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Formulation and Evaluation of Famotidine Gastro-Retentive Floating Matrix Tablets by Using Natural and Synthetic Polymers

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ABSTRACT

Drugs that have narrow absorption window in the gastrointestinal tract (GIT) will have poor absorption. For these drugs, gastro retentive drug delivery systems offer the advantage in prolonging the gastric emptying time. Famotidine belongs to H2-receptor antagonist. It is used widely for the treatment of treatment of gastro-esophageal reflux disease (GERD) and gastric ulceration duodenal ulcer, stress ulcer. The low bioavailability (40-45 %) and short biological half-life (2.5-4.0 hrs) of Famotidine following oral administration favors development of a sustained release formulation. The rapid gastrointestinal transit could result in incomplete drug release from the drug delivery system above the absorption zone leading to poor bioavailability of the drug. The floating tablets were formulated using synthetic polymer like HPMC K15M and natural polymer like chitosan as the release retardant polymers, and sodium bicarbonate as the gas generating agent to reduce the floating lag time. The tablets were prepared by direct compression. The formulated tablets were evaluated for weight variation, hardness, friability, swelling index, floating lag time, total floating time and dissolution rate in pH 1.2. The floating tablets extended the drug release up to 12 h. The drug-polymer interaction was evaluated by Fourier transform infrared spectroscopy (FTIR). The FTIR study indicated the lack of drug-polymer interaction. The optimized formulation (F5), containing drug: HPMC K15M 200mg and Chitosan 75mg showed very good result and extended the release up to 12 h. The drug release from the optimized formulation followed Zero order kinetics and Korsmeyer Peppas equation.

INTRODUCTION

It has been suggested that compounding the drugs with narrow absorption window in a unique pharmaceutical dosage form with gastro retentive properties, would enable an extended absorption phase of these drugs. After oral administration, such a dosage form would be retained in the stomach and release the drug there in a controlled and prolonged manner, so that drug could be supplied continuously to its absorption sites in the upper GIT. This mode of administration would best achieve the known pharmacokinetic and pharmacodynamic advantages of controlled release dosage form for such drugs. [1] Gastro retentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs.

Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in a high pH environment. It is also suitable for local drug delivery to the stomach and proximal small intestines. Gastroretention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patients.[2] Thus one of most feasible approaches for achieving a prolonged and predictable drug delivery profiles in the GIT is to control the gastric residence time, using gastroretentive dosage forms that will provide us with new and important therapeutic options. The need for gastroretentive dosage forms has led to extensive efforts in both academia and industry towards the development of such drug delivery systems.[3] Over the past three decades, the pursuit and exploration of devices designed to be retained in the upper part of GI tract has advanced consistently in terms of technology and diversity, encompassing a variety of systems and devices such as floating systems, swelling systems, bioadhesive systems and high density systems.[4,5] The floating drug delivery system (FDDS) have a bulk density less than gastric fluid and hence, remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents the drug is released slowly at desired rate from the system.[3] After the release of drug, the residual system is emptied from the stomach. This results in an increase in the GRT and a better control of fluctuations in plasma drug concentration. [6] Potential drug candidates for Gastroretentive drug delivery system are:

- Drugs which are locally active in the stomach e.g. antacids, etc.

- Drugs which are used for gastric disorders e.g. Famotidine.
- Drugs that have narrow absorption window in GIT e.g. L-DOPA, para aminobenzoic acid, furosemide, riboflavin, etc.
- Drugs which are unstable in the intestinal or colonic environment e.g. captopril, ranitidine HCl, metronidazole
- Drugs that disturb normal colonic microbes e.g. antibiotics against Helicobacter pylori.
- Drugs that exhibit low solubility at high pH values e.g. diazepam, chlordiazepoxide, verapamil HCl[7],

Famotidine is histamine H2-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 mouth at bedtime, for 4 to 8 weeks. In gastroesophageal reflux disease the recommended dose is 20 mg by mouth twice a daily for 6 to 12 weeks, where gastroesophageal reflux disease is associated with esophageal ulceration; the recommended dose is 40 mg twice daily for similar period. For symptomatic relief of heartburn or non-ulcer dyspepsia a dose of 10 mg up to twice daily is suggested. In the Zollinger-Ellison syndrome the initial dose by mouth is 20 mg every 6 h, increased as necessary, dose up to 80 mg daily have been employed. The low bioavailability (40 – 45%) and short biological half life (2.5 - 4.0 h) of famotidine following oral administration favors development of a sustained release formulation. The gastroretentive drug delivery system can be retained in the stomach and assist in improving oral sustained delivery of drug that have an absorption window in a particular region of gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability.

It has been reported that the oral treatment of gastric disorders with an H2 receptor antagonist like famotidine or ranitidine used in combinations with antacids promotes local delivery of these drugs to the receptor of parietal cell wall. Local delivery also increases the stomach wall receptor site bioavailability and increases efficacy of drugs to reduced acid secretion. Hence this principle may be applied for improving systemic as well as local delivery of famotidine, which would efficiently reduced gastric acid secretion. In the present investigation floating tablets of famotidine were prepared by direct compression using HPMC K4M and Na-CMC as gel forming

and also release retardant agent. The aim of the work was to evaluate the effect of gel-forming polymer HPMC on floating properties and release characteristics of famotidine floating tablets.

MATERIALS AND METHODS

MATERIALS

Famotidine was obtained from Wallace Pvt. Ltd. Goa as a gift sample. Chitosan and HPMC K15M was obtained from Kopran RND Lab. PVP was obtained from Emcure Pharma, Pune, Sodium bicarbonate was procured from Suprime Pharma, Pune. Lactose (DCL), Magnesium stearate and Talc was obtained from Research Fine Lab, Mumbai. All other chemicals used were of analytical grade.

Table no.1 Materials used in the development of Famotidine tablets.

Ingredients	Source
Drug: Famotidine	Wallace Pvt. Ltd. Goa.
Chitosan	Kopran RND Lab.Pune
HPMC K15M	Kopran RND Lab.
PVP	Emcure pharma,Pune
Sodium bicarbonate	Suprime lab, Pune
Citric acid anhydrous	Research fine lab, Mumbai
Lactose (DCL)	Research fine lab, Mumbai
Magnesium stearate	Research fine lab, Mumbai
Talc	Research fine lab, Mumbai

METHODS

Formulation of Controlled Release Matrix Tablets of Famotidine

Matrix tablets of Famotidine with other excipients were prepared by direct compression. Lactose was selected as tablet diluent for increasing the compressibility and flowability of the ingredients. Sodium bicarbonate was incorporated as an effervescent substance to aid buoyancy to the dosage form due to liberation of CO_2 when the tablets come in contact with acidified

dissolution medium which entrapped in the matrix. The detailed compositions of the prepared matrix tablets formulations are given in table 2.

Table 2. Composition of Famotidine controlled release matrix tablet

Sr. NO.	Ingrdients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Famotidine	40	40	40	40	40	40	40	40	40
2	HPMC K15M	200	200	200	175	175	175	150	150	150
3	Chitosan	75	50	25	75	50	25	75	50	25
4	Sodium bicarbonate	30.4	28	28	28	28	28	28	28	28
5	Citric acid	15.2	14	14	14	14	14	14	14	14
6	PVP	10	10	10	10	10	10	10	10	10
7	Maganesium stearate	06	06	06	06	06	06	06	06	06
8	Talc	01	01	01	01	01	01	01	01	01
9	Lactose	2.4	01	026	01	26	50	26	51	76
11	Total	380	350	350	350	350	300	300	300	300

Evaluation of matrices used for preparation of floating tablet of Famotidine

A. Micromeritics Studies

Matrices of different batches were evaluated for different micromeritic properties such as angle of repose, bulk density, tapped density, Carr's compressibility index, Hausner's ratio, etc. before compression.

Various formulations before compression were evaluated for their flow properties in terms of following parameters.

(i) Angle of repose

Static angle of repose was measured according to the fixed funnel and free standing core method of Banker and Anderson. Blends were carefully poured through the Enar reposograph until the apex of the conical pile so formed just reached the tip of the funnel of reposograph. Height of

instrument was fixed to 4 cm.[9] Thus, with r being the radius of the base of the granules conical pile and the angle of repose (θ) was calculated by using the eqn.1

$$\tan\theta = h/r, \text{ therefore, } \theta = \tan^{-1} h/r \ldots (1)$$

(ii) Bulk density/Tapped density

Both bulk density (BD) and tapped density (TD) were determined. A suitable amount of powder blend from each formulation, previously lightly shaken to break any agglomerates formed, was introduced into a 100 mL measuring cylinder. After observing its initial volume, the cylinder in the density tapper instrument and density is measured according to USP method II (up to1250 taps). The tapping was continued until no further change in volume was noted. Volume of packing after tapping was noted. BD and TD were calculated using eqn. 2 and 3 respectively.

$$BD = \text{weight of the powder / volume of the packing} \ldots (2)$$

$$TD = \text{weight of the powder / tapped volume of the packing} \ldots (3)$$

(iii) Compressibility index

Compressibility index of the powder was determined by Carr's compressibility index[10] as given by equation 4

$$\text{Carr's index (\%)} = [(TD - BD) \times 100] / TD \ldots (4)$$

It helps in measuring the force required to break the friction between the particles and the hopper.

(iv) Hausner's ratio

It is the ratio of tapped to bulk density [11] and was calculated by using the eqn. 5

$$\text{Hausner's ratio} = TD/BD \ldots (5)$$

B. Evaluation of Floating Matrix Tablets of Famotidine

The prepared tablets of Famotidine were evaluated for hardness, friability, weight variation, thickness, diameter, swelling index, floating or buoyancy test, drug content uniformity and *in vitro* dissolution studies.

(i) Tablet hardness

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and handling, before usage, depends on its hardness. The crushing strength of prepared tablets was determined for ten tablets of each batch using Monsanto hardness tester.

(ii) Friability

Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the plastic chamber that revolves at 25 rpm for 4 minutes dropping the tablets through a distance of six inches with each revolution. After 100 revolutions the tablets were reweighed and the percentage loss in tablet weight was determined.

% loss = Initial wt. of tablets - Final wt. of tablets/ Initial wt. of tablets x 100… (6)

(iii) Weight variation

Twenty tablets were weighed individually and the average weight was determined. Then percentage deviation from the average weight was calculated. According to USP standards, not more than the percentage shown in table 2 and none deviates by more than twice that percentage.[12]

Table 3: Maximum percentage difference allowed

Average weight of tablets (mg)	Maximum percentage difference allowed
130 or less	10
130-324	7.5
More than 324	05

(iv) Tablet Thickness/ Diameter

Thickness and diameter of tablets were important for uniformity of tablet size. Six tablets were examined for their thickness and diameter using vernier calipers and the mean thickness and diameter value was calculated

(v) Swelling index

Swelling of tablet involves the absorption of a liquid by tablet matrices resulting in an increase in weight and volume of tablet. The extent of swelling can be measured in terms of % weight gain by the tablet. For each formulation batch, one tablet was weighed and placed in a beaker containing 200 mL of 0.1 N HCl. After each time interval, the tablet was removed from beaker and weighed again up to 12 h.[13] The swelling index was calculated using following equation 7.

$$\text{Swelling Index \% (S.I.)} = (Wt-Wo)/Wo*100 \quad \ldots (7)$$

Where, S.I. = Swelling index

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

(vi) Floating or buoyancy test

The time taken for tablet to emerge on the surface of the medium is called the floating lag time (FLT) or buoyancy lag time (BLT) and duration of time the dosage form constantly remains on the surface of the medium is called the total floating time (TFT). The buoyancy of the tablets was studied in USP type II dissolution apparatus at $37^{o}C \pm 0.5^{o}C$ in 900 mL of simulated gastric fluid at pH 1.2. The time of duration of floatation was observed visually.[6]

(vii) Content uniformity

For the content uniformity, ten tablets were weighed and pulverized to fine powder, a quantity of powder equivalent to 100 mg of Famotidine was dissolved in 100 mL methanol and liquid was filtered using Whatman filter paper and diluted up to 50µg/mL. The Famotidine content was determined by measuring the absorbance at 288 nm using UV spectrophotometer, after appropriate dilution with methanol.[14]

(viii) *In-vitro* dissolution studies

In-vitro dissolution studies were conducted to determine the release pattern of the drug from the product. Dissolution test for Famotidine floating matrix tablet was carried out using USP Type II dissolution test apparatus. 900 mL 0.1 N HCl was used as dissolution media at $37^{o}C \pm 0.5^{o}C$ temperature with rotation speed of paddle at 50 rpm. An aliquot of 5 mL sample was withdrawn at different time interval. These samples were filtered and diluted. Absorbance of the resulting solution was measured at 288 nm. Amount of drug release was calculated.[12] Percent drug release was calculated by using the eqn. 8 as follows

$$\% \text{ Drug release} = K \times \text{Absorbance} \ldots (8)$$

Where K can be calculated by using eqn. 9 as follows

$$K = \text{Std. conc.} \times \text{vol. of dissolution media} \times \text{dilution factor} \times 100 / \text{std. abs.} \times \text{dose} \times 1000 \ldots (9)$$

Kinetic analysis of drug dissolution data. The dissolution profile of most satisfactory formulation was fitted to zero order, first order, Higuchi's model and Korsmeyer-Peppas model to ascertain the kinetic modeling of the drug release.

The methods were adopted for deciding the most appropriate model.

Percent drug released versus time (Zero order kinetic model)[15]

Log percent drug remaining versus time. (First-order kinetic model)[16]

Percent drug released versus square root of time (Higuchi's model)

Log percent drug released versus log time (Korsmeyer-Peppas model)[17]

Drug excipient compatibility studies

(IX) Fourier transform infra-red (FTIR) studies

FTIR spectra of the drug and its physical mixtures with polymer blend of selected best formulation were recorded using an FTIR spectrophotometer.

C. Accelerated stability studies

It is imperative that the final product be sufficiently rugged for marketing worldwide under various climate conditions including tropical, subtropical temperature. Stability testing is done to check the physical, chemical and physiological properties of the product. Accelerated stability testing was carried out as per ICH guidelines (40^0C/75% RH)[14] to ascertain the product stability for longer period in a shorter period of time. The most satisfactory formulation sealed in aluminum packing and kept in humidity chamber maintained at 40^0C/75% RH for three months. At the end of studies, samples were analysed for % drug content.

RESULTS AND DISCUSSION

Micromeritic properties of matrices

Table 4: Micromeritic properties of Famotidine matrices

Formulation Code	Bulk Density (gm/ml)	Tap Density (gm/ml)	Carr's Index (%)	Hausner's ratio	Angle of Repose (Deg)	Flow Rates (gm/sec)
F1	0.511±0.005	0.56±0.008	8.75±2.235	1.09±0.005	34.30±0.001	1.02
F2	0.51±0.002	0.53±0.007	5.20±0.646	1.03±0.01	30.5±0.000	1.21
F3	0.52±0.003	0.53±0.007	6.32±0.489	1.00±0.005	39.35±0.02	1.06
F4	0.52±0.007	0.58±0.003	10.30±0.740	1.11±3	27.47±0.012	1.17
F5	0.49±0.004	0.58±0.008	14.77±0.738	1.17±3	30.96±0.01	1.23
F6	0.47±0.006	0.52±0.004	9.21±0.455	1.10±0.005	30.54±0.020	1.12
F7	0.43±0.008	0.47±0.008	7.13±1.908	1.08±0.020	37.59±0.022	8.51
F8	0.45±0.002	0.52±0.007	13.42±00780	1.15±0.01	29.68±0.00	1.28
F9	0.39±0.005	0.45±0.004	13.3±0.34	1.15±0.005	27.92±0.00	1.82

Table 5: Post compression parameters of Floating matrix tablet

Formulation Code	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Floating Lag Time (Sec)	Total Floating time (hrs)
F1	2±0.115	10	5.8±0.1	0.5	30	12
F2	1.1±0.1	10	5.4±0.1	0.9	25	11
F3	.2±0.25	10	5.5±0.404	1.3	60	14
F4	1.5±0.057	10	5.3±0.3	0.8	50	10
F5	1±0.00	10	5.8±0.00	0.6	16	12
F6	1±0.00	10	5.5±0.305	0.9	90	12
F7	1±0.00	10	5.5±0.305	0.8	60	12
F8	1±0.00	10	5.6±0.251	0.9	120	13
F9	1±0.00	10	5.2±0.1	0.4	50	10

(n=3; mean S.D) (n=20; mean S.D.),

All batches of tablet passes weight variation test.

Table 6: *In-vitro* % drug release of Floating matrix tablet of Famotidine (F1-F9)

Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
01	17.65	13.15	13.67	10.6	13.82	5.21	6.18	4.68	5.51
02	19.41	28.43	26.14	21.2	25.52	5.92	12.03	14.79	15.05
03	28.2	34.57	34.2	29.83	34.79	14.34	20.04	20.34	18.56
04	36.44	41.23	41.45	50.59	42.19	21.41	25.39	26.79	29.66
05	42.1	47.89	50.54	50.67	48.62	26.41	28.69	34.33	39.53
06	51.11	52.35	54.83	54.46	53.01	32.9	34.94	36.83	40.11
07	52.27	54.59	55.96	60.96	56.33	39.16	40.6	41.98	42.05
08	55.57	54.27	57.8	57.88	58.38	41.96	46.78	48.29	47.43
09	57.4	55.39	62.27	60.91	62.41	47.59	53.46	54.53	57.61
10	65.11	57.21	68.95	96.67	71.09	49.45	57.85	60.55	64.75
11	68.55	61.54	74.21	75.63	74.36	56.45	74.21	68.55	70.67
12	80.81	80.81	80.81	88.55	96.29	73.78	80.81	81.52	73.78

From *in-vitro* drug release profile of Famotidine matrix tablet, it was found that more than 20% of drug was released till 1 h from F1 to F9 formulations. After 8 h more than 60% of the drug was released from all the formulations. After 12 h the release rate decreased slightly and a sustained release pattern was observed for 12 h. The hydrophilic matrix of HPMC K15Mcontrolled the Famotidine release effectively for 12 h.

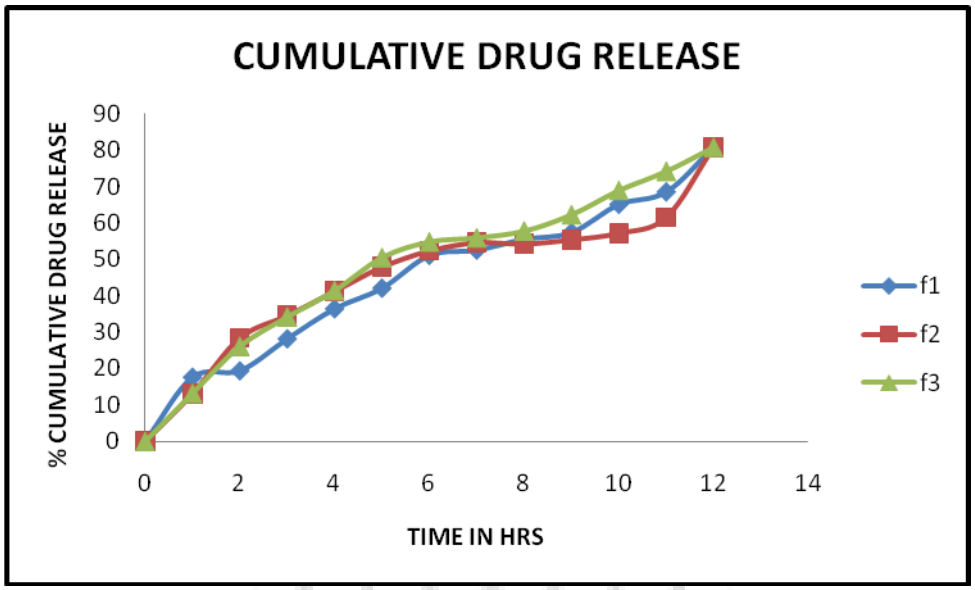

Fig.1- *In-vitro* Release Profile of F1, F2, and F3 Batch

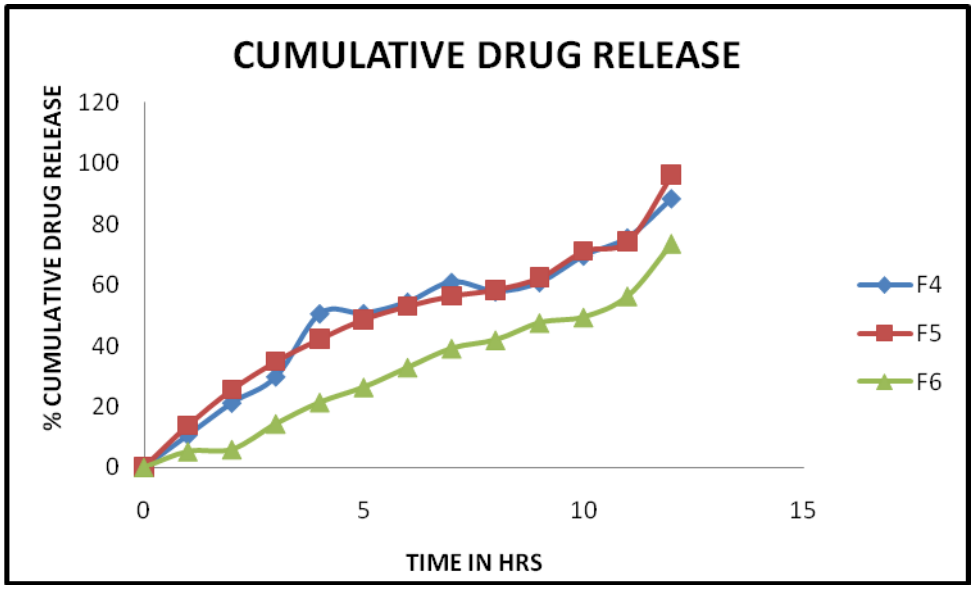

Fig.2- *In-vitro* Release Profile of F4, F5, and F6 Batch

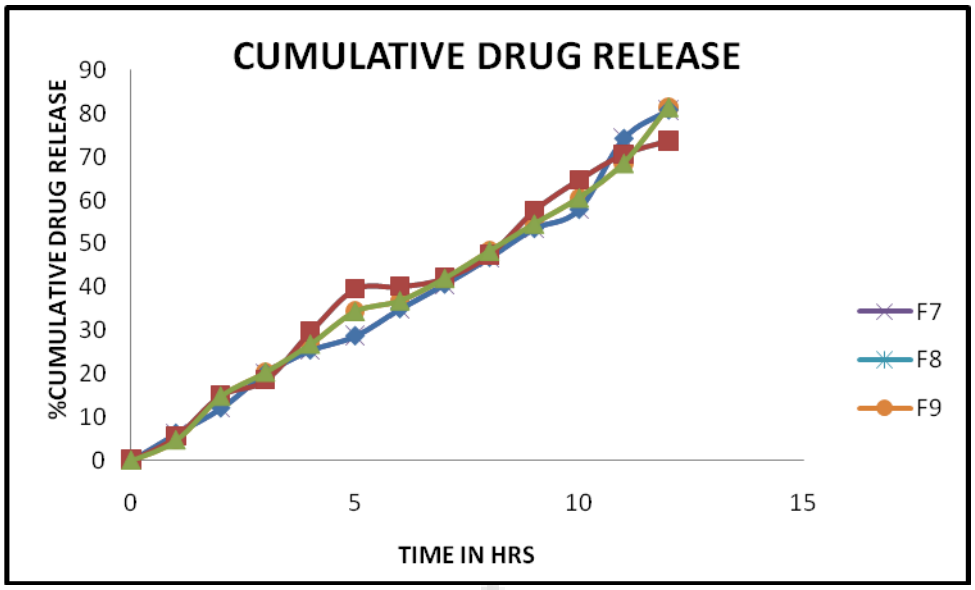

Fig.3- *In-vitro* Release Profile of F7, F8, and F9 Batch

Figure 4: Initial Floating, Float in 16 sec, FLT MT 12hrs.

C. Kinetic Analysis of Dissolution Data

The *in-vitro* drug release data of all nine formulations (F1 to F9) were fitted into zero order, Korsmeyer-Peppas model and the values of slope, intercept and r^2 were calculated in each case.

These values are shown in table 6 and the plots obtained for optimized formulation (F7) are given in Fig.2 to 5. On the basis of kinetic analysis it can be concluded that the drug release from

the formulation followed Korsmeyer-Peppas model as it has highest value of r^2. Hence, we can say that diffusion is the predominant mechanism of drug release from Famotidine formulations. From the Korsmeyer-Peppas plots, it has been observed that regression value (n-value) of all the formulations (F1 to F9) ranges from 0.3870 to 0.5038, suggesting that the drug was released by Fickian diffusion in all the cases.

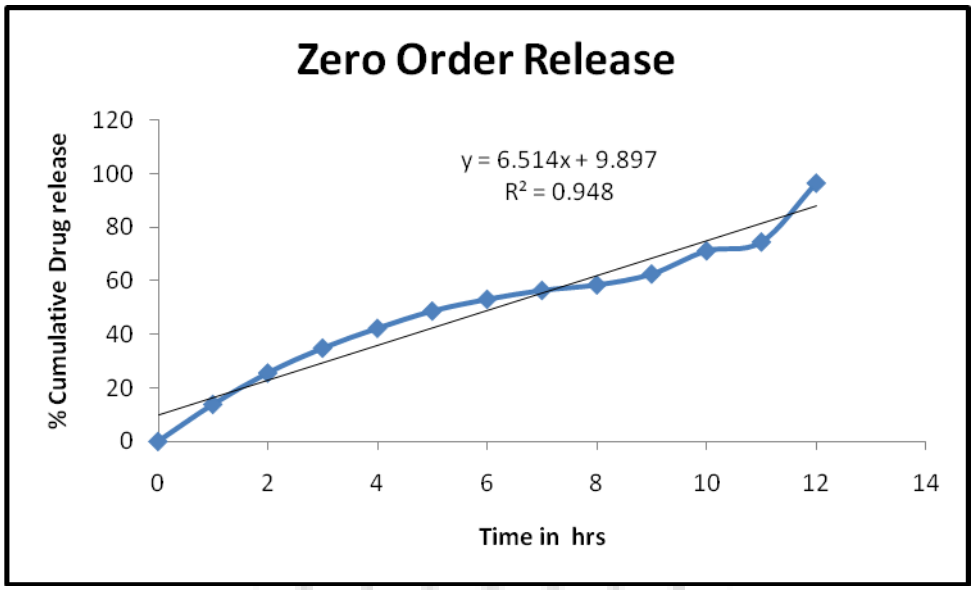

Fig. 5: % Drug release vs time plot of F5 showing zero order kinetics.

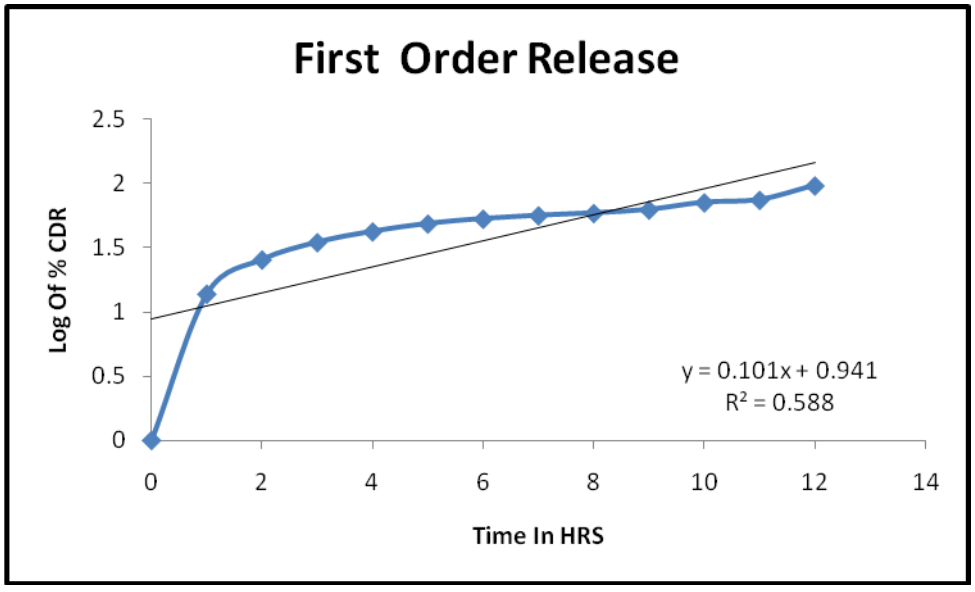

Fig. 6: Log % drug remained vs time plot of F5 showing first order kinetics.

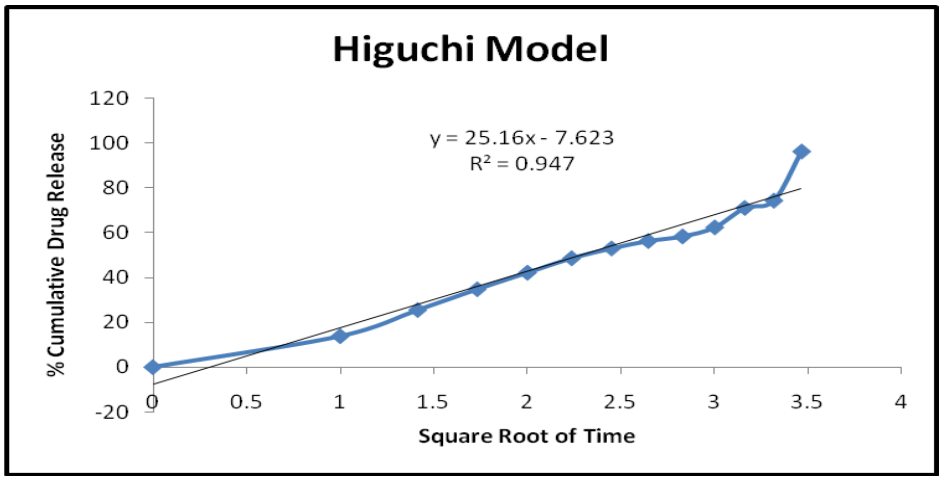

Fig. 7: % Drug release vs square root of time plot of F5 showing Higuchi's model

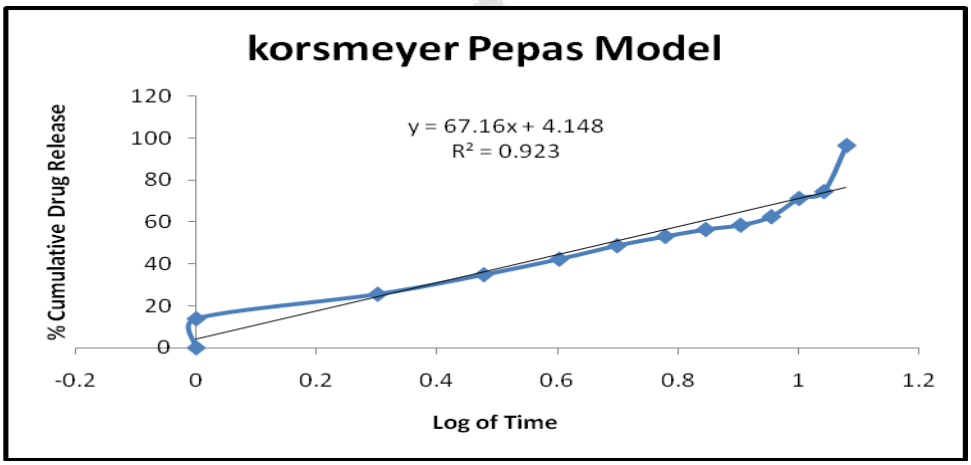

Fig. 8: Log % drug release vs time plot of F5 showing Korsmeyer-Peppas model

This study discusses the preparation of floating tablets of famotidine. The addition of gel forming polymers HPMC K15M, Chitosan and gas generating agent Sodium bicarbonate was essential to achieve *in vitro* buoyancy. Polymer swelling is crucial in determining the drug release rate and is also important for flotation. The dissolution studies of nine formulations showed that the formulation having lesser amount of polymer exhibits better drug release. Formulations containing HPMC K15M in concentration of 175 mg and 50 mg showed more release in comparison to formulation containing HPMC K15M and chitosan in less concentration. As the concentration of HPMC K15M decreased from 90 mg to 70 mg, the release rate of drug increased. All formulation contains 8% sodium bicarbonate with 4% citric acid which shows the Floating time less than 120 sec.

Table 7: Modeling of dissolution data of all formulations (F1-F9)

Batch	Regression coefficient (R^2)										Best Fit Model
	Zero order		First order		Higuchi		Korsmeyer-Peppas		Hixon-Crowell		
	k	R^2	k	R^2	k	R^2	k	R^2	k	R^2	
F1	0.0943	0.9901	-09503	-0.0021	-3.345	0.982	1.159	0.983	-0.972	-0.005	Zero order
F2	0.0956	0.9838	-0.0022	-0.948	-3.395	0.977	0.756	0.986	-0.0005	-0.952	Korsmeyer-Peppas
F3	0.0821	0.9863	-0.0015	-0.957	2.209	0.976	0.522	0.986	0.0004	-0.971	First order
F4	0.0695	0.9885	-0.0010	-0.971	0.245	0.977	0.214	0.995	-0.0003	-0.979	Korsmeyer-Peppas
F5	0.0468	0.9898	-0.0006	-0.981	1.650	0.975	0.133	0.995	-0.0002	-0.984	Korsmeyer-Peppas
F6	0.0313	0.9922	-0.0004	-0.987	1.097	0.972	0.017	0.995	-0.0001	-0.985	Korsmeyer-Peppas
F7	0.0169	0.9880	-0.0002	-0.985	0.636	0.969	0.0036	0.993	-0.0001	-0.986	Korsmeyer-Peppas
F8	0.1058	0.9953	-0.0021	-0.960	3.732	00.982	0.161	0.995	-0.006	-0.978	Korsmeyer-Peppas
F9	0.1043	0.9928	-0.975	-0.0021	3.697	0.984	0.176	0.994	-0.0005	-0.984	Korsmeyer-Peppas

Swelling Study of formulation Batches

Table.8- Swelling Study of F4 and F5 Batches

TIME (Hrs.)	F4	F5
1	11.42±0.02%	26.76±0.03%
2	15.71±0.05%%	38.02±0.02%
3	48.57±0.07%	54.92±0.06%
4	80±4%	81.97±0.012%
5	99.71±0.01%	101.40±0.05%
6	111.42±0.06%	117.18±0.04%

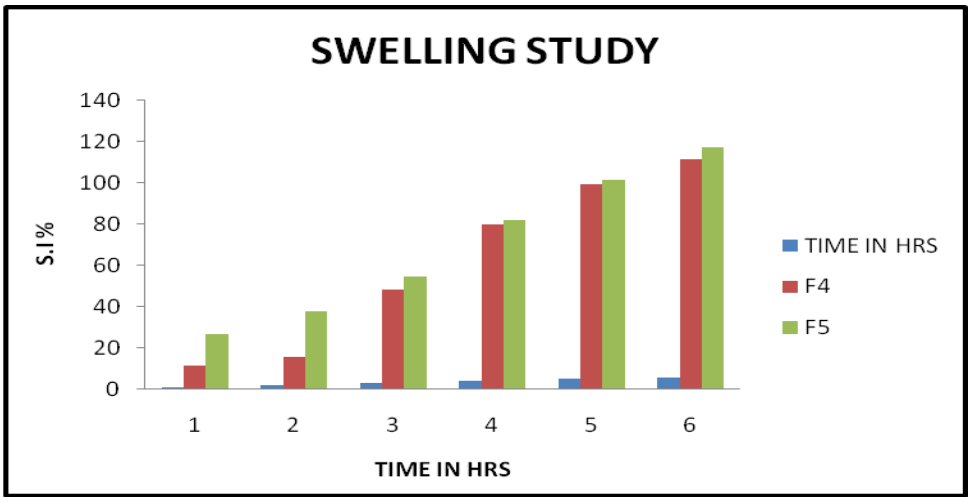

Fig. No.9- Swelling Study of F4 and F5 Batches

D. Drug Excipients Compatibility Studies

To check the interaction between drug and polymers, used in the formulations, FTIR studies were performed. In FTIR study, it was found that all the prominent peaks which were present in individual graphs of Famotidine and polymers were also present in IR of physical mixture of drug and polymers. Thus we can say that there was no significant interaction between drug and polymer were observed. The FTIR spectrum of famotidine exhibits a peak at 3400.50 cm^{-1} due to the N-H stretching of sulphonamide group and peaks at 1286.55 cm^{-1} and 1147.03 cm^{-1} due to S-O stretching, confirms the structure of the drug. The C-H absorption frequency was noticed at 2924.2 cm^{-1} in confirmation of presence of alkyl moieties.

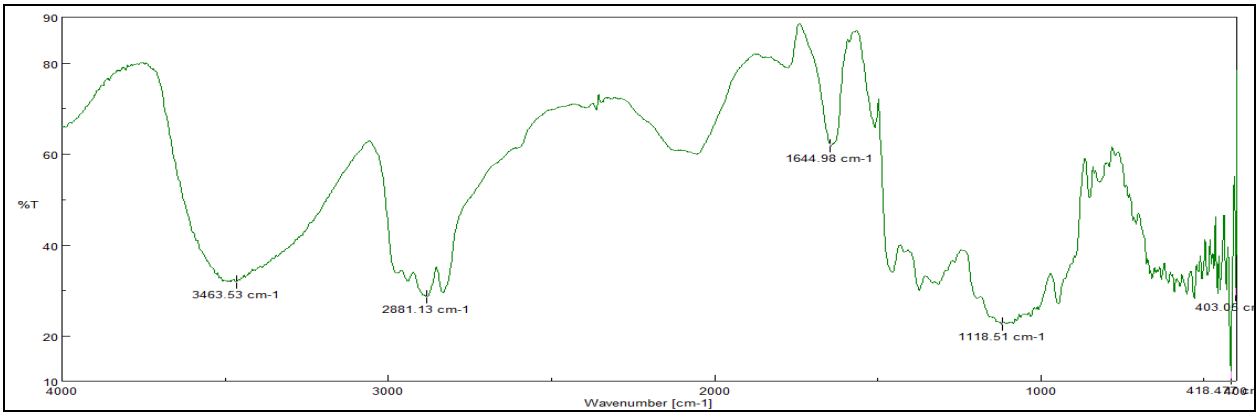

Fig. 10: FTIR Spectra of pure Famotidine

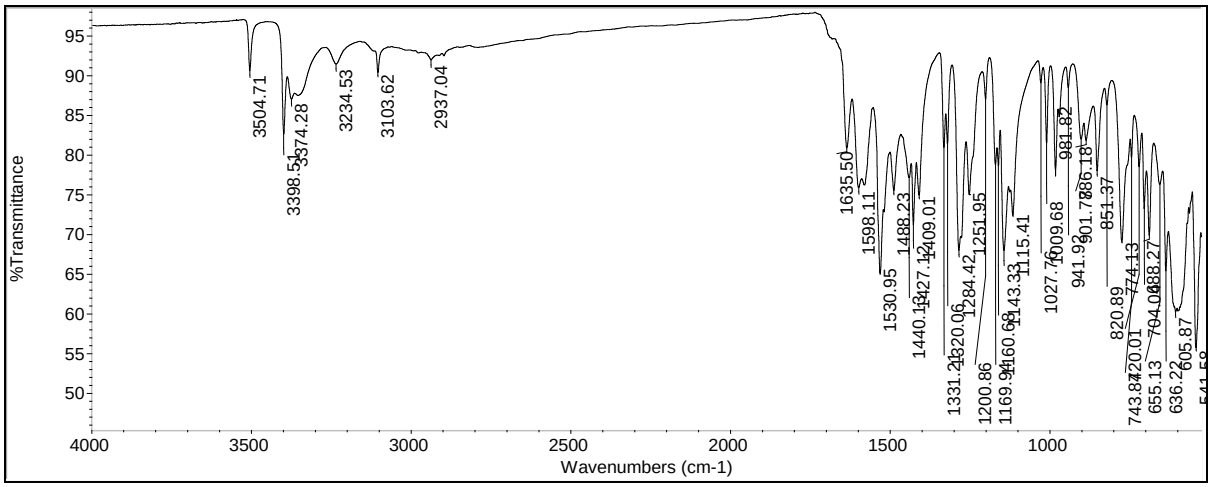

Fig. 11: FTIR Spectrum of HPMC K15M

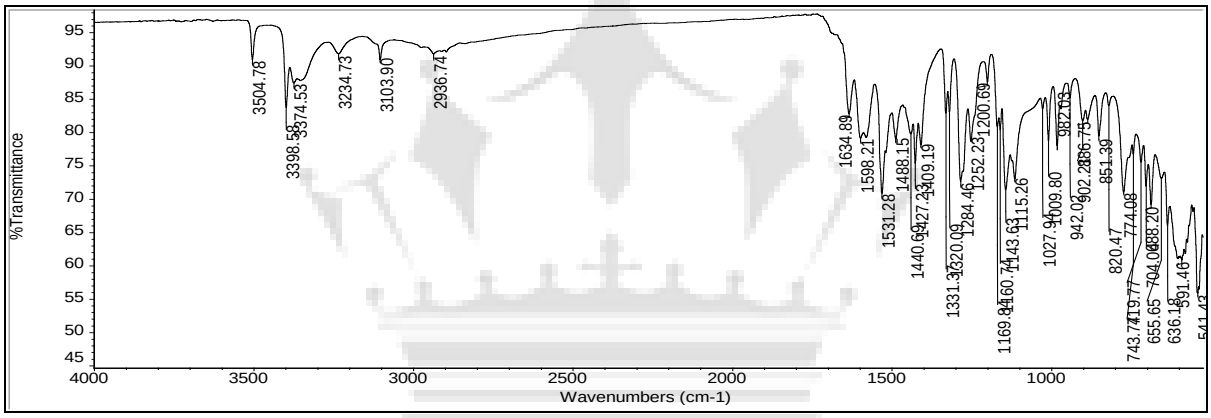

Fig. 12- FTIR Spectrum of Famotidine+HPMC K15M

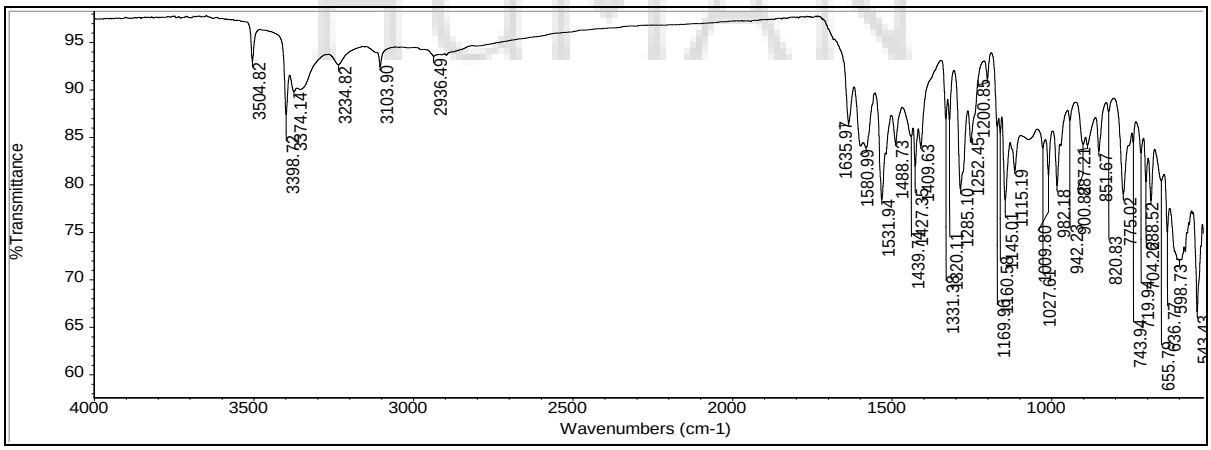

Fig. 13- FTIR Spectrum of Famotidine+Chitosan

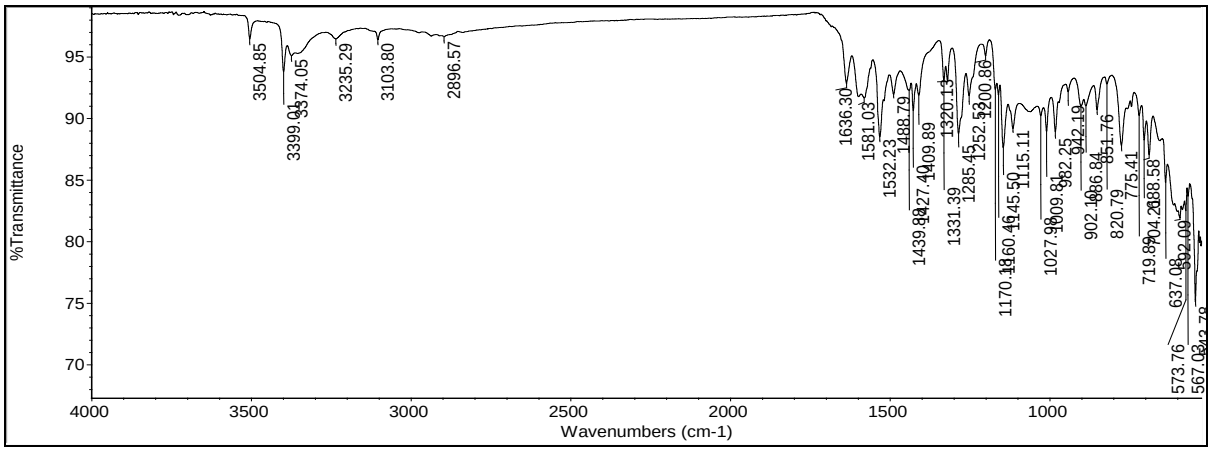

Fig. 14-FTIR Spectrum of Famotidine+HPMC K15M+Chitosan

Table.9 - Interpretation of Drug and Polymer (Fig. 28)

Sr.No.	Wavelength(cm^2)	Interpretation
1	901.78	N-H
2	1331.27	$-SO_2$
3	1635.50	O-C-O
4	2937.04	C-H STRECH
5	3103.62	C-H
6	3234.53	-OH
7	3398.51	-NH
8	35.4.71	$-NH_2$

D. Stability studies:

Table.10- Stability study all formulation Batches

Sr.no	Time	DRUG CONTENT %w/w								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	98.53	97.05	95.53	94.61	97.25	88.02	97.66	85.88	106.90
2	After one Month	90.86	91.26	94.61	93.40	95.43	83.55	96.44	84.72	97.05

E. CONCLUSION

Controlled release gastroretentive floating matrix tablets of Famotidine can be successfully prepared using various polymers like HPMC K15M and Chitosan. The effervescent based floating drug delivery was a promising approach to achieve *in-vitro* buoyancy. The addition of gel forming polymer and gas generating agent sodium bicarbonate along using citric acid was essential to achieve *in vitro* buoyancy. In the present study, an attempt was made to retain the dosage form in stomach for longer period of time. This can be achieved by developing gastro-retentive drug delivery system i.e., floating drug delivery system. These tablets mainly prepared by reduction of lag time and may also increase the bioavailability of the drugs by utilizing the drug to full extent avoiding unnecessary frequency of dosing. For the formulation of floating tablets HPMCK15M and Chitosan were used as matrix forming agent. Other excipients used are PVP, talc, sodium bicarbonate and citric acid (gas generating agent), talc and magnesium stearate (lubricating agent). Fourier transform infrared spectroscopy confirmed the absence of any drug/polymer/excipients interactions.

The prepared floating tablets were evaluated for hardness, weight variation, thickness, friability, drug content uniformity, buoyancy lag time, total floating time, swelling index and *in vitro* dissolution studies. Among all the 9 formulations F1, F2, F3, F4, F4, F6, F8, F9 showed good floating property while formulations F5, F7, showed moderate floating while all the 9 formulations showed controlled drug release. Stability studies were carried out for F2 and F9, both the formulations showed good stability. It was observed that F4 and F5 gave maximum drug release up to 96.29% within 12 hrs. All the 9 formulations were subjected for five different models viz. zero order, first order, Higuchi model, Peppas model, Hix.Crowell. It was revealed that concentration of polymers and gas generating agent had significant influence on drug release and floating ability. Thus conclusion can be made that stable dosage form can be developed for Famotidine for the controlled release .Swelling index study indicates that all the formulations showed significant swelling.

- Sodium bicarbonate has predominant effect on the buoyancy lag time, while HPMC K15M and Chitosan have predominant effect on total floating time and drug release.
- *In-vitro* release rate studies showed that the maximum drug release was observed in F4 and F5 formulations up to 12 hrs.

- The release of Famotidine from the prepared formulations was found to follow Zero order kinetics and Korsmeyer Peppas Kinetics.
- The mechanism of drug release was found to be diffusion controlled.
- Results of the stability studies showed that there were no significant changes in the drug content and physical appearance.
- Combinations of HPMC grades are good polymer systems for the formulation of floating matrix system.
- The drug-polymer compatibility and their compatibility with process condition was evaluated on the basis of FTIR spectroscopy and there was no sign of any interaction between drug and polymers and within the prepared system.
- The prepared floating tablets of Famotidine showed satisfactory physicochemical properties and floating behavior.

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