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Research Article

Formulation Development and Invitro Evaluation of Famotidine Gastroretentive Tablets

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Abstract:

The present study involves the formulation and evaluation of gastroretentive drug delivery of Famotidine tablets. This type of drug delivery helps to retain the drug in the stomach. The swelling property of the formulation helps to retain the drug in the stomach, by swelling to such an extent so that cannot pass out of the stomach. Preformulation studies which include Organoleptic properties, Bulk and Tapped densities, Carr‘s index, Hausner‘s ratio, Melting point, pH, Solubility, were carried out are as per IP specifications. Drug-excipient compatibility studies were performed which shows that there is no interaction between drug and polymers. Evaluation studies have been performed for tablets include friability, hardness, weight variation, content uniformity, buoyancy studies are as per IP specifications. Drug release studies have been performed by using 0.1N HCl for 12 hrs. These studies have shown that the formulation F4 gave better drug release upto 12 hrs. which is formulated with HPMC K100 M.

Introduction

Dosage forms that can be retained in the stomach are called gastro retentive drug delivery system (GRDDS). GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site. Control of placement of a drug delivery system (DDS) in a specific region of the GI tract offers advantages for a variety of important drugs characterized by a narrow absorption window in the GIT or drugs with a stabilityproblem. [(1)]

The need for gastro retentive dosage forms (GRDFs) has led to extensive efforts in both academia and industry towards the development of such drug delivery systems. These efforts resulted in GRDFs that were designed, in large part, based on the following approaches:

(a) Low density form of the DF that causes buoyancy in gastric fluid.

(b) High density DF that is retained in the bottom of the stomach.
(c) Bioadhesion to stomach mucosa.
(d) Slowed motility of the gastrointestinal tract by concomitant administration ofdrugs or Pharmaceutical excipients.
(e) Expansion by swelling or unfolding to a large size which limits emptying of the DF through the pyloric sphincter.(2)
Famotidine, is a histamine H2 receptor antagonist that inhibits stomach acid production. It is commonly used in the treatment of peptic ulcer disease and gastroesophageal reflux disease. The aim of the present study is to formulate and evaluate gastro retentive tablet of famotidine for the treatment of peptic ulcer, thus the action would be specifically in the stomach.(3)

Material and Methods

Famotidine was received as gift sample from Trojan Pharma, Baddi, India. Hydroxypropyl methylcellulose (HPMC K4M, HPMC K15M, HPMC K100M) was procured from local suppliers. PVP K30 was purchased from S.D fine chemicals, Mumbai. Sodium bicarbonate, Bees wax, Lactose, Magnesium state, Talc were purchased from CDH. Other solvents and chemicals used in the research were of LR grade. All the studies were carried in distilled water.

Methods

The composition of different formulation of ranitidine hydrochloride floating tablets is shown in Table 1. Famotidine and all other ingredients were weighed separately and passed through sieve no. 25. The active ingredient, HPMC K100LV, HPMC K15M, HPMC K100M, and 50% of the lubricants were mixed together. The mixture was then compacted in a slugging machine to form the compacts. The compacts were then milled and passed through sieve no. 18 followed by sieve no. 60. The particles that retained on sieve no. 60 were taken as granules and those passing through the sieve were fines. The fines were again compacted, milled and sieved through sieve no. 18 and 60. The cycle of compaction-milling- sieving was repeated until the granules and fines were obtained in the ratio of about 70:30. The granules and fines were then mixed together and the remaining ingredients except magnesium stearate were added to it and mixed. The remaining lubricant i.e. magnesium stearate was then added and mixed to the above mixture to form the final blend. The final blend was compressed into tablets.(4)

Table 1: Formulation of Famotidine tablets

Ingredients (in mg)	Formulation Batches							
	FF1	**FFF2**	**FF3**	**FF4**	**FF5**	**FF6**	**FF7**	**FF8**
Famotidine	40	40	40	40	40	40	40	40
HPMC K100LV	0	30	0	0	30	30	0	30
HPMC K15M	0	0	30	0	30	0	30	30
HPMC K100M	0	0	0	30	0	30	30	30
$NaHCO_3$	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

All the formulated sustained release tablets were evaluated for following official and unofficial parameters.

1. Weight Variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of twenty tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight by more than the percentage shown in a none deviate by more than twice the percentage shown.

Table 2: Weight variations Specification as per IP

Average weight of tablets(mg)	Maximum % difference allowed
Less than 80	10
80- 250	7.5
Above 250	5

2. Dimensions

Control of physical dimension of the tablets thickness is essential for consumer acceptance and to maintain tablet to tablet uniformity. The dimensional specifications were measured using digital Vernier calipers. The thickness of tablets is mostly related to the tablet hardness can be used as initial control parameter. Six tablets were randomly selected from each batch and their thickness was measured by using Digital Vernier caliper.[5]

3. Hardness

It is determined to get perfect compactness during shipping, coating, and packaging and to get proper shape and design. Hardness was measured by using hardness tester. (Pfizer hardness tester) for each batch six tablets were tested. The force required to break the tablet is recorded by the unit is Kg/cm^2.

4. Friability

Twenty tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25 rpm for every 4 minutes. After revolution the tablets were dedusted and weighed again. The percentage friability was measured using the formula,

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

Where, %F=friability in percentage W=initial weight of tablets after revolution [6]

5. Buoyancy Lag Time

It is determined in order to assess the time taken by the dosage form to float on the top of the dissolution medium, after it is placed in the medium. These parameters can be measured as a part of the dissolution test.The results were tabulated in table. [7]

6. Floating Time

Test for buoyancy is usually performed in SGF-Simulated Gastric Fluid maintained at 37^0C. The time for which the dosage form continuously floats on the dissolution media is termed as floating time. [8]

7. Dissolution study:

Preparation of buffer:

Measure 8.5 ml of HCL in a 1000 ml volumetric flask and make up the volume to 1000 ml using distilled water.

Requirements:

Perform the test on six tablets one tablet in each dissolution vessel containing 900 ml of 0.1 N HCL maintained at 37^0c $\pm 0.5^0$c. at specific time withdrawn required amount of sample and replace same amount of 0.1N HCL (maintain sink condition), then

absorbance was taken and calculate percentage release.

8. Assay:

Crush 20 tablets and weigh equivalent to 20 mg Famotidine and dissolved in 0.1NHcl and make up the volume to 100 ml. From that, withdraw 10 ml and diluted to 100 mlwith 0.1 N HCl. Read the absorbance at 266 nm in UV spectrophotometer. [9]

9. Kinetics of drug release

The invitro dissolution profile of all batches were fitted to Zero order, first order, Higuchi model and Koresmeyer-Peppas model to ascertain the kinetic modeling of drug release. Correlation coefficient (R^2) values were calculated for linear curves obtained by the regression analysis of the above plot. [10]

Result and Discussion

Organoleptic properties:

The tests were performed as per the procedure. The results were tabulated below.

Table 3: Organoleptic properties

Test	Specifications/limits	Observations
Colour	White to pale yellow	White powder
odour	Odourless	Odourless

The result complies as per specifications.

Angle of repose:

It was determined as per procedure. The results were tabulated below.

Table 4: Flow properties

Material	Angle of repose
Famotidine	27.140

The results show that the drug having poor flow.

Bulk density and tapped density:

It was determined as per procedure. The results were tabulated below.

Table 5: Bulk density and tapped density

Material	Bulk density(gm/ml)	Tapped density(gm/ml)
Famotidine	0.48	0.44

Powder compressibility:

It was determined as per procedure. The results were tabulated below.

Table 6: Powder compressibility

Material	Compressibility index	Hausner's ratio
Famotidine	11.27	1.44

Melting point:

It was determined as per procedure. The results were tabulated below.

Table 7: Melting point

Material	Melting point range	Result

Famotidine	163.5 ° C	163 0c

The result indicates that the Famotidine drug was pure one.

Solubility:

It was determined as per procedure. The results were tabulated below.

Table 8: Solubility

Material	Test	Specification	Observation
Famotidine	Solubility	Freely soluble in glacial acetic acid, slightly soluble in methanol, very slightly soluble in water, and practically insoluble in ethanol.	Complies

Drug-excipient compatibility studies:

The FT-IR peaks were observed that there is no change in the spectrum representing that there is no interaction between the drug and polymers and other excipients. These peaks play a vital role with respect to drug release. (11)

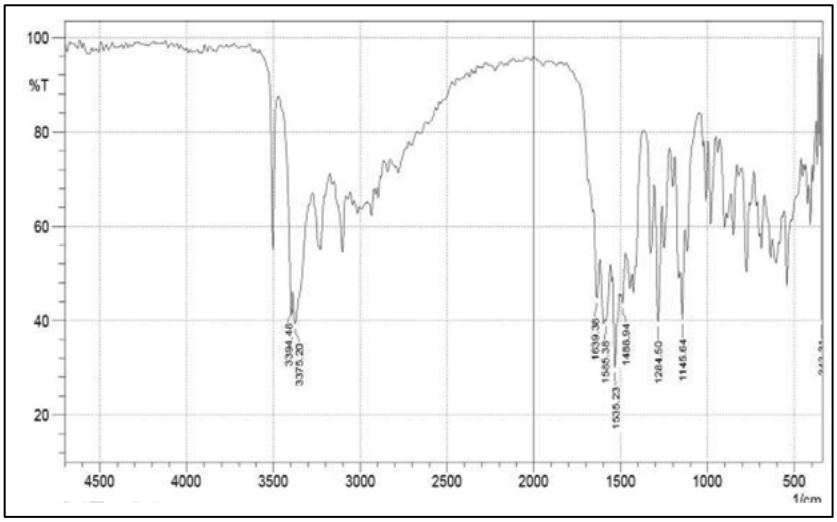

Figure 1: FTIR of Famotidine

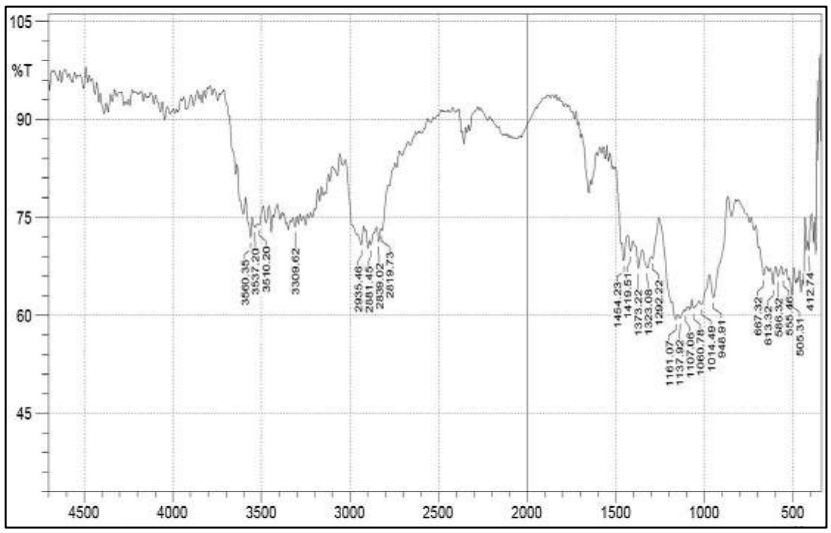

Figure 2: FTIR of HPMC

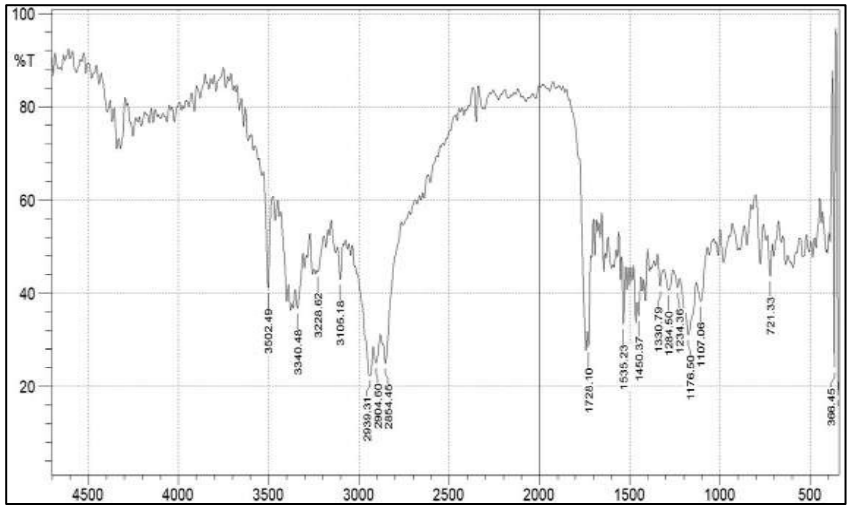

Figure 3: FTIR of Famotidine + excipients

Evaluation of Granules:

Table 9: Showing results of angle of repose, bulk and tapped density, Carr's index, hausner ratio

Batch no.	Angle of repose(0)	Bulk density (gm/ml)	Tapped density (gm/ ml)	Carr's index (%)	Hausner ratio
FF1	26˚32	0.2891	0.3503	14.04	1.21
FF2	24˚64	0.2845	0.3394	15.68	1.22
FF3	28˚59	0.2924	0.3349	11.94	1.13
FF4	26˚12	0.2875	0.3446	13.96	1.16
FF5	23˚62	0.2862	0.3420	15.13	1.19
FF6	24˚74	0.2677	0.3214	13.92	1.15
FF7	24˚77	0.2743	0.3242	15.42	1.19

FF8	26˚56	0.2847	0.3177	10.38	1.11

The angle of repose for the formulations FF1-FF8 was found to be in the range 23˚62 to 28˚59 shows good flow. Compressibility index for the formulations FF1-FF8 found between 10.38% to 15.6% indicating that the blend has good flow property for compression.[7]

Evaluation of Famotidine Tablets

The weight variation of the tablets are in the range of 1.23 to 3.09% (below 5%) complying with the pharmacopoeial standards. The friability of the tablets are in the range of 0.18 % to 0.34% (below 1%) complying with the pharmacopoeial standards. The content uniformity of the tablets is in the range of 99.37 to 100.38% complying with the pharmacopoeial standards. The thickness of the formulations was found to be in the range of 5.1+0.01 to 5.5+0.01 mm. The hardness of the tablets was found to be in the range of 6.2 to 7.5 kg/cm2 indicating a satisfactory mechanical strength. [7]

Buoyancy Lag Time and Total Floating Time

Table 10: Showing buoyancy lag time and total floating time

Batch no.	Buoyancy lag time	Total buoyancy time(hrs)
FF1	624	15
FF2	96	3
FF3	90	6
FF4	84	12
FF5	171	5
FF6	63	10
FF7	44	15
FF8	39	14

From the results formulations FF1, FF4, FF7, FF8 shows good buoyancy, all formulations showed buoyancy upto 12 hrs.

In-vitro release Profile:

Table 11: In-Vitro release profile

Time (hrs)	FF1	FF2	FF3	FF4	FF5	FF6	FF7	FF8
1	8.65	24.79	15.13	7.24	21.32	13.76	5.91	12.25
2	13.12	58.12	34.67	12.09	43.13	24.27	11.64	16.79
3	17.75	95.39	46.21	17.62	67.08	30.14	17.08	22.47
4	25.34	-	63.90	23.98	96.34	39.51	25.42	26.75
5	29.59	-	76.39	31.56	-	46.24	29.32	30.54
6	34.23	-	96.14	39.34	-	53.69	31.13	37.67
7	41.09	-	-	47.87	-	67.76	36.41	43.34
8	47.23	-	-	55.23	-	80.09	40.69	49.50
9	53.98	-	-	64.42	-	89.13	46.86	54.71
10	58.14	-	-	73.7	-	97.43	53.63	60.92
11	61.17	-	-	84.54	-	-	57.20	68.43
12	67.91	-	-	96.78	-	-	62.32	72.19

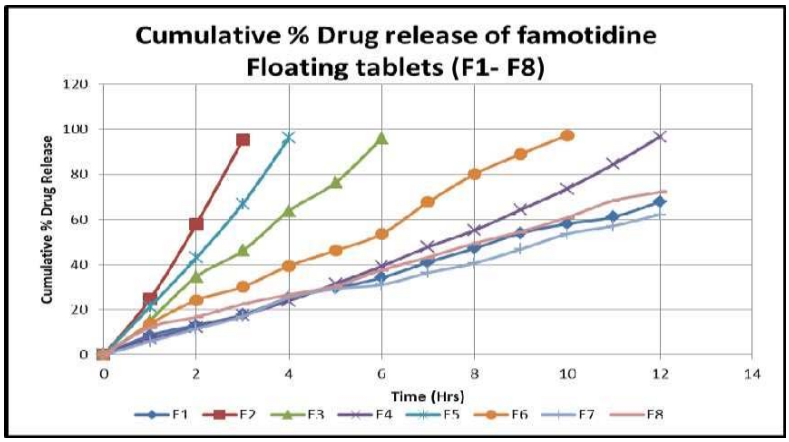

Figure 4: Showing in-vitro drug release profile for FF1-FF8 formulations

From the in-vitro dissolution study of all formulations, formulation FF1 gave 84% release at the end of 24th hour, hence FF1 have chosen as best formulation. [8]

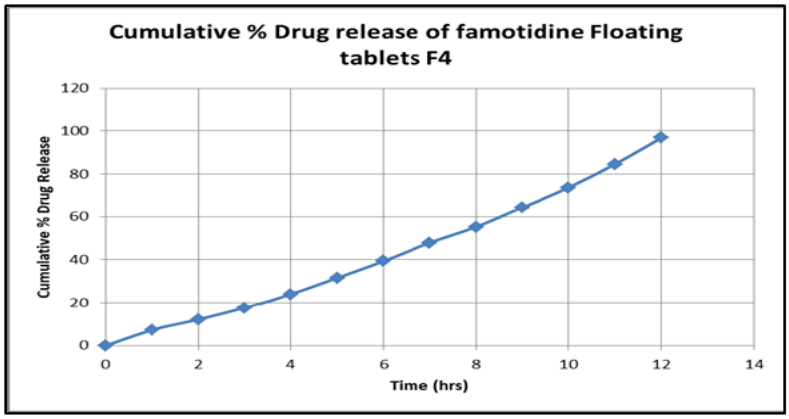

Figure 5: Showing in-vitro release profile of best formulation (FF4)

Drug Release Kinetics:

Figure 12: Drug release kinetics

Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released
0	0	100	0.000	2.000	0.000	0.000	100
1	7.24	92.76	1.000	1.967	0.000	0.860	7.24
2	12.09	87.91	1.414	1.944	0.301	1.082	4.85
3	17.62	82.38	1.732	1.916	0.477	1.246	5.53
4	23.98	76.02	2.000	1.881	0.602	1.380	6.36
5	31.56	68.44	2.236	1.835	0.699	1.499	7.58
6	39.34	60.66	2.449	1.783	0.778	1.595	7.78
7	47.87	52.13	2.646	1.717	0.845	1.680	8.53
8	55.23	44.77	2.828	1.651	0.903	1.742	7.36
9	64.42	35.58	3.000	1.551	0.954	1.809	9.19
10	73.7	26.3	3.162	1.420	1.000	1.867	9.28

11	84.54	15.46	3.317	1.189	1.041	1.927	10.84
12	96.78	3.22	3.464	0.508	1.079	1.986	12.24

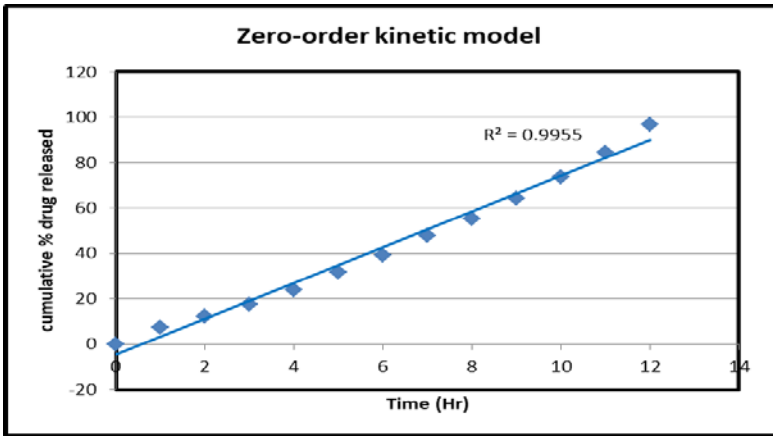

Figure 6: Zero Order Kinetic Model

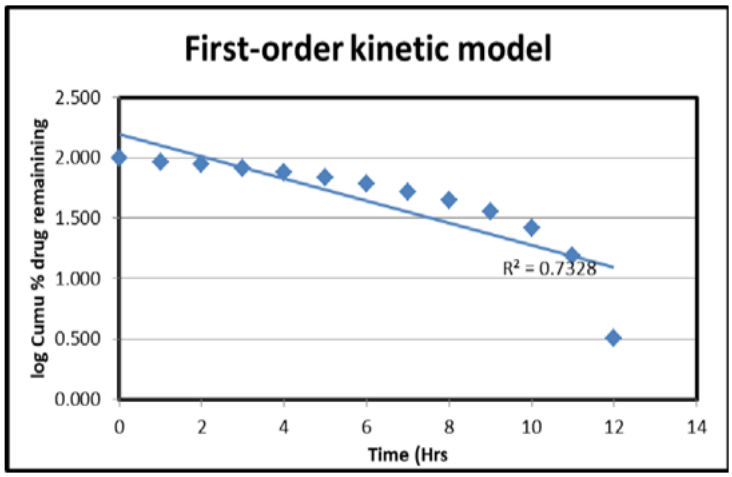

Figure 7: First Order Release Kinetics

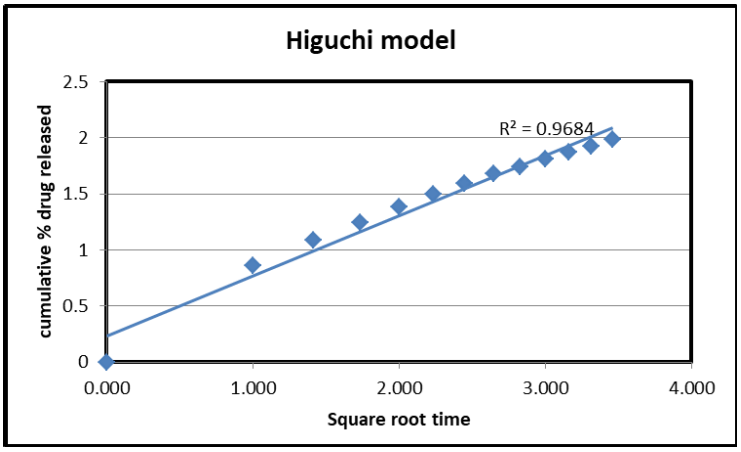

Figure 8: Higuchi model

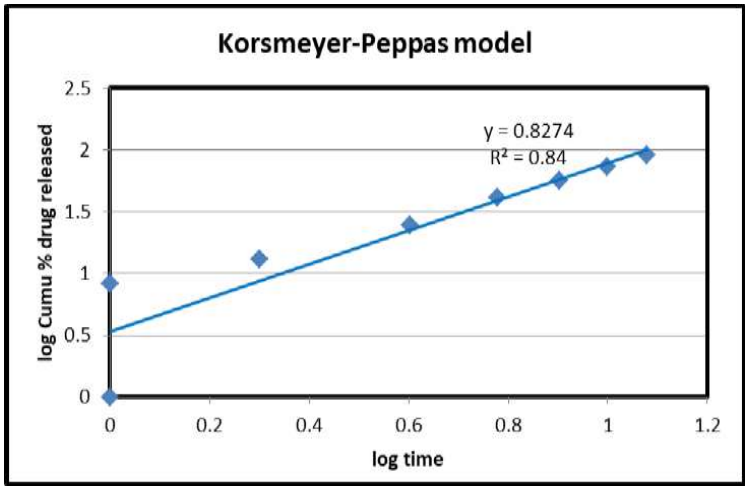

Figure 9: Korsemeyer Peppas Model

Table 13: Regression coefficient of FF4

Formulation	Regression coefficient (R2) value			
	Zero-order	First order	Higuchi	Korsmeyer – Peppas (n value)
Famotidine tablets	0.9955	0.7328	0.9684	0.84 (0.8274)

N value = 0.8274

The regression coefficient values and n values show that the drug releases follow Non - Fickian release.

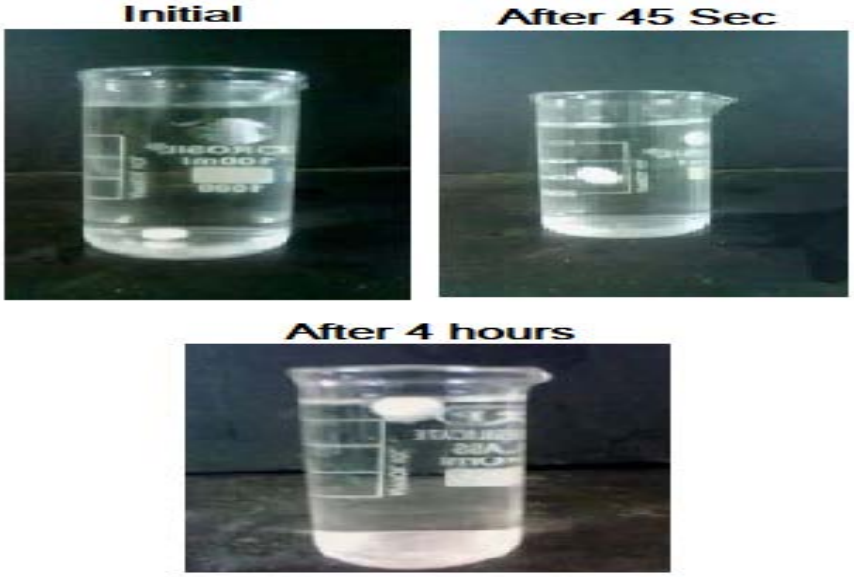

Figure 10: Buoyancy of formulation FF4.

Summary and Conclusion

The present study involves the formulation and evaluation of gastroretentive drug

delivery of Famotidine tablets. This type of drug delivery helps to retain the drug in the stomach. The swelling property of the formulation helps to retain the drug in the stomach, by swelling to such an extent so that cannot pass out of the stomach. Preformulation studies which include Organoleptic properties, Bulk and Tapped densities, Carr‘s index, Hausner‘s ratio, Melting point, pH, Solubility, were carried out are as per IP specifications. Drug-excipient compatibility studies were performed which shows that there is no interaction between drug and polymers. Evaluation studies have been performed for tablets include friability, hardness, weight variation, content uniformity, buoyancy studies are as per IP specifications. Drug release studies have been performed by using 0.1N Hcl for 12 hrs. These studies have shown that the formulation FF4 gave better drug release upto 12 hrs. Which is formulated with HPMC K100 M?

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