IJMPR 2021, 5(3), 92-101

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Research Article
SJIF Impact Factor: 5.273

DEVELOPMENT AND EVALUATION OF GASTRORETENTIVEFLOATING MATRIX TABLETS OF FAMOTIDINE

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Received on: 31/03/2021
Revised on: 20/04/2021
Accepted on: 10/05/2021

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ABSTRACT

The objective of the study is to prolong the gastric residence time, increase drug bioavailability and also to target the gastric ulcer for local drug action. A floating drug delivery system of famotidine was developed using hydroxy propyl methyl cellulose K4M, Xanthum gum, guar gum in various ratios. The tablets were prepared by wet granulation. The formulated tablets were evaluated for weight variation, hardness, buoyancy lag time. The prepared tablets exhibit satisfactory physical characteristics. All formulations showed good in vitro buoyancy. The results of the invitro release studies show that the formulation remain buoyant for more than 12 hrs. Finally, the tablet formulation was found to be economical and will overcome the draw backs associated with the drug during its absorption.

KEYWORDS: *Residence time, Buoyant, gastric ulcer, Bioavailability.*

INTRODUCTION

Oral route is the most preferred route of drug delivery due to ease of administration and greater patient compliance, although studies revealed that this route is subject to two physiological influences, a short gastric residence time (GRT) and variable gastric emptying time (GET), which may lead to unpredictable bioavailability and times to achieve peak plasma levels. Furthermore, the brief GET in humans, which normally averages 2-3 h through the major absorption zone (stomach and upper part of the intestine), can result in incomplete drug release from the drug delivery system leading to diminished efficacy of the administered dose. Thus, control of placement of a drug delivery system in a specific region of the gastro intestine (GI) tract offers numerous advantages like improved bioavailability and therapeutic efficacy, local delivery of drug and possible reduction of dose size. All these considerations have led to the development of oral controlled release (CR) dosage forms possessing gastric retention capabilities. Gastroretentive systems can remain in the gastric region for several hours and significantly prolong the gastric residence of the drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, improve solubility of drugs that are less soluble in a high pH environment. It has application also for local drug delivery to the stomach and proximal small intestine. Famotidine is a histamine H_2- receptor antagonist. It is widely prescribed in gastric ulcers, duodenal ulcers, Zollinger-Ellison syndrome and gastroesophageal reflux disease. In the management of benign gastric and duodenal ulceration the dose is 40 mg daily by oral route at bedtime, for 4 to 8 weeks. In gastroesophageal reflux disease the recommended dose is 20 mg by oral route twice daily for 6 to 12 weeks. Famotidine is incompletely absorbed from GI tract, the low bioavailability (40-45%) and short biological half-life (2.5-3.5 hrs) of famotidine following oral administration favours developmentof a sustained release formulation.[1]

MATERIAL AND METHOD

Formulation of Grt of Famotidine: Gastroretentive tablets was prepared by wet granulation method: The respective powder, famotidine, releasing retarding polymers (HPMC K4M, Carbopol 934, guar gum, Xanthum gum, Sodium carboxyl methylcellulose), Gas - forming agent (sodium bicarbonate) was passed through sieved no.20, separately for each formulation. mixing of powder was carried out using pestle mortar for 10 minutes to the above blend added HPMC 2% granulating agent then again mixing of powder. magnesium stearate, talc was then added to the powder blend mixture. mixing is continued for another 3 min, finally tablets was punched to desired tablets. the composition of formulated batches in table 1.

Evaluation of Gastroretentive Drug Delivery System: Pre compression Parameters

Evaluation of blend for the following parameters carried out before compression

- **Angle of repose:** The angle of repose gives an indication of the flow ability of the substance. Funnel was adjusted such that the stem of the funnel lies 2 cm above the horizontal surface. The drug powder was allowed to flow from the funnel under the gravitational force till the apex of the pile just touched the stem of the funnel, so the height of the pile is taken as 2 cm. drawing a boundary along the circumference of the pile and taken

the average of six diameters determined the diameter of the pile. These values of height and diameter are then substituted in thefollowing equation:

$\tan \theta = h/r$

$\theta = \tan^{-1} hr$.....E.q.1

Where, θ = Angle of repose, h = Height of the cone and r = Radius of the heap

Values of θ less than 40º indicate responsible flow property to the powder and value greater than 50º indicates difficulty in flow. The Angle of Repose and Quality of Flow given in table 1.2.

- **Bulk density and tapped density**

20 g of the granules (W) from each formula was introduced into a 20 ml measuring cylinder, and the initial volume was observed. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated by using E.q.2

Bulk density = W/V_O, Tapped density = W/V_F.....E.q.2

Where, W= weight of the granules, Vo= initial volume of the granules, V_F= final volume of the granules as shown in table 1.3.

- **Compressibility index (Carr's index)**

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated by using E.q.3. as shown in table 1.4

$C = (\rho t - \rho b)/\rho t * 100$…… E.q.3

Where ρt- tapped density and ρb- untapped bulk density

- **Hausner's ratio**

Hausner's ratio is an index of ease of powder flow; it is calculated by using E.q.4.as shown in table1.5

Hausner's ratio= ρt/ρb E.q.4

Where ρt- Tapped density, ρb- Untapped bulk density.[2][3]

CHARACTERIZATION OF GRT OF FAMOTIDINE

Post Compression Parameters

- **General Appearance:** Appearance is the first most required quality for the acceptance of tablet. General elegance and its identity play a major role for the consumer acceptance. Acceptance of the appearance of batches of the tablet was done based on the measurement of the following factors like size, color, shape, presence or absence of odor, taste etc.
- **Weight variation Test:** The weight variation test was done by weighing 20 tablets. First the total weight of 20 tablets from each formulation was determined and then individually calculated average weight and compared the individual weight to the average. The tablets met the IP specification that not more than 2 tablets are outside the percentage limits and no tablets differ by more than 2 times the percentage limit as shown in table 1.6
- **Thickness:** The thickness of tablets was determined by using digital screw and the standard deviation was calculated as shown in table 1.7.
- **Hardness Test:** Hardness of a tablet is defined as the force applied across the diameter of the table tin order to break the tablet. Pfizer hardness tester is the instrument which is used to determine the hardness of tablet. It is expressed in Kg/cm^2. Tablets were taken from each formulation randomly and their hardness was measured. Then the mean and standard deviation values were calculated as shown in table 1.7.
- **Friability:** Ten tablets are weighed and placed in the Roche Friabilator apparatus which rotated at 25 rpm for 4 min. After revolution the tablets dusted and weighed. The friability was calculated by the formula given below:

$F = (1 - W_i/W_f) \times 100$

Where, **W_i** is the weight of the tablets before the test and **W_f** is the weight of the tablet after the test. as shown in table 1.7.

- **Disintegration test:** Disintegration time of prepared tablets is determined in disintegrationtest apparatus. One tablet from each formulation was placed in each tube and the basket rack was positioned in a 1liter beaker containing phosphate buffer pH 6.8 maintained at temperature 37 ± 2°C. The tablet should remain 2.5 cm below the surface of the liquid. The time taken for the complete disintegration of the tablets was noted.[4][5]
- **Drug content:** Ten tablets are powdered and then blended equivalent to 20 mg was weighed and dissolved in suitable quantity of Phosphate buffer of pH 6.8. The solution was filtered, suitably diluted and the drug content was analyzed spectrophotometrically.[12] as shown in table 1.8.
- **In vitro drug release/ dissolution study:** In vitro drug release studies was carried out using Type 2 apparatus at 50 rpm 500 ml of HCl 0.1Nwas used as the dissolution medium. The temperature of the dissolution medium was maintained at 37 ± 0.5ºC. An aliquot 5 ml of dissolution medium was withdrawn at specific time intervals, filtered, and suitably diluted prior to spectrophotometrically analysis. The medium was replenished with an equal amount 5ml of dissolution medium. The absorbance of these solutions was analyzed by UV spectroscopy.
- **Buoyancy Lag time and Duration of buoyancy:** In vitro buoyancy was determined by USP - II type dissolution apparatus (paddle type) in 0.1N HCl (pH 1.2). the time interval between the introduction of the tablets into the dissolution medium and its buoyancy to the of the dissolution medium was taken as buoyancy lag time or floating time and the time in which tablets constantly floats on the

dissolution media that is 0.1N HCl surface was taken as the duration of buoyancy and was observed visually the data id reported .

- **Stability:** The stability study of formulation was carried out at 40º C ± 5ºC /75% ± 2% RH for one months. The tablets were wrapped in the aluminum foil and stored in a stability chamber at accelerated conditions. The drug content was checked at regular time intervals of 7,14,21,28 and 30 days respectively and was evaluated for physical appearance. There was no significant change in physical appearance, Drug content at the end of one month as shown in table 1.14

percentage swelling index = (W_t -W_0 / W_0) * 100

where W_0 is the initial weight of tablets and W_t **is** the weight of tablets at time t.

CONCLUSION AND SUMMARY

The present research was executed in two phases. In the first phase, Preformulation study was carried out for drug characterization and drug-excipient compatibility study. In the second phase, gastroretentive tablets were prepared and evaluated on the basis of various parameters. Famotidine was evaluated for organoleptic properties whose results are shown in table 3.1. The melting point data is given in table 3.2 and it is in accordance with the value reported in literature. The absorption maximum of drug was observed at 260nm. Standard calibration curve of Famotidine was prepared in Phosphate buffer pH 6.8 and HCl pH 1.2. Samples were scanned at 260nm using UV spectrophotometer and the absorbance data is presented in table 3.3 respectively. The calibration curve is shown in fig 3.3. The regression coefficient (r^2) value in HCl pH 6.8 is 0.994 which indicated linear relationship between the two parameters. The solubility of the drug was determined in various solvents and data is reported in table 3.4. The purity of the drug sample was assured by FTIR spectrum of the drug sample, which is in agreement with standard IR spectrum of drug. Drug and the various polymers were initially analyzed for any compatibility. There was no discoloration, liquefaction, clump formation and has no significant shifts in the peaks corresponding to the drug or polymer. It has been observed that the sample was pure and there was no chemical interaction between the drug and the polymers procured. Hence, they can be successfully incorporated in the formulation. The results are shown in table 3.5 and the FTIR spectrums of pure drug, mixture of drug-polymer i.e. HPMC K4M, Xanthum gum, guar gum is shown in fig 3.2, 3.3 and 3.4 respectively.[6]

Characterization of Gastroretentive Tablets

Gastroretentive tablets was prepared using the formula given in table 4.4. Initially all the formulations F1 to F9 blends was characterized for flow properties shown in table 5.2. The results shown in Table showed that the prepared formulations were within the limits for further studies. The pre-compression parameters such as weight variation, thickness, hardness, friability, wetting time, water absorption ratio, in vitro dispersion time, Disintegration time and drug content for all the formulations was in the specified range shown in table 5.3 and 5.4 The maximum drug release was found to be in the formulation F2 containing Xanthum gum with 97±0.49 % of drug release. results revealed that with the increase in concentration of polymer there is decreased in disintegration time. Therefore, F2 was selected asthe best formulation. The results of % drug release is shown in table 5.4 and the graph is shown in fig 5.2. The comparative study between formulation F2 with the marketed formulation of Famotidine was also performed. The time of the marketed formulation was found to be 10 hrs. and 85% drug was released.[7][8]

STABILITY STUDY

Stability study of the prepared gastroretentive tablets was carried out for 30 days at 40 ºC ± 5ºC/ 75 % ± 2 % RH. Formulation F2 was placed to stability chamber for specific period of time and was observed for any physical change and drug content. Finally, it was observed that there was no physical and chemical change. No significant change in terms of physical characteristics (no discoloration and no change in shape) and drug content under all the storage conditions. The results are shown in table 5.11.

SUMMARY

In the present research work, an attempt was made to formulate gastrotentive tablets of famotidine. Famotidine is a BCS Class II drug with low solubility and high permeability. The tablets were prepared by wet granulation method using natural polymer and synthetic polymers.The selection of suitable polymer for the preparation of the gastroretentive tablet was highly effective and Xanthum gum significantly enhanced characteristics of the tablet when in contact with water. Nine formulations of gastroretentive tablets were prepared. All the formulations F1 to F9 were subjected to in vitro release studies and in vitro disintegration time and formulation F2 showed maximum release of 97 ± 0.80%. As the tablets disintegrate in the oral cavity, this could decline clinical efficacy of drug through pre-gastric absorption from the mouth, pharynx and esophagus, which leads to an increase in less solubility and longer sustain by avoiding first pass metabolism. The results of comparative study with that of marketed formulation also revealed that the formulation F2 shows better results. It can thus be concluded that the gastroretentive tablets containing Famotidine with Xanthum gum could prove a better dosage form for treatment of peptic ulcer /gastric ulcer.[9][10]

Table 1.1: Formulation Composition of Floating Tablets (mg).

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug (Famotidine)	150	150	150	150	150	150	150	150	150
HMPCK4M	100	100	75	25	100	75	100	75	150
Xanthum gum	100	50	-	-	-	-	-	-	-
Guar gum	-	-	75	100	-	-	-	-	-
SCMC	-	-	-	-	100	25	-	-	--
Carbopol934	-	-	-	-	-	-	100	25	-
$NaHCO_3$	50	50	50	50	50	50	50	50	50
Citric acid	10	10	10	10	10	10	10	10	10
Mg stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Stearic acid	5	5	5	5	5	5	5	5	5

Table 1.2: Angle of Repose and Quality of Flow.

S. No.	Angle of Repose	Quality of flow
1.	<25	Excellent
2.	25-30	Good
3.	30-40	Passable
4.	>40	Very poor

Table 1.3: Carr's Index and Quality of Flow.

S. No.	Carr's Index	Quality of flow
1.	5-12	Free flowing
2.	12-16	Good
3.	18-21	Fair
4.	23-35	Poor
5.	33-38	Very poor
6.	>40	Extremely poor

Table 1.4: Hausner's ratio and Quality of Flow.

S. No.	Hausner's ratio	Nature of flow
1.	0-1.2	Free flowing
2.	1.2-1.6	Cohesive powder

Table 1.5: Weight variation of Tablet.

S. No.	Average Weight of the Tablet(mg)	Maximum % Deviation Allowed
1.	130mg or less	10%
2.	More than 130 mg but less than350 mg	7.5%
3.	350 mg or more	5%

Table 1.6: Pre-Compression Parameters.

F. Code	Bulk Density (g/ml)	Tapped density*(g/ml)	Carr's index* (%)	HauserRatio*	Angle ofrepose(º)
F1	0.330 ± 0.64	0.454 ± 0.21	16.74 ± 0.321	1.20 ± 0.34	29.74 ± 0.97
F2	0.458 ± 0.52	0.514 ± 0.26	21.71 ± 0.214	1.26 ± 0.001	30.91 ± 0.88
F3	0.369 ± 0.74	0.406 ± 0.37	11.12 ± 0.32	1.13 ± 0.39	30.69 ± 0.97
F4	0.474 ± 0.64	0.666 ± 0.18	28.63 ± 0.45	1.45 ± 0.96	34.11 ± 0.63
F5	0.313 ± 0.49	0.370 ± 0.21	15.46 ± 0.15	1.18 ± 0.36	29.36 ± 0.82
F6	0.334 ± 0.52	0.415 ± 0.32	16.87 ± 0.46	1.22 ± 0.25	28.21 ± 0.46
F7	0.456 ± 0.55	0.473 ± 0.23	15.87 ± 0.87	1.16 ± 0.24	34.18 ± 0.56
F8	0.454 ± 0.51	0.656 ± 0.24	31.73 ± 0.91	1.47 ± 0.24	40.6 ± 0.98
F9	0.945 ± 0.53	0.357 ± 0.25	17.23 ± 0.87	1.21 ± 0.36	29.73 ± 0.91

* All readings are in triplicate (n=3) and SD= Standard Deviation

Table 1.7: Characterization data of the formulated batches.

F. code	Weight Variation (mg)±SD	Hardness(Kg/cm^2) ±SD	Thickness (mm)±SD	Friability(%) ±SD
F1	400.63 ± 0.78	5.5 ± 0.145	4.03 ± 0.05	0.29 ± 0.10
F2	367.5 ± 0.21	5.8 ± 0.154	3.96 ± 0.1	0.39 ± 0.08
F3	401 ± 0.39	5.9 ± 0.214	4.06 ± 0.05	0.38 ± 0.12
F4	397.5 ± 0.56	5.6 ± 0.230	3.98 ± 0.24	0.28 ± 0.10
F5	394 ± 0.24	5.4 ± 0.357	3.92 ± 0.32	0.36 ± 0.07
F6	403 ± 0.28	5.6 ± 0.412	4.12 ± 0.18	0.31 ± 0.05
F7	398 ± 0.36	6.3 ± 0.231	3.95 ± 0.25	0.26 ±0.05
F8	391 ± 0.39	5.6 ± 0.287	3.92 ± 0.26	0.51 ± 0.14
F9	398 ± 0.45	5.2 ± 0.312	3.97 ± 0.36	0.45±0.09

Table 1.8: Observations of Post-compression parameter of Gastroretentive tablet.

F. code	Drug contents (%)	Floating time (mean) (sec)	Swelling time (sec)
F1	99.25 ± 0.92	290 ± 10	345 ± 0.11
F2	98.34 ± 0.34	260 ± 5.7	341 ± 0.15
F3	97.71 ± 0.55	310 ± 10	289 ± 0.14
F4	98.34 ± 0.65	280 ± 6.8	300 ± 0.10
F5	98.21 ± 0.23	290 ± 8.2	279 ± 0.17
F6	98.41 ± 0.25	280 ± 5.8	262 ± 0.07
F7	97.60 ± 0.89	410 ± 3.3	184 ± 0.05
F8	99.20 ± 0.75	310 ± 2.3	207 ± 0.12
F9	98.33 ± 0.25	260 ± 3.6	175 ± 0.09

Table 1.9: % Cumulative drug released (CDR) vs Time (hrs.) in 0.1N HCl.

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	2.48	2.49	3.41	1.24	3.78	2.36	1.51	1.34	4.23
2	4.36	4.78	7.8	2.26	5.26	5.13	2.58	3.4	6.12
3	6.41	6.54	10.2	4.45	7.41	8.74	4.64	5.29	6.56
4	9.43	8.6	14.23	6.48	10.32	10.26	6.48	7.32	12.35
5	13.23	12.32	16.3	9.42	14.87	12.37	6.48	10.5	19.85
6	17.32	16.54	28.33	10.37	17.45	16.98	9.42	11.28	20.58
7	20.15	20.15	32.14	14.07	28.98	23.89	10.32	13.28	25.87
8	25.28	26.89	38.21	16.54	32.12	26.58	14.28	17.98	30.21
9	29.65	30.23	45.24	22.98	35.89	28.30	19.38	19.22	37.21
10	32.46	44.65	55.55	29.36	47.48	32.33	22.31	20.78	39.56

Table 1.10: % Cumulative drug released vs Time (hrs.) in pH 6.8 Phosphate buffer

Table 1.11: Log Cumulative Drug retained vs Time (hrs.).

Time (hrs.)	Log % Cumulative Drug retained								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	2	2	2	2	2	2	2	2	2
1	1.90	1.85	1.85	1.95	1.91	1.9	1.84	1.85	1.92
2	1.83	1.84	1.78	1.92	1.87	1.86	1.82	1.78	1.9
3	1.8	1.68	1.78	1.91	1.85	1.83	1.77	1.75	1.89
4	1.74	1.69	1.72	1.90	1.77	1.76	1.73	1.73	1.84
5	1.67	1.61	1.66	1.83	1.71	1.69	1.66	1.66	1.76
6	1.61	1.54	1.59	1.82	1.68	1.59	1.6	1.59	1.69
7	1.48	1.45	1.52	1.71	1.53	1.57	1.55	1.51	1.61
8	1.40	1.30	1.34	1.69	1.47	1.41	1.40	1.31	1.52
9	1.15	0.99	1.08	1.49	1.25	1.18	1.16	1.11	1.43
10	0.80	0.72	0.76	1.43	0.99	0.87	0.83	0.77	1.38

Table 1.12: Log Cumulative Drug retained vs Time (hrs.)

Time (hrs.)	Log % Cumulative Drug retained								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	2	2	2	2	2	2	2	2	2
1	1.90	1.85	1.85	1.95	1.91	1.9	1.84	1.85	1.92
2	1.83	1.84	1.78	1.92	1.87	1.86	1.82	1.78	1.9
3	1.8	1.68	1.78	1.91	1.85	1.83	1.77	1.75	1.89
4	1.74	1.69	1.72	1.90	1.77	1.76	1.73	1.73	1.84
5	1.67	1.61	1.66	1.83	1.71	1.69	1.66	1.66	1.76
6	1.61	1.54	1.59	1.82	1.68	1.59	1.6	1.59	1.69
7	1.48	1.45	1.52	1.71	1.53	1.57	1.55	1.51	1.61
8	1.40	1.30	1.34	1.69	1.47	1.41	1.40	1.31	1.52
9	1.15	0.99	1.08	1.49	1.25	1.18	1.16	1.11	1.43
10	0.80	0.72	0.76	1.43	0.99	0.87	0.83	0.77	1.38

Table 1.13: Cumulative drug release vs Time (hrs.) from formulation F1-F9.

Time (Sqrt) hrs.	% CDR								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	20.36	28.65	28.76	10.42	17.34	19.38	21.81	28.76	15.12
1.41	31.43	30.64	38.62	15.32	25.12	27.38	33.665	38.62	20.45
1.73	36.11	32.2	39.02	17.32	29.21	31.10	39.51	39.15	21.45
2	44.23	51.62	46.58	20.32	39.82	41.36	45.82	46.58	30.41
2.23	52.85	58.63	53.65	31.42	48.51	50.65	53.84	53.65	41.92
2.44	59.12	64.55	60.85	31.12	57.6	60.25	59.84	60.85	50.64
2.64	69.23	71.42	67.64	48.41	65.41	67.42	64.56	67.61	58.54
2.82	74.21	79.54	79.56	50.62	70.65	73.44	74.12	79.23	66.42
3	85.63	90.2	87.67	68.44	82.15	84.62	85.45	87.14	72.64
3.16	92.52	99.87	94.22	72.44	90.12	92.41	93.12	94.15	79.44

Table 1.15: Log % Cumulative drug release (CDR) vs log Time (hrs.).

Log Time(hrs.)	Log % Cumulative drug release (CDR)			
	F1	F2	F3	F4
∞	0	0	0	0
0	1.30	1.45	1.44	1
2	1.49	1.48	1.57	1.17
0.47	1.55	1.50	1.59	1.23
0.6	1.71	1.70	1.63	1.30
0.69	1.77	1.76	1.72	1.49
0.77	1.83	1.80	1.77	1.48
0.84	1.86	1.85	1.82	1.68
0.9	1.92	1.89	1.89	1.69
0.95	1.96	1.95	1.93	1.83
1	1.90	1.82	1.92	1.77

Table 1.16: Log% CDR vs Time (hrs.) of F5-F9.

Percentage Swelling									
Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	32±0.30	36±0.54	35±0.21	40±0.82	35±0.32	29±0.20	33±0.26	48±0.71	42±0.50
2	39±0.12	46±0.64	42±0.51	51±0.84	42±0.41	32±0.78	38±0.28	59±0.70	51±0.23
3	41±0.56	56±0.21	49±0.45	62±0.64	48±0.22	48±0.52	43±0.94	65±0.98	67±0.36
4	49±0.14	64±0.91	57±0.23	73±0.50	55±0.85	59±0.30	49±0.51	78±0.23	76±0.65
5	56±0.89	77±0.87	68±0.87	90±0.61	66±0.61	62±0.24	65±0.63	82±0.25	91±0.98

Table 5.10: Swelling index (%) of Tablets of batches F1 to F9.

Log Time (hrs)	Log % Cumulative drug release (CDR)				
	F5	F6	F7	F8	F9
∞	0	0	0	0	0
0	1.24	1.28	1.32	1.46	1.17
2	1.40	1.43	1.55	1.57	1.30
0.47	1.46	1.49	1.59	1.59	1.32
0.6	1.59	1.69	1.65	1.66	1.47
0.69	1.68	1.77	1.72	1.72	1.61
0.77	1.75	1.82	1.77	1.77	1.69
0.84	1.81	1.86	1.80	1.82	1.76
0.9	1.84	1.92	1.85	1.89	1.81
0.95	1.91	1.96	1.92	1.93	1.85
1	1.95	1.97	1.96	1.97	1.89

* All readings are in triplicate (n=3) and SD= Standard Deviation

Table 5.11: Drug Content data during Stability Study.

Time (days)	Accelerated conditions (40ºC ± 5ºC / 75% ± 2% RH)	
	Physical appearance	Drug content (%)
7	+	98.13 ± 0.03
14	+	97.64 ± 0.18
21	+	97.03 ± 0.04
28	+	96.45 ± 0.01
30	+	95.79 ± 0.06

CONCLUSION AND SUMMARY

The present research was executed in two phases. In the first phase, Preformulation study was carried out for drug characterization and drug-excipient compatibility study. In the second phase, gastroretentive tablets were prepared and evaluated on the basis of various parameters. Famotidine was evaluated for organoleptic properties whose results are shown in table 3.1. The melting point data is given in table 3.2 and it is in accordance with the value reported in literature. The absorption maximum of drug was observed at 260nm. Standard calibration curve of Famotidine was prepared in Phosphate buffer pH 6.8 and HCl pH 1.2. Samples were scanned at 260nm using UV spectrophotometer and the absorbance data is presented in table 3.3 respectively. The calibration curve is shown in fig 3.3. The regression coefficient (r^2) value in HCl pH 6.8 is 0.994 which indicated linear relationship between the two parameters. The solubility of the drug was determined in various solvents and data is reported in table 3.4. The purity of the drug sample was assured by FTIR spectrum of the drug sample, which is in agreement with standard IR spectrum of drug. Drug and the various polymers were initially analyzed for any compatibility. There was no discoloration, liquefaction, clump formation and has no significant shifts in the peaks corresponding to the drug or polymer. It has been observed that the sample was pure and there was no chemical interaction between the drug and the polymers procured. Hence, they can be successfully incorporated in the formulation. The results are shown in table 3.5 and the FTIR spectrums of pure drug, mixture of drug-polymer i.e. HPMC K4M, Xanthum gum, guar gum is shown in fig 3.2, 3.3 and 3.4 respectively.

CHARACTERIZATION OF GASTRORETENTIVE TABLETS

Gastroretentive tablets was prepared using the formula given in table 4.4. Initially all the formulations F1 to F9 blends was characterized for flow properties shown in table 5.2. The results shown in Table showed that the prepared formulations were within the limits for further studies. The pre-compression parameters such as weight variation, thickness, hardness, friability, wetting time, water absorption ratio, in vitro dispersion time, Disintegration time and drug content for all the formulations was in the specified range shown in table 5.3 and 5.4 The maximum drug release was found to be in the formulation F2 containing Xanthum gum with 97±0.49 % of drug release results revealed that with the increase in concentration of polymer there is decreased in disintegration time. Therefore, F2 was selected as the best formulation. The results of % drug release is shown in table 5.4 and the graph is shown in fig 5.2. The comparative study between formulation F2 with the marketed formulation of Famotidine was also performed. The time of the marketed formulation was found to be 10 hrs. and 85% drug was released.

STABILITY STUDY

Stability study of the prepared gastroretentive tablets was carried out for 30 days at 40 ºC ± 5ºC/ 75 % ± 2 % RH. Formulation F2 was placed to stability chamber for specific period of time and was observed for any physical change and drug content. Finally, it was observed that there was no physical and chemical

change. No significant change in terms of physical characteristics (no discoloration and no change in shape) and drug content under all the storage conditions. The results are shown in table 5.11.

SUMMARY

In the present research work, an attempt was made to formulate gastrotentive tabletsof famotidine. Famotidine is a BCS Class II drug with low solubility and high permeability. The tablets were prepared by wet granulation method using natural polymer and synthetic polymers.The selection of suitable polymer for the preparation of the gastroretentive tablet was highly effective and Xanthum gum significantly enhanced characteristics of the tablet when in contact with water. Nine formulations of gastroretentive tablets were prepared. All the formulations F1 to F9 were subjected to in vitro release studies and in vitro disintegration time and formulation F2 showed maximum release of 97 ± 0.80%. As the tablets disintegrate in the oral cavity, this could decline clinical efficacy of drug through pre-gastric absorption from the mouth, pharynx and esophagus, which leads to an increase in less solubility and longer sustain by avoiding first pass metabolism. The results of comparative study with that of marketed formulation also revealed that the formulation F2 shows better results.

It can thus be concluded that the gastroretentive tablets containing Famotidine with Xanthum gum could prove a better dosage form for treatment of peptic ulcer /gastric ulcer.

LIST OF TABLES AND FIGURES

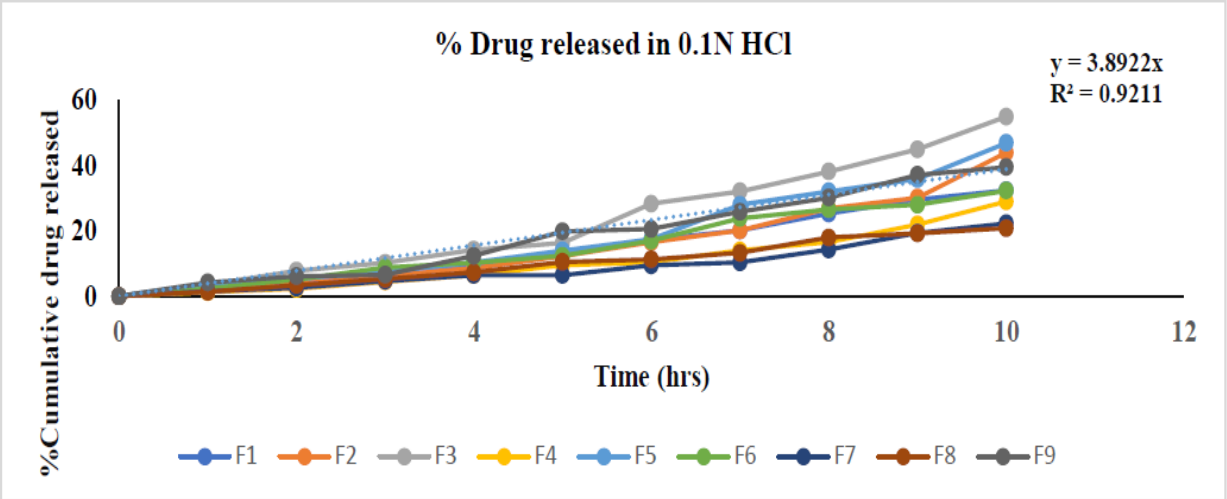


Fig 1.1: % drug release vs Time (hrs).

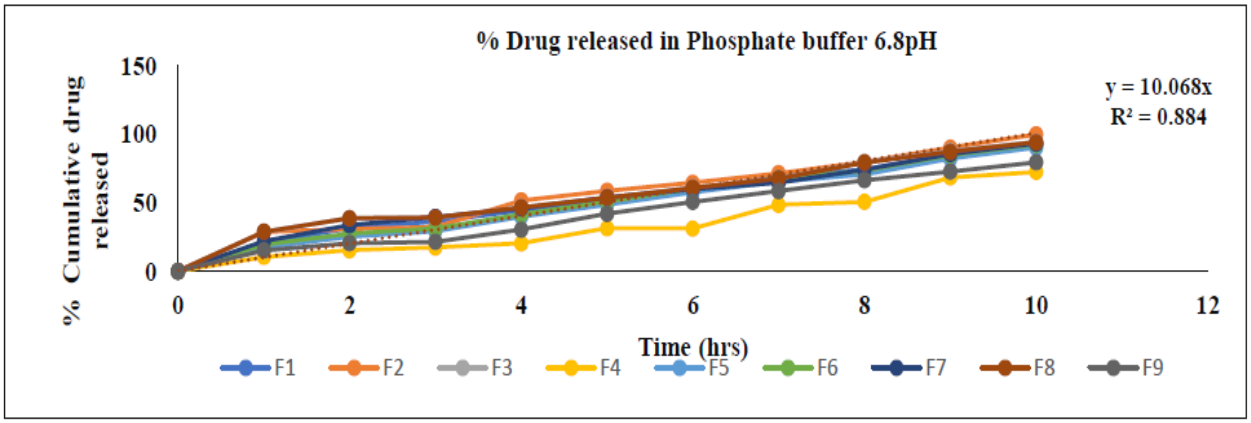


Fig 1.2: % drug release vs Time (hrs).

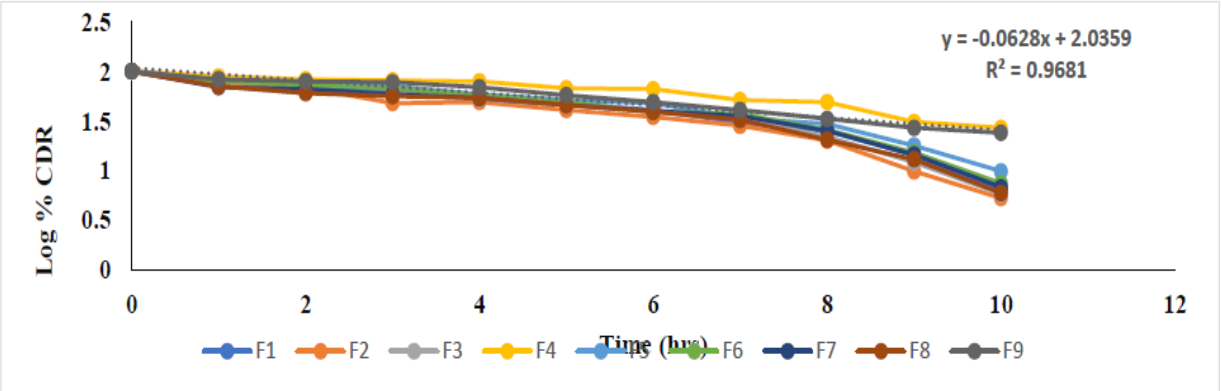


Fig 1.3: Log% CDR vs Time(hrs).

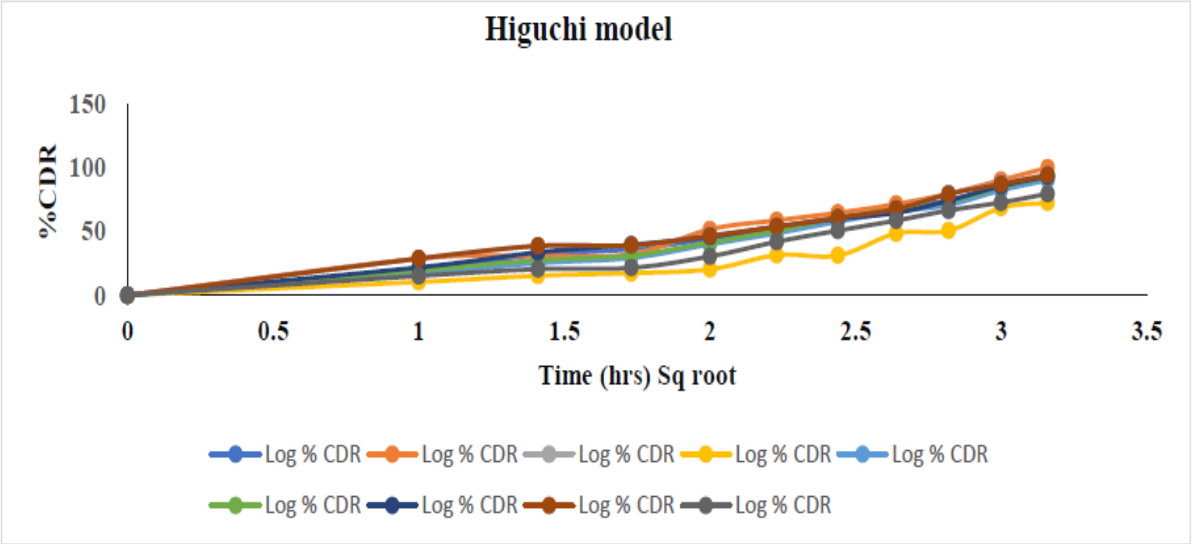


Fig 5.4: Log % Cumulative drug release (CDR)vs Time (hrs.) (sq root)

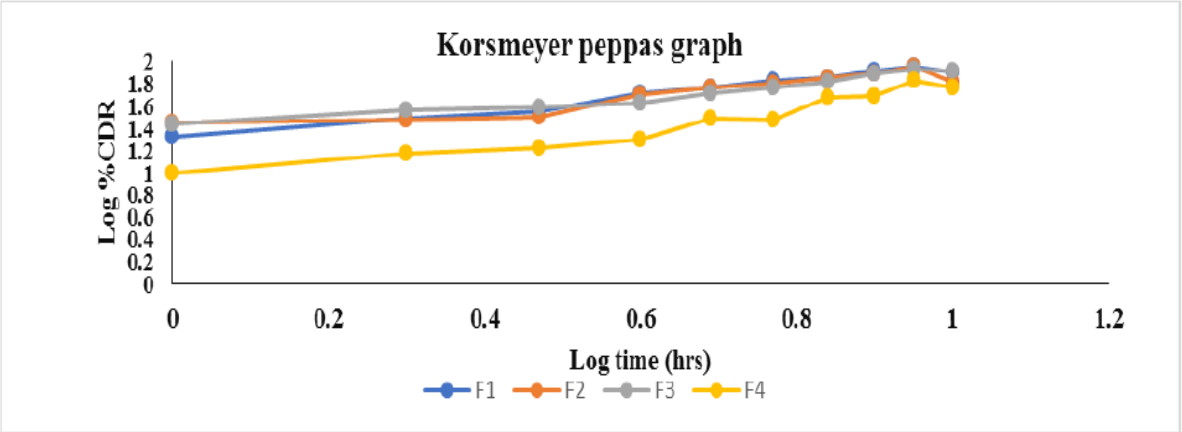


Fig 5.5: Log% CDR vs Log Time (hrs.) of F1-F4.

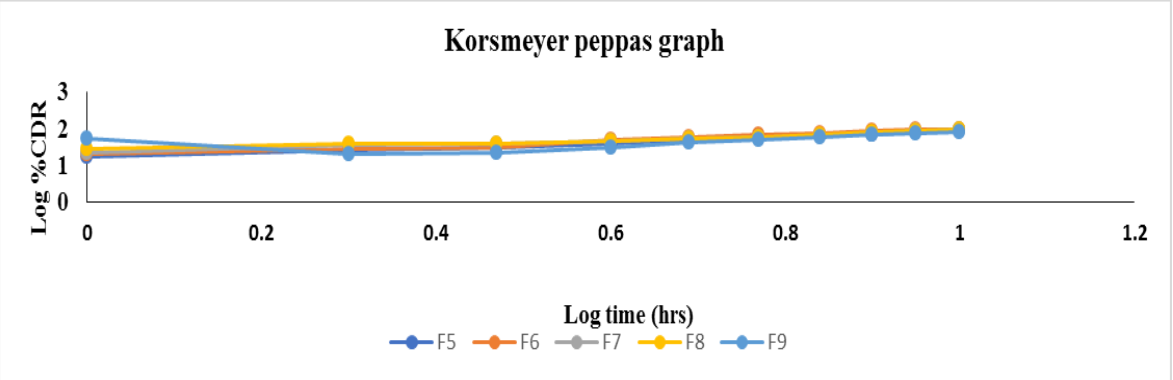
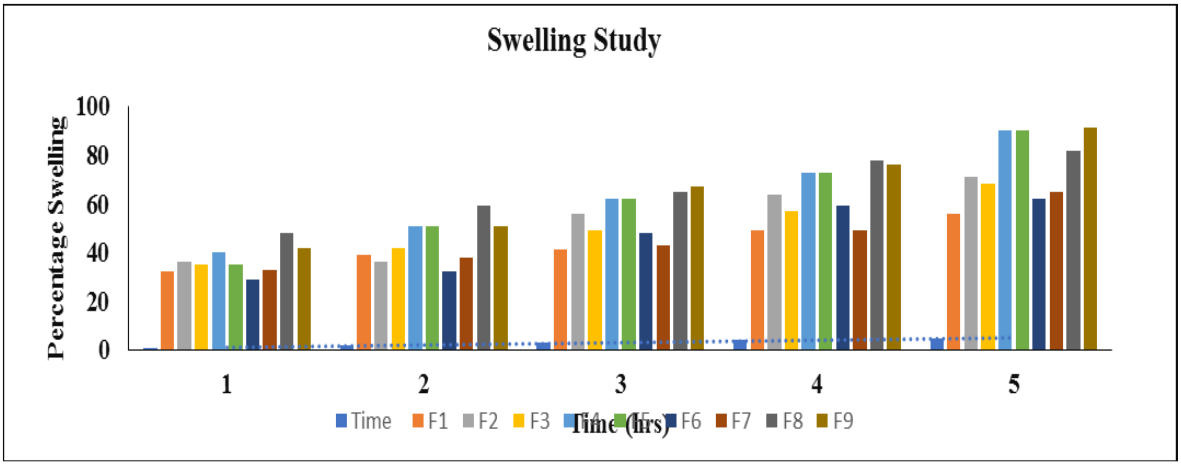


Fig 5.6: Log% CDR vs Log Time (hrs) of F5-F9.



ACKNOWLEDGEMENTS

Famotidine was obtained as a gift sample from Srinivasan Pharmaceuticals Pvt. Ltd, Hyderabad, for providing the gift sample of Famotidine

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