CODEN (USA): IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF

PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com Research Article

FORMULATION AND EVALUATION OF GASTRO-RETENTIVE EFFERVESCENT FLOATING TABLETS OF FAMOTIDINE HCL

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Abstract:

The objective of the present investigation was to prepare gastro retentive drug delivery systems of Famotodine floating tablets. Famotidine binds competitively to H_2-receptors located on the basolateral membrane of the parietal cell, blocking histamine affects. This competitive inhibition results in reduced basal and nocturnal gastric acid secretion and a reduction in gastric volume, acidity, and amount of gastric acid released in response to stimuli including food, caffeine, insulin, betazole, or pentagastrin. The drug has low bioavailability (40-45%.), shorter biological half life (2.5-3.5 hours) and it has better solubility in the acidic medium. In the preparation of Famotodine floating tablets sodium bicarbonate was incorporated as a gas generating agent. The tablets were formulated using direct compression technology by employing various grades of HPMC polymers such as HPMC K4M, K15M and K100M.The prepared tablets exhibited satisfactory physical parameters and good in vitro buoyancy. The in-vitro drug release of floating tablets followed first order kinetics with non fickian diffusion mechanism. The formulations prepared with HPMC K15 M were evaluated for in vitro floating time, which shows the floating property up to 12 hours. The DSC and FTIR study shows that there is no drug polymer interaction.

Keywords: *Floating Tablets, Famotidine HCl, HPMC*

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Please cite this article in press as B.Heeralal and P.Shashikala, ***Formulation and Evaluation of Gastro-Retentive Effervescent Floating Tablets of Famotidine Hcl****, Indo Am. J. P. Sci, 2016; 3(12).*

INTRODUCTION:

Gastroretentive dosage forms are drug delivery systems which remain in the stomach for an extended period of time and allow both spatial and time control of drug liberation. Basically gastroretentive systems swells following ingestion and is retained in the stomach for a number of hours, while it continuously releases the incorporated drug at a controlled rate to preferred absorption sites in the upper intestinal tract. Their application can be advantageous in the case of drugs absorbed mainly from the upper part of GIT or unstable in the medium of distal intestinal regions. They can also be used beneficially in the local therapy of the stomach. Prolonged gastric retention of the drugs may offer numerous advantages including improved bioavailability, therapeutic efficacy and possible reduction of dosage size[1].

However standard controlled release dosage forms offer only limited advantages for drugs that have an absorption window in the upper small intestinal. (Eg: Levodopa, Furosemide, and Riboflavin). Once emptied from the stomach, the passage through this region is rapid, thus limiting the extent of absorption at this site. In order to increase the bioavailability of this type of drugs, the residence time of the controlled-released dosage forms in the upper GIT needs to be prolonged[2].

Drugs that would benefit from GRDDS

1) CNS drugs (for Parkinson disease, epilepsy, alzheimer and migraine).
2) Anti-viral products (for HIV, herpes and hepatitis) and certain antibiotics.
3) Anti-hypertension drugs.
4) Anti-diabetic agents for Type 2 diabetes.
5) Drugs for local treatment of GI infections and gastric enzyme replacement[3].

MATERIALS AND METHODS:

Famotidine HCl was obtained as gift sample from Zydus Cadila Healthcare, India. HPMC-K4M, K15M, K100M were obtained as gift samples from Danmed Pharmaceutical,Hyd. Microcrystalline cellulose was obtained as gift sample from Aurobindo Pharma, Hyderabad.Magnesium stearate was purchase from Himedia Pvt Ltd, Mumbai, Aerosil was purchased from S.D. Fine Chemicals Pvt Ltd, Mumbai.

Experimental Methodology:

Formulation of Effervescent Floating Tablets of Famotidine HCl[12,13,14]

Procedure for floating tablet preparation:

Floating matrix tablets containing Famotidine Hydrochloride were prepared by direct compression technique using varying concentrations of different grades of polymers.

Direct compression:

Famotidine Hydrochloride (10 mg) and all the ingredients were accurately weighed and passed through sieve # 40. Famotidine Hydrochloride was well mixed with weighed quantity of polymer and then mixed with remaining ingredients i.e., sodium bicarbonate and micro crystalline cellulose in geometric proportions. Mixed homogeneously in a polybag for about 5 -10min.Then lubricated with the previously weighed and sieved magnesium stearate and aerosil to obtain the blend for compression. Then the lubricated blend was subjected to compression on a sixteen station rotary tablet punching machine using 8mm circular standard faced punches.

Table 1: Composition of Famotidine HCl floating tablets containing HPMC K15 M with 20%, 25%, 30% & 35% Sodium Bicarbonate

Ingredients	Quantity (mg) present in formulation			
	F 1	F 2	F 3	F 4
Famotidine HCl	10	10	10	10
Sodium Bicarbonate	40	50	60	70
HPMC K 15 M	70	70	70	70
MCC	75	65	55	45
Aerosil	2.5	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5	2.5
Total (mg)	200	200	200	200

Table 2: Composition of Famotidine HCl floating tablets containing 20% (F 5) 30% (F 6) & 40% (F 7) HPMC K 4 M

Ingredients	Quantity (mg) present in formulation		
	F 5	F 6	F 7
Famotidine HCl	10	10	10
Sodium Bicarbonate	60	60	60
HPMC K 4 M	40	60	80
MCC	85	65	45
Aerosil	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5
Total (mg)	200	200	200

Table 3: Composition of Famotidine HCl floating tablets containing 15 %(F8), 20% (F 9), 30% (F 10) & 40% (F 11) HPMC K 15 M

Ingredients	Quantity (mg) present in formulation			
	F 8	F 9	F 10	F 11
Famotidine HCl	10	10	10	10
Sodium Bicarbonate	60	60	60	60
HPMC K 15 M	30	40	60	80
MCC	95	85	65	45
Aerosil	2.5	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5	2.5
Total (mg)	200	200	200	200

Table 4: Composition of Famotidine HCl floating tablets containing 20% (F 12), 30% (F 13) & 40% (F 14) HPMC K 100 M

Ingredients	Quantity (mg) present in formulation		
	F 12	F 13	F 14
Famotidine HCl	10	10	10
Sodium Bicarbonate	60	60	60
HPMC K 100 M	40	60	80
MCC	85	65	45
Aerosil	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5
Total (mg)	200	200	200

Table 5: Composition of Famotidine HCl floating tablets containing HPMC K 15 M & K 100 M in the ratios of 2:1, 1:1, 1:2

Ingredients	Quantity (mg) present in formulation		
	F 15	F 16	F 17
Famotidine HCl	10	10	10
Sodium Bicarbonate	60	60	60
HPMC K 15 M	40	30	20
HPMC K 100 M	20	30	40
MCC	65	65	65
Aerosil	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5
Total (mg)	200	200	200

- MCC was used as filler in all formulations.
- All the above formulas were compressed at hardness of 3-4kg/cm^2.

Construction of Theoretical release Profile

Theoretical release profile of a drug is constructed when any marketed preparations are not available, to check whether the formulations are releasing the drug similar to the predicted profile. Theoretical release profile of a drug is plotted on basis of the loading dose and the drug availability rate (Raghuram Reddy et al., 2003).The total dose of Famotidine for sustained release formulation was calculated by the following equation

$$D_t = \text{Dose}\ [1+0.693 \times t / t_{1/2}]$$

Where D_t = total dose of drug

Dose = dose of the immediate release part (3.24mg)

t = time (hours) during which the sustained release is desired (12 hours)

$t_{1/2}$ = half life of the drug (4.1 hrs)

For 10 mg dose of Famotidine

Table 6: Theoretical release profile of Famotidine HCl

Time in hrs to be released	Amount of Famotidine (mg)	% Release
0	0	0
1	3.24	32.4
2	3.854	38.54
3	4.468	44.68
4	5.052	50.52
6	6.31	63.1
8	7.538	75.38
10	8.78	87.8
12	9.994	99.94

A) Standard graph of Famotidine hydrochloride

The calibration curve is based on the spectrophotometry.

Standard solution:

Determination of λmax:

Stock solution (1mg/ml) of famotidine was prepared in methanol. This solution was appropriately diluted with 0.1N HCL (pH 1.2) to obtain a concentration of 10µg/ ml. The resultant solution was scanned in the range of 200nm to 400nm on UV-Visible spectrophotometer. The drug exhibited a λmax at 265nm.

Preparation of standard calibration curve of famotidine in 0.1 n HCL :

Famotidine (10 mg) was dissolve in 0.1 N HCl and volume is made up to 100 mL in volumetric flask.1 mL of stock solution (100 µg/ml) was further diluted with 0.1N HCl to obtained solution of 10 µg/mL to 25 µg/ml. Absorbance of each solution was measured at 265 nm using Shimadzu UV-1601 UV/Vis double beam Spectrophotometer (Kyoto, Japan) and 0.1 N HCl as a reference standard. The standard curve was generated for entire range from 10 to 25 µg/ml. The experiment was performed in triplicate and based on average absorbance; the equation for the best line was generated.

Evaluation of Effervescent Floating Matrix Tablets of Famotidine HCl (10 mg)

B) Evaluation of Physical Properties of Tablets [15, 16]

The prepared effervescent floating matrix tablets were evaluated for the following parameters.

i) Tablet thickness

ii) Weight variation

iii) Tablet hardness

iv) Friability

v) Content uniformity

vi) Buoyancy / Floating Test

The in vitro buoyancy was determined by floating lag time, as per the method described by a Rosa et al., 1994. Here, the tablets were placed in a 100-mL beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and to float was determined as floating lag time and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

vii) *Invitro* Drug Release

The dissolution conditions used for studying the drug release from the effervescent floating tablets of Famotidine HCl.

Apparatus : Dissolution test apparatus (USP XXIII)

Method :USP type 2 apparatus (paddle method)

Dissolution medium : 0.1N HCl

Volume : 900 ml

Temperature : 37 ± 0.5 °C

Speed : 50 rpm

λ_{max} : 265 nm

Procedure

The *invitro* dissolution studies were performed for the formulated efferevescent floating tablets of Famotidine HCl over a period of 12 hours, using USP dissolution test apparatus 2 (paddle method) at 50 rpm, [Electro lab , TDT – 082].A minimum of 3 tablets per each batch was tested. The dissolution medium consists of 900 ml of 0.1 N HCl and temp was maintained at 37 ± 0.5 °C. The tablets were placed inside the dissolution vessel. An aliquot (5ml) of sample was withdrawn at specific time intervals of 60, 120, 180, 240, 360, 480, 600 and 720 minutes. The volume of dissolution fluid adjusted to by replacing 5ml of dissolution medium after each sampling. Each sample was analyzed at 265 nm using double beam UV and Visible Spectrophotometer against reagent blank. The drug concentration was calculated using standard calibration curve.

viii) Kinetic Analysis of Dissolution Data

To analyze the *in vitro* release data various kinetic models were used to describe the release kinetics: Zero order rate, First order, Higuchi, Hixson-Crowell cube root.

ix) Calculation of Similarity Factor (f_2)

Different dissolution profiles were compared to establish the effect of formulation or process variables on the drug release as well as comparison

of test formulations to the theoretical release profile. The dissolution similarity was assessed using FDA recommended approaches F2 96.The similarity factor is a logarithmic, reciprocal square root transformation of the sum of squared errors and it serves as a measure of the similarity of 2 respective dissolution profiles. The data were analyzed by the following formula ((Bolton and Bon., 2004)

$$f_2 = 50 \log \{[1+ (1/N) \sum (R_i - T_i)^2]^{-0.5} \times 100\}$$

Where N = number of time points

Ri = % release from marketed product or Theretical release profile

Ti = % release from test formulation at time i

If f_2 value is in between 50-100, it is to be considered that 2 products share similar drug release behaviors.

Fourier transform infrared spectroscopy

The infrared spectra of Famotidine hydrochloride pure drug, physical mixture of drug and excipients and placebo were recorded between 400 to 4000cm^{-1}on FTIR. The IR spectra for the test samples were obtained using KBr disk method using an FTIR spectrometer.

Differrentential scanning colorimetry

Thermal properties of pure drug and the formulation were evaluated by Differrentential scanning colorimetry (DSC) using a diamod (DSC) (Mettler star sw8.10).The analysis were performed at a rate 50c min-1 to 200ºc temperature range under nitrogen flow of 25ml min^{-1}.

RESULTS AND DISCUSSIONS:

Standard curve for Famotidine hydrochloride: Determination of λmax

A solution of 10µg/ml of Famotodine was scanned in the range of 200 to 400nm. The drug exhibited a λmax at 265nm in simulated gastric fluid pH 1.2 and had good reproducibility. Correlation between the concentration and absorbance was found to be near to 0.9992, with a slope of 0.0152.

Calibration curve of Famotidine in 0.1N HCl

Table below shows the calibration curve data of Famotidine in 0.1N HCl of pH 1.2 at 265nm. The figure below shows the standard calibration curve with a regression value of 0.9992, slope of 0.028 and intercept of 0.004 . The curve was found to be linear in the concentration range of 10-25 µg/ml.

CONCENTRATION (µg /ml)	ABSORBANCE
0	0
10	0.155
15	0.231
20	0.309
25	0.38

Table 6 : Standard values of Famotidine 0.1N HCl

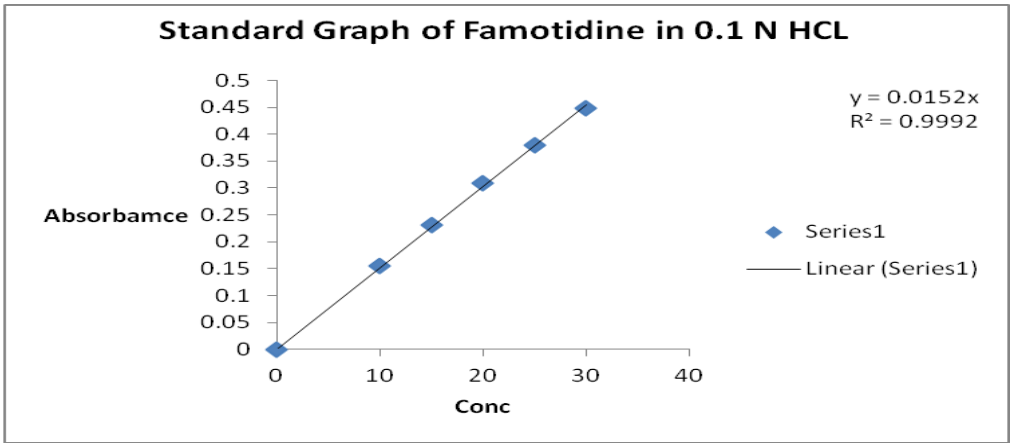


Fig 1: Standard curve of Famotidine hydrochloride in 0.1N HCl

Evaluation of prepared tablets for physical parameters

All formulations were tested for physical parameters like hardness, thickness,weight variation, friability, and found to be with in the pharmacopoeial limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within permissilble limit.

Hardness of the tablet was in between 3-4 kg/cm^2 and was maintained for all the batches in order to minimize the effect of hardness on the drug release because; the effect of polymer concentration is the only area of interest.

Tablet thickness was also used to assess the quality of tablets. Under uniform conditions of manufacture, the total weight of tablet and thickness were linearly related. The thickness of floating tablets ranged from 3.23 to 3.45 mm and linearly correlated with the weight of the tablets.

Drug content uniformity in all formulations was calculated and the percent of active ingredient ranged from 95-98%. The study indicated that all the prepared formulations were good.

Table 7: Physicochemical evaluation of Famotidine HCl tablets formulated using HPMC K4M

Evaluation Parameter	Formulation code			
	F 1	F 2	F 3	F 4
Weight variation (mg)	200±1.8	203±5.7	197±3.8	196±3.9
Tablet Hardness kg/cm^2	3.4±0.9	3.5±0.4	3.3±0.5	3.4±0.3
Tablet diameter (mm)	8±0.01	8±0.03	8±0.02	8±0.01
Thickness (mm)	3.31±0.04	3.18±0.1	3.28±0.02	3.31±0.08
Friability (%)	0.36	0.29	0.31	0.32
Drug Content (%)	97.87±2.3	94.37±0.1	96.39±2.6	98.12±2.1

Evaluation Parameter	Formulation code		
	F 5	F 6	F 7
Weight variation (mg)	202±2.3	205±6.3	198±4.3
Tablet Hardness kg/cm^2	3.5±0.7	3.4±0.6	3.5±0.5
Tablet diameter (mm)	8±0.02	8±0.02	8±0.02
Thickness (mm)	3.40±0.05	3.20±0.09	3.32±0.05
Friability (%)	0.40	0.32	0.35
Drug Content (%)	98.91±2.8	95.42±.09	97.41±2.3

Table 8: Physicochemical evaluation of Famotidine HCl tablets formulated using HPMC K15M

Evaluation Parameter	Formulation code			
	F 8	F 9	F 10	F 11
Weight variation (mg)	205±5.6	202±3.3	202±6.2	201±4.3
Tablet Hardness kg/cm^2	3.5±0.2	3.5±0.5	3.5±0.3	3.5±0.5
Tablet diameter (mm)	8±0.02	8±0.02	8±0.02	8±0.02
Thickness (mm)	3.33±0.02	3.26±0.02	3.44±0.16	3.40±0.05
Friability (%)	0.38	0.41	0.21	0.38
Drug Content (%)	97.69±2.4	97.35±1.7	96.55±2.4	94.48±1.8

Table 9: **Physicochemical evaluation of Famotidine HCl tablets formulated using HPMC K100M**

Evaluation Parameter	Formulation code		
	F 12	F 13	F 14
Weight variation (mg)	205±2.3	198±2.9	205±8.3
Tablet Hardness kg/cm^2	3.6±0.4	3.5±0.5	3.5±0.5
Tablet diameter (mm)	8±0.02	8±0.02	8±0.02
Thickness (mm)	3.20±0.09	3.32±0.05	3.34±0.02
Friability (%)	0.41	0.52	0.34
Drug Content (%)	95.42±.09	95.99±1.3	98.91±2.8

Table 10: Physicochemical evaluation of Famotidine HCl tablets formulated using Combination of Polymers HPMC K15 M & K100M

Evaluation Parameter	Formulation code		
	F 15	F 16	F 17
Weight variation (mg)	203±3.8	201±4.9	204±8.3
Tablet Hardness kg/cm^2	3.6±0.4	3.5±0.3	3.5±0.1
Tablet diameter (mm)	8±0.02	8±0.02	8±0.02
Thickness (mm)	3.31±0.02	3.36±0.02	3.22±0.02
Friability (%)	0.45	0.25	0.28
Drug Content (%)	98.46±3.2	97.41±2.1	97.97±2.6

Effect of sodium bicarbonate concentration on floating lag time

The tablets were prepared by using different concentrations of sodium bicarbonate along with same concentrations of remaining other components (F1, F2, F3, F4 Formulations).

Table 11: Effect of sodium bicarbonate concentration on floating lag time

Total weight of tablet 200 mg.

Formulation	NaHCO3 (mg)	Concentration (%)	Floating lag time (sec)
1	40	20	170 - 176
2	50	25	148 -157
3	60	30	125 -140
4	70	35	90 - 105

From the results shown in Table 19 it can be conclude that as concentration of sodium bicarbonate increased the floating lag time decreased (F1, F2, F3, F4 formulations mentioned in table). Both were inversely proportion. The concentration of sodium carbonate at 20% shown increased lag time when compared with 25 and 30 % respectively. This is due to the fact that as sodium bicarbonate increased the ability to produce CO_2 in the formulation was also increased which made tablets buoyant. The intermediate concentration of sodium bicarbonate was selected because it showed less lag time and the tablets remained rigid throughout the study where as the tablets with higher concentration showed very less lag time but the tablet integrity was lost during the study of 6 – 8 hours.

Table 12: Floating Properties of Famotidine HCl tablets

Formulations	Floating lag time(sec)	Floating time (hrs)
F1	170 - 176	4
F2	148 -157	4
F3	125 -140	4
F4	90 - 105	4
F5	450	4
F6	435	6
F7	430	8
F8	126	> 12
F9	120	> 12
F10	130	> 12
F11	136	> 12
F12	128	> 12
F13	139	> 12
F14	140	> 12
F15	139	> 12
F16	135	> 12
F17	138	> 12

***In vitro* drug release studies of Famotidine HCl floating tablets formulated using HPMC K4M**

The *In vitro* dissolution studies were conducted in 900ml of 0.1 N HCl using USP-II apparatus. The results indicated that as the polymer concentration of HPMC K4M increases the drug release rate was retarded. F-5 formulation containing 20% of polymer retards the drug release only for 4 hours. F-6 formulation containing 30% of polymer retarded the drug release for about 6 hours, F-7 formulation containing 40% of polymer retards the drug release for 8 hours .The formulations were failed to retard the drug release up to 12 hours. Further the tablet integrity was also poor, total buoyancy was found to be 6-8 hours. So attempts were made to improve the retardation of drug release, total buoyancy time as well as tablet integrity by employing high viscosity grade polymers like HPMC K15 M,HPMC K 100M and combinations of both polymers.

Table 13: Cumulative percent drug release of formulations with HPMC K4M

Sampling time (hr)	Formulation code		
	F 5	**F 6**	**F 7**
1	23.94±2.04	20.42±1.21	18.22±2.12
2	45.45±1.98	35.54±1.89	30.32±2.12
3	55.15±1.78	58.44±1.90	45.35±2.13
4	97.65±2.12	76.25±2.09	62.23±1.78
6		98.45±2.67	83.51±2.31
8			97.23±1.97

Data represents mean ± SD (n=3)

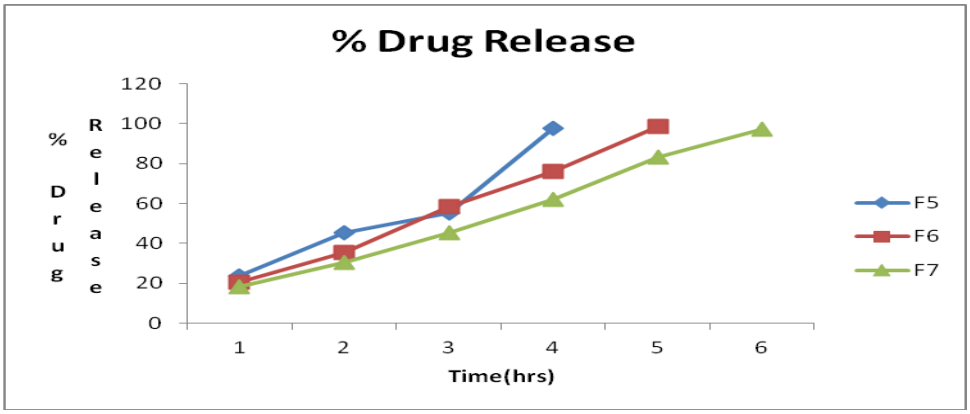


Fig 2: Cumulative % drug release of HPMC K4M formulations

***In vitro* drug release studies of Famotidine HCl floating tablets formulated using HPMC K15M**

The *In vitro* dissolution studies were conducted in 900ml of 0.1 N HCl using USP-II apparatus. The results indicated that as the polymer concentration of HPMC K15M increases the drug release rate was retarded. F-8 formulation containing 15% of polymer has showed 100 % drug in 10 hours. F-9, F-10 & F-11 formulations containing 20%, 30% and 40% of polymer retarded the drug release up to 12 hours.

The dissolution data of formulations were fitted to various kinetic models such as zero-order, first-order, and Higuchi, and Peppas models. Table 22 describes the invitro drug release kinetic of Famotidine HCl. The release kinetics of all the formulations follows first order kinetics.

The diffusion exponent n values of Korsmeyer-Peppas model of the best formulations are in between 0.55-0.85. Therefore the most probable mechanism that the release patterns of the formulations followed was non-fickian diffusion or anomalous diffusion.

The results of in vitro dissolution and release kinetics of the prepared Famotidine HCl floating matrix tablets were summarized in the table 22 .Figure 14 shows the plots of the cumulative % release vs time profile of the prepared matrix tablets.

Sampling time (hr)	Table 14: Cumulative % drug release of formulations with HPMC K15 M Formulation code			
	F 8	F 9	F 10	F 11`
0	0	0	0	0
1	24.01±1.72	22.12±2.12	8.56±2.11	7.13±2.12
2	34.23.06±2.2	30.03±2.31	17.18±1.78	12.27±2.09
3	43.94±2.1	39.18±1.96	28.19±1.94	19.42±1.89
4	64.97±2.23	45.44±1.89	36.42±2.12	29.24±1.98
6	84.60±1.98	60.83±2.10	48.77±1.75	44.86±2.12
8	97.15±1.68	73.25±2.21	62.27±1.51	57.70±1.89
10	100.01±1.73	84.67±2.12	75.21±2.09	71.28±2.06
12		95.14±1.98	86.31±1.98	81.64±1.79
Kinetics				
Zero order (r^2)	0.885	0.919	0.932	0.949
First order(r^2)	0.958	0.988	0.977	0.969
Higuchi(r^2)	0.935	0.922	0.916	0.936
Peppas(n)	0.62	0.74	0.56	0.63

Data represents mean ± SD (n=3)

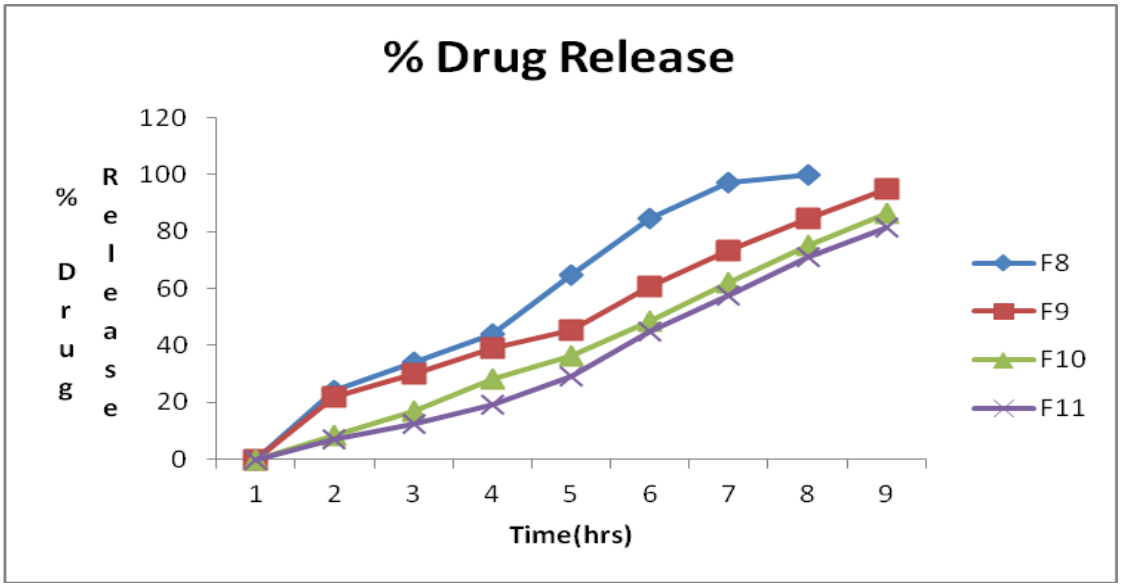


Fig 3: Cumulative % drug release of HPMC K 15 M formulations

5.6. *In vitro* drug release studies of Famotidine HCl floating tablets formulated using HPMC K 100 M

The *In vitro* dissolution studies were conducted in 900ml of 0.1 N HCl using USP-II apparatus. The results indicated that as the polymer concentration of HPMC K100M increases the drug release rate was retarded. F-12 formulation containing 20 % of polymer has showed 91 % drug release in 12 hours. F-13 & F-14 formulations containing 30% and 40% of polymer also retarded the release up to 12 hours.

The dissolution data of formulations were fitted to various kinetic models such as zero-order, first-order, and Higuchi, and Peppas models. Table 23 describes the invitro drug release kinetic of Famotidine HCl. The release kinetics of all the formulations follows first order kinetics.

The results of in vitro dissolution and release kinetics of the prepared Famotidine HCl floating matrix tablets were summarized in the table 23. Figure 15 shows the plots of the cumulative % release vs time profile of the prepared matrix tablets.

The diffusion exponent n values of Korsmeyer-Peppas model of the best formulations are in between 0.55-0.85. Therefore the most probable mechanism that the release patterns of the formulations followed was non-fickian diffusion or anomalous diffusion.

Table 15: Cumulative % drug release of formulations with HPMC K100 M

Sampling time (hr)	Formulation code		
	F 12	**F 13**	**F 14**
0	0	0	0
1	6.92±2.11	5.37±2.12	4.85±2.31
2	11.99±1.78	10.28±2.12	9.12±1.96
3	18.93±1.94	16.81±2.13	13.74±1.89
4	29.71±2.12	26.85±1.78	21.34±2.10
6	38.05±1.75	36.93±2.31	30.58±2.21
8	55.09±1.51	48.34±1.97	44.24±2.12
10	75.80±2.09	69.05±2.21	60.99±1.98
12	91.09±1.78	82.65±2.09	75.80±2.23
Kinetics			
Zero order (r^2)	0.936	0.932	0.908
First order(r^2)	0.962	0.952	0.946
Higuchi(r^2)	0.926	0.906	0.923
Peppas(n)	0.67	0.64	0.59

Data represents mean ± SD (n=3)

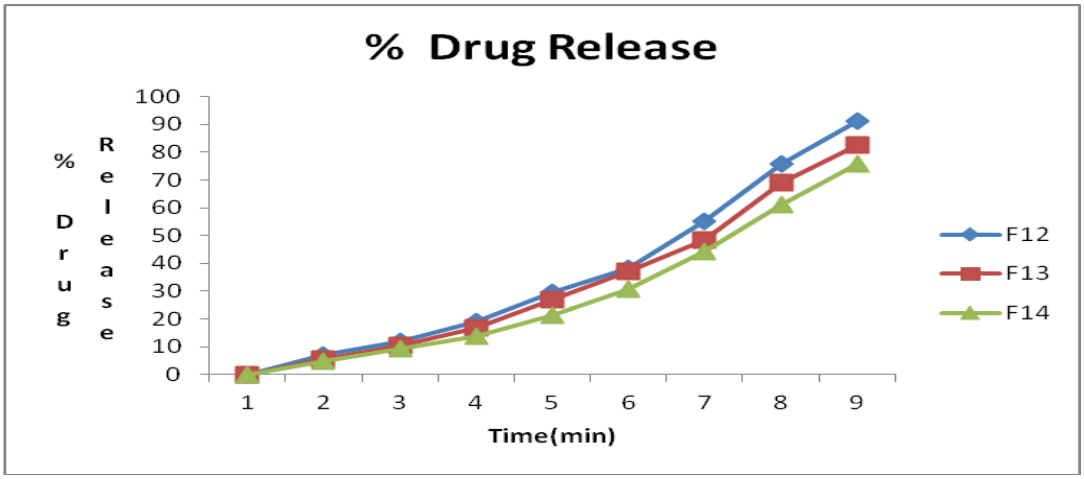


Fig 4: Cumulative % drug release of HPMC K 100 M formulations

***In vitro* drug release studies of Famotidine HCl floating tablets formulated using combinations of polymers HPMC K15 M& K 100 M**

The *In vitro* dissolution studies were conducted in 900ml of 0.1 N HCl using USP-II apparatus. Drug release profiles of the formulations containing combinations of HPMC K 15M and K100M (F15, F16, F17) were reported. The polymers were in 2:1, 1:1 and 1:2 ratios respectively. All the three formulations have shown more retardation extending the drug release up to 12 hours.

The dissolution data of formulations were fitted to various kinetic models such as zero-order, first-order, and Higuchi, and Peppas models. Table 24 describes the invitro drug release kinetic of Famotidine HCl. The release kinetics of all the formulations follows first order kinetics.

The diffusion exponent n values of Korsmeyer-Peppas model of the best formulations are in between 0.55-0.85. Therefore the most probable mechanism that the release patterns of the formulations followed was non-fickian diffusion or anomalous diffusion.

Table 16: Cumulative % drug release of formulations with combinations of HPMC K 15 M & K 100 M
Data represents mean ± SD (n=3)

Sampling time (hr)	**Formulation code**		
	F 15	**F 16**	**F 17**
0	0	0	0
1	8.27±2.12	6.19±2.11	5.87±2.12
2	12.72±2.12	11.45±1.78	10.81±2.31
3	20.37±2.13	17.50±1.94	16.74±1.96
4	32.47±1.78	30.88±2.12	26.74±1.89
6	44.42±2.31	41.24±1.75	34.46±2.10
8	59.08±1.97	55.73±1.81	50.90±2.21
10	74.21±2.12	71.28±2.09	67.20±2.12
12	87.43±2.09	82.65±1.78	76.10±1.98
Kinetics			
Zero order (r^2)	0.913	0.868	0.894
First order(r^2)	0.973	0.941	0.939
Higuchi(r^2)	0.926	0.910	0.915
Peppas(n)	0.69	0.56	0.54

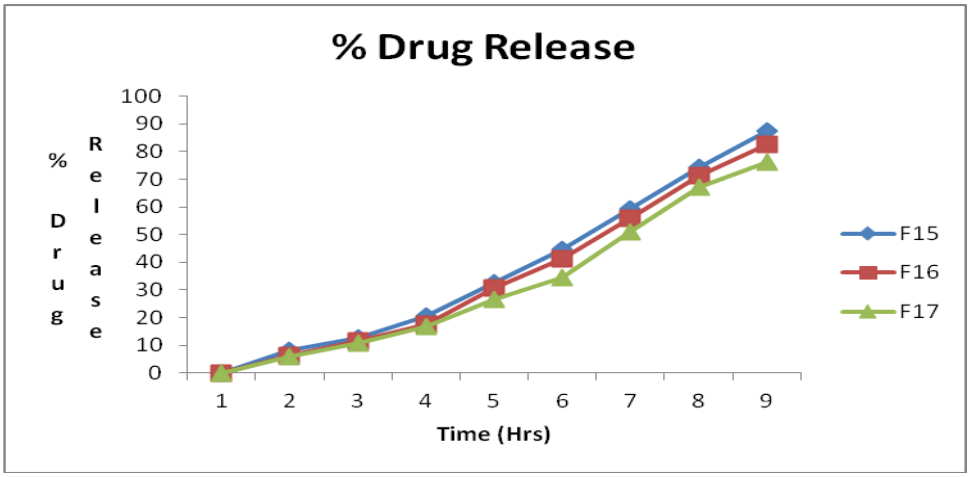


Fig 5: Cumulative % drug release of formulations with combinations of HPMC K 15 M & K 100 M

5.8. Selection of formulations for further study

Some formulations were selected from the dissolution release data and release kinetics. The formulation containing HPMC K15M in 20% conc (F-9) retarded the drug release up to 12 hours and showed above 95 % drug release in 12hours. The drug release was also retarded in case of formulations prepared with polymer HPMC K100M (F12) in the conc of 20%, showed maximum of about 91 % drug release in 12 hours. Where as the formulation containing combination of polymers HPMC K15 M & K100 M in 2:1 ratio (F-15) retarded the drug release at optimum rate and showed above 87% drug release in 12 hours. Hence the formulations F-9,F -12 & F-15 were selected for the comparative study.

***In vitro* buoyancy studies**

In vitro buoyancy study was evaluated for the selected formulations (F-9 & F-15). The tablets were dropped into 200 ml of 0.1 N HCl taken in 250 ml of beaker. The tablets were observed for the floating time. Digital photographs were taken at initial, 2min, 2nd, 4th, 8th and 12th hour. The floating matrix tablets of both formulations were floats about 12 hours and more in the media. Figure 17shows the photo graphs of floating property in the 0.1 N HCl.

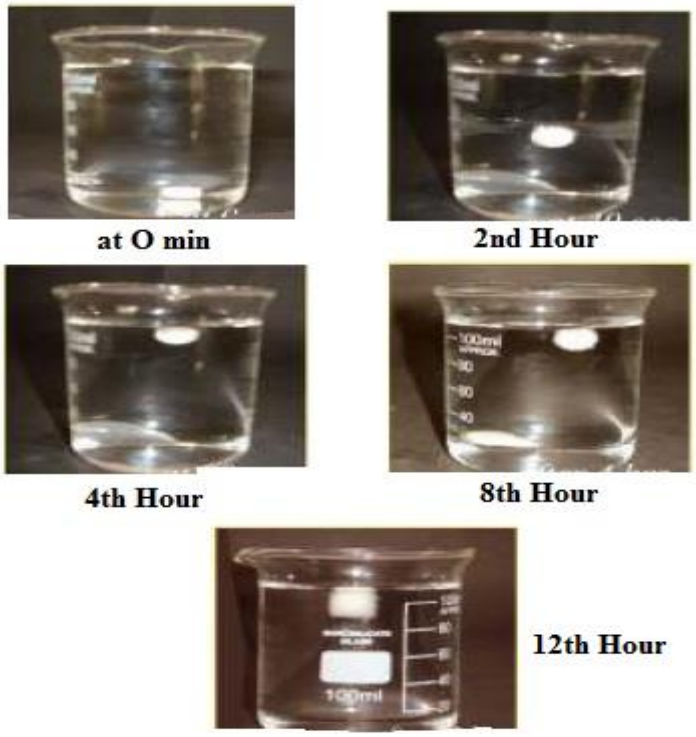


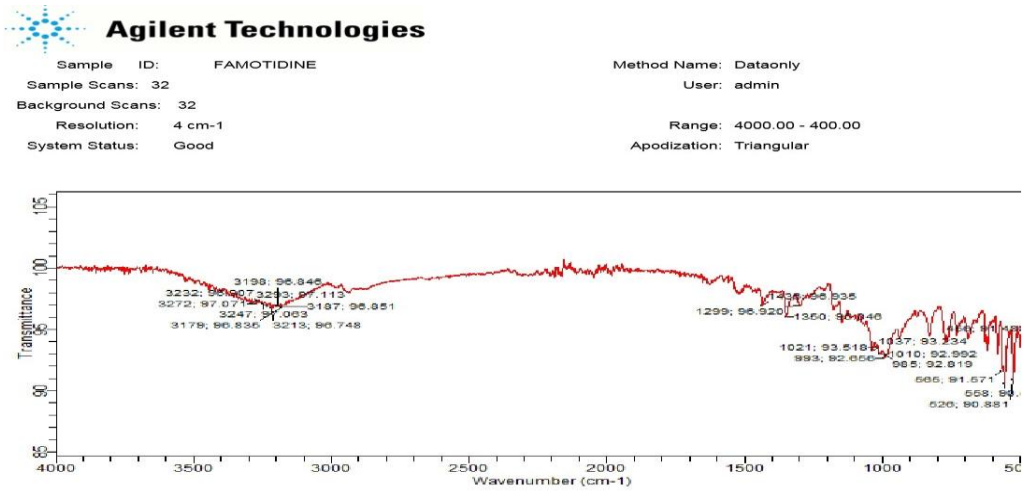
Fig 6: *In-vitro* buoyancy study of Famotidine floating tablet.

Fourier Transform Infrared spectroscopic studies (FTIR)

FTIR spectral analysis

A base line correction was made using dried potassium bromide. Weighed amount of the drug was mixed thoroughly with potassium bromide (dried at 40°-50° C) which was then compressed under 10 ton pressure in a hydraulic press to form a pellet which was then scanned from 4000–400 cm-1 using FTIR 410 PC spectrophotometer. The same procedure was repeated for polymers and formulations. The FTIR spectrum of Famotidine was compared with the FTIR spectrum of Famotidine and polymers show no significant interaction between drug and polymers. The obtained spectra were shown in the figure

A



B

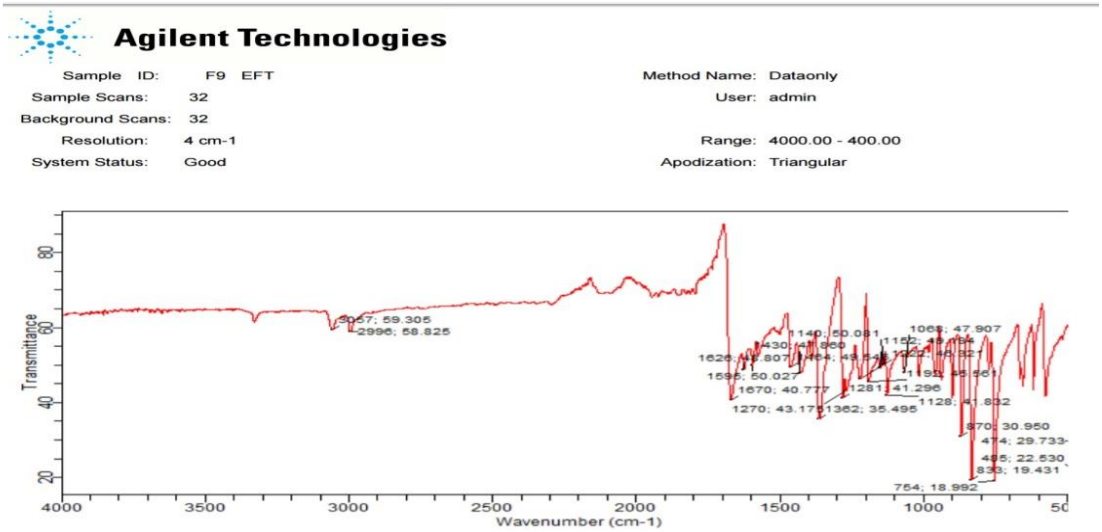


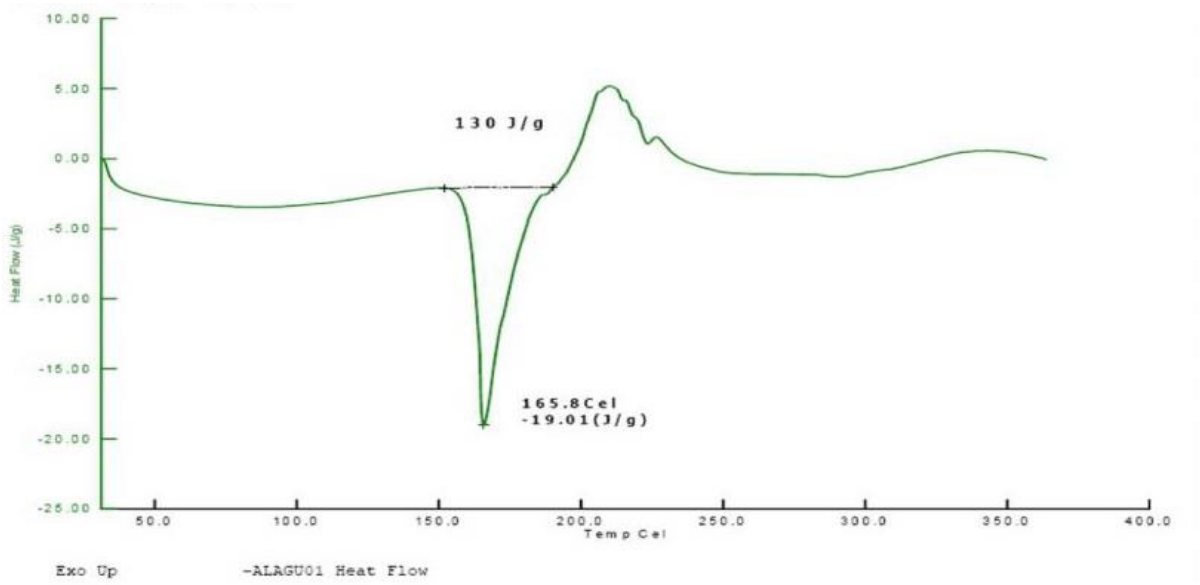
Fig 7: FTIR spectra of (A) Model drug Famotidine HCl, (B) Drug loaded optimized formulation.

Differential scanning calorimetric study (DSC)
DSC study was conducted on the selected formulation. DSC thermogram of pure Famotidine HCl shows sharp endothermic peak at 165.8 °C. Similar endothermic peaks were obtained at 165.2 °C for the formulation prepared with HPMC K15 M, at 165.2°C for the formulation prepared with combination of HPMC K15 M & K100 M The DSC thermograms were given in the following section.

Table 17: DSC melting points of the selected formulations.

Formulations	DSC melting point in °C
Pure Famotidine HCl	165.8
Famotidine+ Polymer mix	165.3

A



B

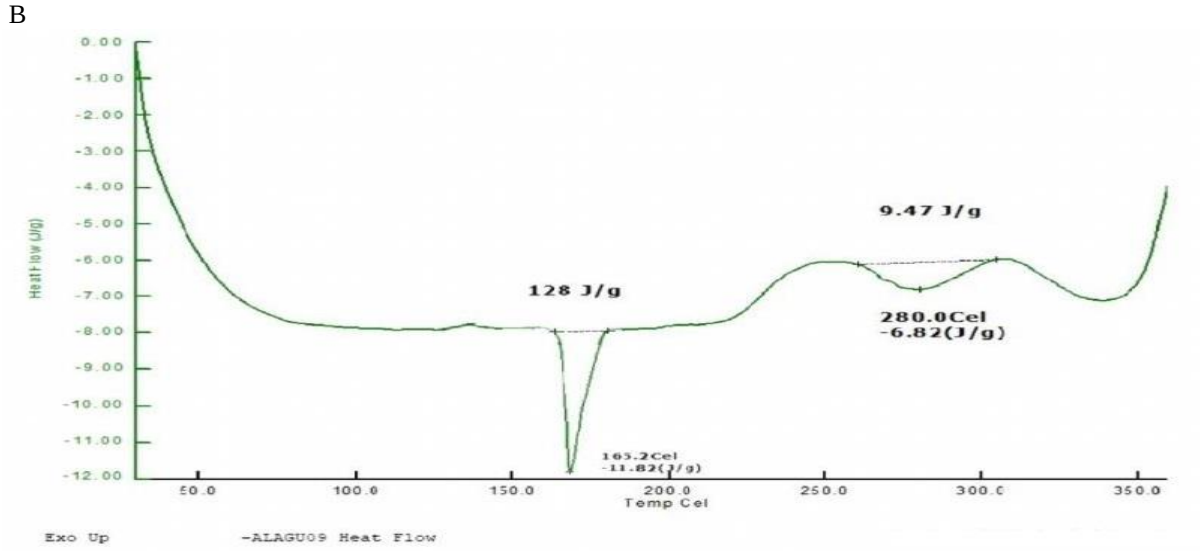


Fig 7: DSC Thermograms of (A) Pure drug, (B) Drug +Polymer mix,

CONCLUSIONS:

In conclusion, the effervescent based FDDS is a promising approach to achieve *in vitro* buoyancy by using gel forming polymers HPMC K15M, HPMC K 100 M and combination of both the polymers in low concentration by employing Sodium bicarbonate as gas generating agent. Among the various FDDS formulations studied, the formulation prepared with HPMC K15 M in the concentration of 20% showed the best result in terms of the required lag time (120 sec) and floating duration of 12 h and releasing 95.14 ± 1.98% of the drug in 12 h and is considered as the ideal formulation. The dosage form can control the release, avoid dose dumping and extend the duration of action of a drug with prolonged floating time.

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