage of drug released against the square root of time, a straight line is formed, indicating that drug release is controlled by diffusion processes. Slope, or K, is given by its numerical value [22].

Korsmeyer – Peppas model

"Fitting the invitro release data to the well-known exponential equation (Korsmeyer – Peppas model), which is often used to characterize the drug release behavior from polymeric systems, allowed researchers to learn more about the mechanism of drug releasefrom the microspheres [23].

$M_t/M_\alpha = Ktn$

M_t/M_α - The fraction of drug released at time't'

K-Constant taking into account structural and geometrical aspects of the drug/polymer system

Mechanism-related N-diffusion exponent for drug release

If you plot the data as the log of the percentage of drug released vs the log of the time, youwill get a straight line with a slope equal to n, and you can calculate K by finding the point where the line crosses the y-axis [24].

The Korsmeyer-Peppas Equation and the Release Mechanism of Drugs / Paul J."

Table 1. Mechanism of drug release

S. No	n value	Drug release
1	0 –0.5	Fickian release
2	0.5 – 1.0	Non-Fickian release
3	>1.0	Class II transport

RESULT AND DISCUSSION

Evaluation of granules

Table 3. Showing results of angle of repose, bulk and tapped density, Carr'sindex, hausner ratio

Batchno.	Angle of repose (^{0})	Bulk density(gm/ml)	Tapped density(gm/ ml)	Carr's index(%)	Hausner ratio
F1	26 ° 32'	0.2891	0.3503	14.04	1.21
F2	24º 64'	0.2845	0.3394	15.68	1.22
F3	28º 59'	0.2924	0.3349	11.94	1.13
F4	26º12'	0.2875	0.3446	13.96	1.16
F5	23º 62'	0.2862	0.3420	15.13	1.19
F6	24º74'	0.2677	0.3214	13.92	1.15
F7	24 ° 77'	0.2743	0.3242	15.42	1.19
F8	26 ° 56'	0.2847	0.3177	10.38	1.11

The formulas F1-F8 have excellent flow, with an angle of repose between 230.62 and 280.59 degrees. The compressibility index ranged from 10.38 percent to 15.6

percent for formulations F1 through F8, showing that the mix had desirable flow properties for compression.

EVALUATION OF FAMOTIDINE TABLETS

The aforementioned pills conform to pharmacopoeial requirements, with a weight fluctuation of less than 5% (in the range of +1.23% to +3.09%). The tablets meet pharmacopoeial requirements for lack of friability [21], which are specified as being between 0.18 and 0.34 percent. The tablets have a content uniformity of between 99.37% and 100.38%, which is well within the acceptable limit set by the pharmacopoeia

Table 4. evaluation data of Floating Tablet.

Batch no.	Weight variation	Friability (%)	Content uniformity (%)
F1	456+ 1.52	0.22	98.65
F2	458±2.37	0.34	96.74
F3	470+ 1.87	0.56	97.34
F4	450+ 1.41	0.36	98.44
F5	480±1.86	0.17	100.38
F6	502±2.56	0.48	98.96
F7	510+2.35	0.39	94.47
F8	490±1.93	0.38	98.35

Thickness and hardness

The formulations' thicknesses were measured to be between 5.1 and 5.5 micrometers (mm) on average. The mechanical strength of the tablets was determined to be adequate, with a hardness inthe range of 6.2 to 7.5 kg/cm2.

Table 5. Evaluation data of hardness and Thickness.

Batch no.	Thickness (mm)	Hardness(kg/cm^2)
F1	5.2±0.021	6.4
F2	5.1±0.12	7.2
F3	5.3±0.21	6.54
F4	5.2±0.23	6.6
F5	5.2±0.14	6.7
F6	5.5±0.13	7.5
F7	5.5±0.16	7.8
F8	5.4±0.35	6.5

Drug-excipient compatibility studies

By analyzing the FT-IR spectra, we found that the drug's peaks did not shift, indicating that the drug did not interact with the polymers or the other excipients. These peaks are quite important in terms of how the medication is released.

Drug-excipient compatibility

Table 6. Compatibility data of drug excipient study.

Drug + Excipients	Initial	After 1 month at		Compatible
		40^0C/75%RH	60^0C	
Drug	White powder	No change	No change	Yes
Drug + HPMC K4 M	White powder	No change	No change	Yes
Drug + HPMC K15 M	White powder	No change	No change	Yes
Drug + HPMC K100 M	White powder	No change	No change	Yes

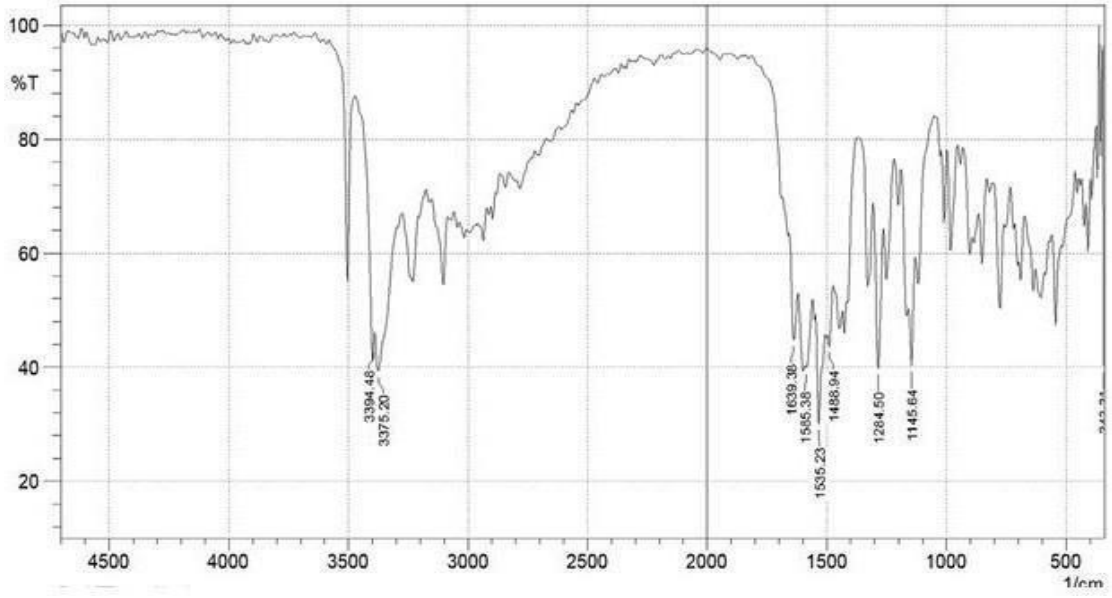

Figure 1. FTIR of Famotidine

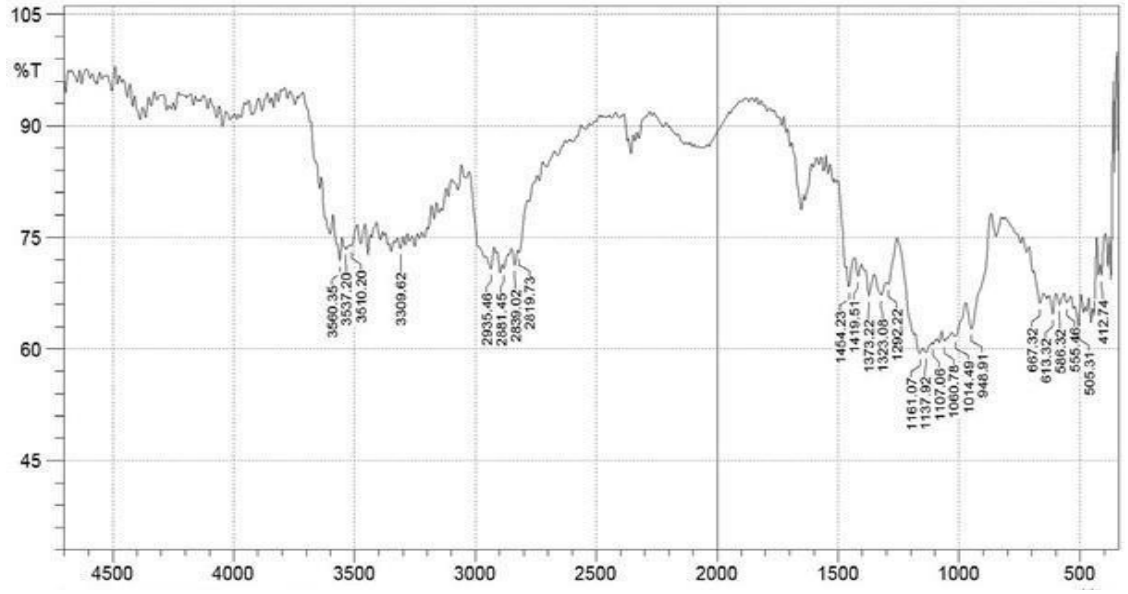

Figure 2. FTIR of HPMC

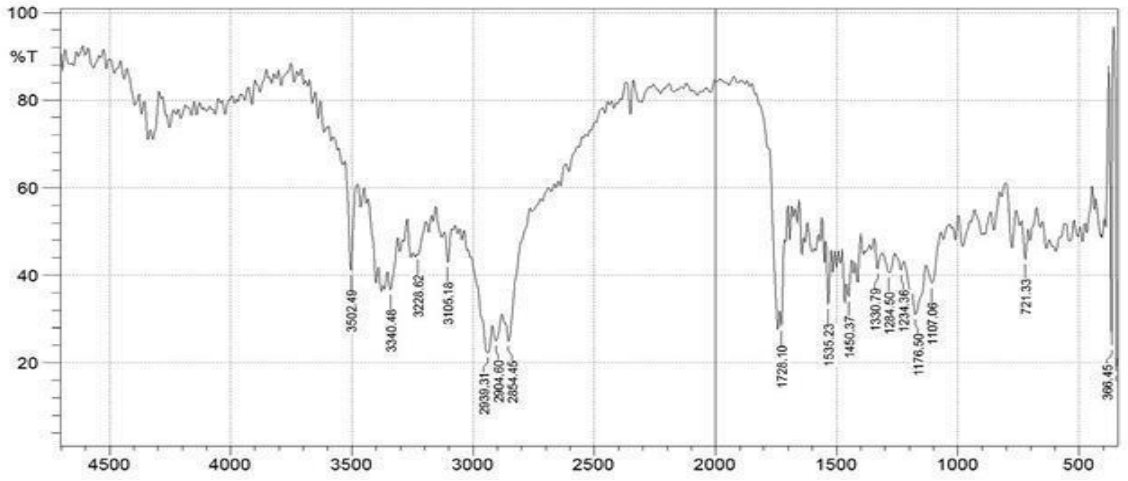

Figure 3. FTIR of Famotidine + excipients

Buoyancy Lag Time and Total Floating Time

According to the data, formulations F1, F4, F7, and F8 had excellent buoyancy, and all ofthe formulations tested floated for at least 12 hours.

Table 7. Showing buoyancy lag time and total floating time.

Batch no.	Buoyancy lag time	Total buoyancy time(hrs)
F1	614	14
F2	95	8
F3	90	7
F4	83	13
F5	174	10
F6	63	11
F7	54	15
F8	49	13

In-vitro release profile

Formulation F1 was selected as the optimal formulation because it achieved 84% release after 24 hours in an in-vitro dissolution assay.

Table 8. Drug release graph of Fomatidin floating tablet.

Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8
1	7.65	11.79	14.13	7.24	21.32	13.76	5.91	12.25
2	12.12	14.12	33.67	12.09	43.13	24.27	11.64	16.79
3	16.75	20.39	45.21	17.62	67.08	30.14	17.08	22.47
4	24.34	23.67	62.90	23.98	69.34	39.51	25.42	26.75
5	28.59	26.09	75.39	31.56	71.09	46.24	29.32	30.54
6	33.23	27.13	95.14	39.34	73.67	53.69	31.13	37.67
7	40.09	30.27	95.13	47.87	80.09	67.76	36.41	43.34
8	46.23	35.64	96.24	55.23	81.98	80.09	40.69	49.50
9	52.98	40.79	97.32	64.42	84.08	89.13	46.86	54.71
10	57.14	56.62	98.14	73.7	85.47	97.43	53.63	60.92
11	60.17	66.08	98.08	84.54	89.39	96.34	57.20	68.43
12	66.91	70.14	99.47	96.78	90.69	98.50	62.32	72.19

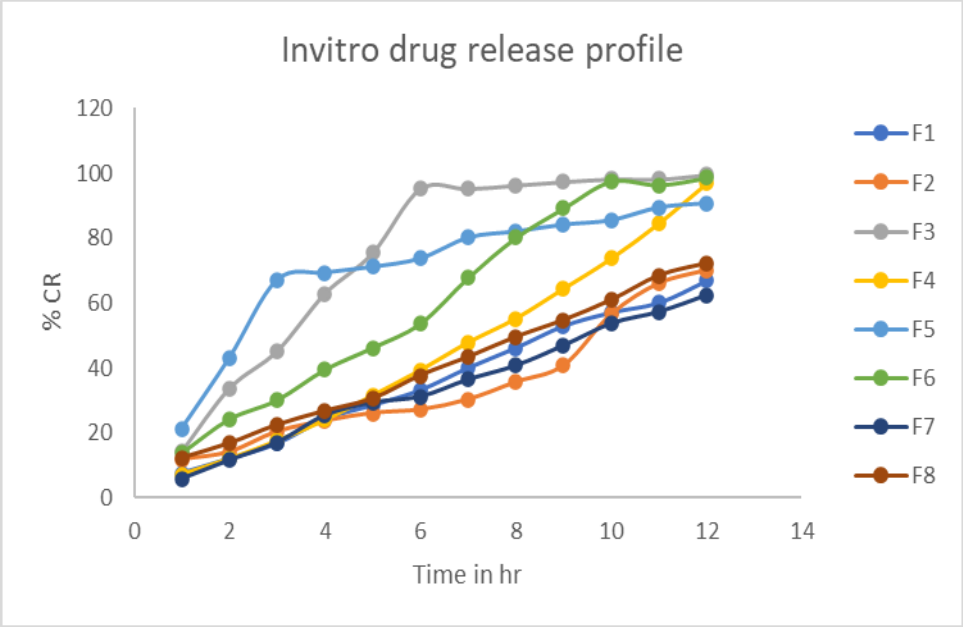

Figure 4. Showing in-vitro drug release profile for F1-F8 formulations

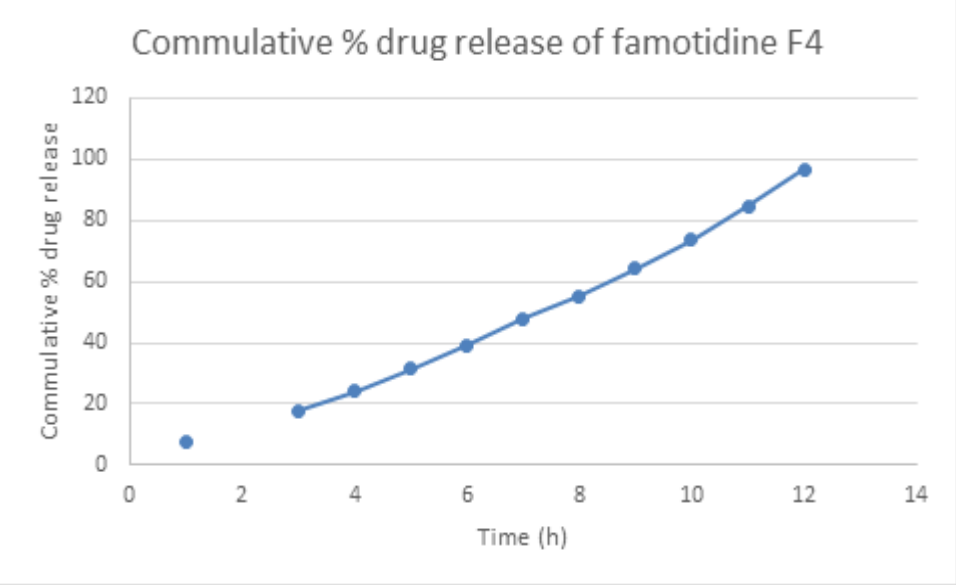

Figure 5. Showing in-vitro release profile of best formulation (F4)

DRUG RELEASE KINETICS

Drug release kinetics

Table 9. Drug release kinetics data.

Formulation	Regression coefficient (R^2) value			
	Zero-order	First order	Higuchi	Korssmeyer – Peppas (n value)
Famotidine tables	0.9955	0.7328	0.9684	0.84 (0.8274)

N value = 0.8274"

The values of the regression coefficients and the n values demonstrate that the drug release follows a non-Fickian distribution.

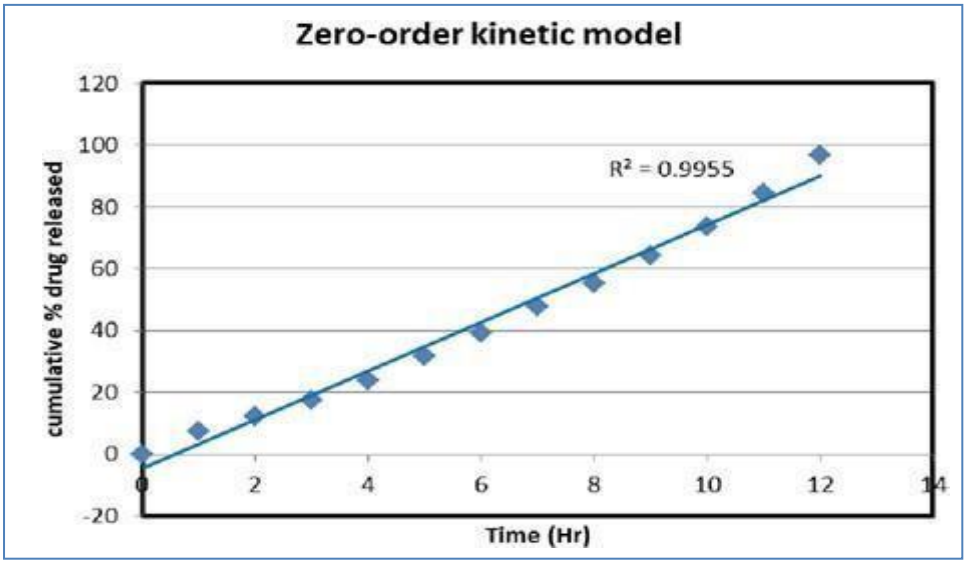

Figure 6. Zero Order Kinetic Model

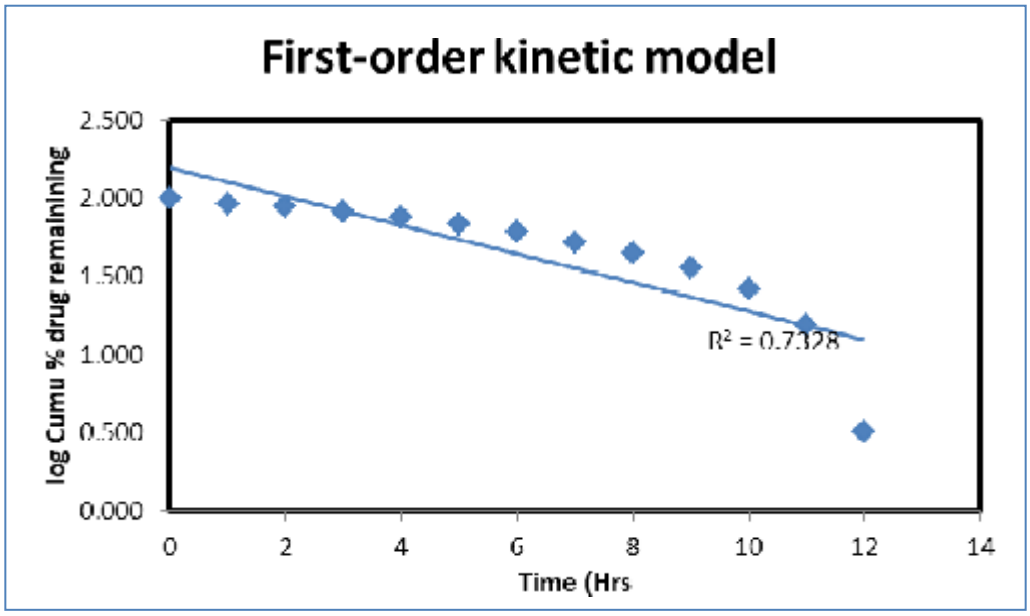

Figure 7. First Order Release Kinetics

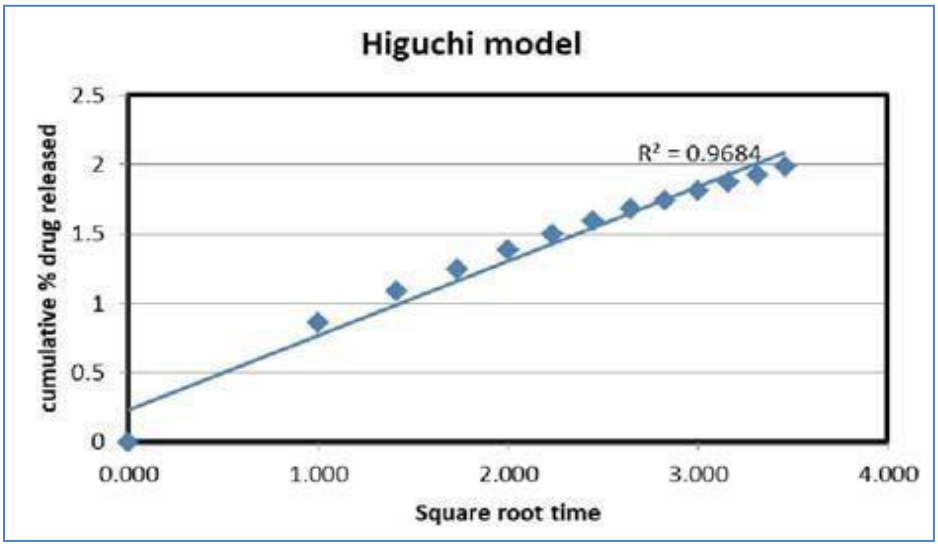

Figure 8. Higuchi model

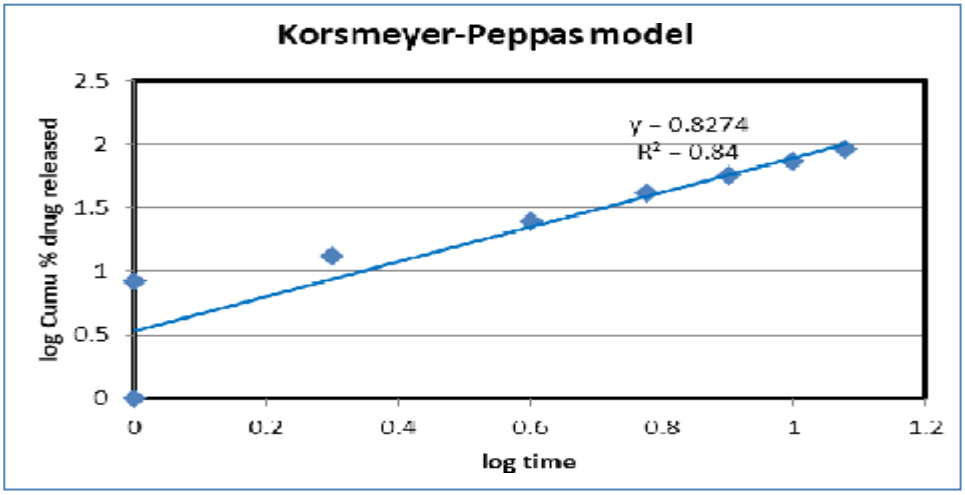

Figure 9. Korsemeyer Peppas

CONCLSUION

Famotidine tablet biopolymer formulation and assessment for gastroretentive drug administration is the focus of the current investigation. In order to keep the medicine in the stomach, this method of drug administration is recommended. To keep the medicine in the stomach, this formulation has a swelling feature that makes it impossible for the drug to be expelled from the stomach. Organoleptic characteristics, bulk density and tapped density, Hausner ratio, Carr's index, melting point, solubility, PH, were all examined as part of the Preformulation process in accordance with IP guidelines. Excipient compatibility investigations have shown that the medicine and polymers do not interact at all.

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