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Original Research Article

FORMULATION AND EVALUATION OF FLOATING TABLETS OF FAMOTIDINE

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ABSTRACT

The objective of the present investigation is to formulate floating tablets of Famotidine. A histamine H_2 receptor antagonist widely prescribed in ulcers like duodenal and gastric Ulcer. The short biological half-life (2.5 - 4 hours) and maximum absorption in initial part of small intestine, colonic metabolism of Famotidine favors' development of gastro retentive floating dosage form. In the present study Famotidine floating tablets were prepared by effervescence method using sodium bicarbonate as a gas generating agent. The tablets were formulated using direct compression technology by employing polymers like HPMC K4M, HPMC K15M, HPCM K 100M and carbopol 934p. The drug-excipient compatible studies were performed by FTIR, The FTIR study revealed that there is no drug-excipient interaction. The prepared floating tablets were evaluated for various physicochemical parameters such as flow properties, hardness, weight variation, friability, *in vitro* buoyancy (floating lag time, total floating time), swelling studies, drug content and *in-vitro* drug release. The *in vitro* drug release pattern of Famotidine floating tablets was fitted to different kinetic models which showed highest regression for zero order kinetics with higuchi mechanism. Out of all formulations the one prepared with carbopol 934p and HPMC K100Mcombination was optimized based on desired sustained release time (12hrs) followed by acceptable swelling and floating properties.

Key words: Famotidine, Floating tablets, HPMC, Carbopol 934p, Sodium bicarbonate, direct compression, sustained release.

INTRODUCTION

The design of oral control drug delivery systems (DDS) should be primarily aimed to achieve more predictable and increased bioavailability [1]. Approximately 505 of the drug available in the market are oral DDS and these systems have more advantages due to patient's acceptance and ease of administration. Nowadays most of the pharmaceutical scientist is involved in developing the ideal DDS. This ideal system should have advantage of single dose for the whole duration of treatment and it should deliver the active drug directly at the specific site. Scientists have succeeded to develop a system and it encourages the scientists to develop control release systems. Control release implies the predictability and reproducibility to control the drug release, drug concentration in target tissue and optimization of the therapeutic effect of a drug by controlling its release in the body with lower and less frequent dose [2,3]. Under certain circumstances prolonging the gastric retention of a delivery system is desirable for achieving greater therapeutic benefit of the drug substances. For example, drugs that are absorbed in the proximal part of the gastrointestinal tract [4], and the drugs that are less soluble or are degraded by the alkaline pH may benefit from the prolong gastric retention [5,6]. In addition, for local and sustained drug delivery to the stomach and the proximal small intestine to treat certain conditions, prolonging gastric retention of the therapeutic moiety may offer numerous advantages including improved bioavailibility, therapeutic efficacy and possible reduction of the dose size [7,8]. Famotidine is a competitive, reversible inhibitor of the action of histamine at the histamine H_2-receptors on the basolateral membrane of parietal cells, including receptors on the gastric cells. The H_2-receptor antagonist predominantly inhibits basal acid secretion, which accounts for its efficacy in suppressing nocturnal acid secretion. Famotidine is not an anticholinergic agent. Famotidine is having a half-life of 2.5-4 hrs. Famotidine is 40-50 % absorbed after oral administration [9].

MATERIALS AND METHODS

Materials:

Famotidine was received as gift sample from Natco Pharma Ltd, Hyderabad. Mico crystalline cellulose (PH 101 and PH 102) from Brahmar cellulose Pvt Ltd., Cuddalore, HPMC K4M HPMC K15M, HPMC K100Mfrom S.D Fine Chem., Mumbai, Carbopol 934p, Sodium bicarbonate were obtained from Signet chemical corporation Pvt Ltd.Mumbai, Magnesium stearate and Lactose were obtained from Vijilak pharma, Mumbai. All the reagents and chemicals used were of analytical grade.

Pre compression parameters:

1. Angle of repose: Angle of repose is defined as the maximum angle possible between the surface of a pile of the

powder and the horizontal plane. The flow characteristics are measured by angle of repose.

$$\theta = \tan^{-1} h/r$$

Where h = height of pile, r = radius of the base of the pile = angle of repose.

Angle of repose below 25^0 indicates an excellent powder flow.

2. Bulk density: The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the part of the interparticulate void volume. It is expressed as gm/ml and calculated using the equation.

$$P = W/V_b$$

Where P = bulk density. W = mass of the powder blend. V_b = bulk volume of powder blend.

3. Tapped density: Tapped density is the ratio of mass of powder to the tapped volume. It is calculated using the following equation and expressed as gm/ml.

$$P_{b,\,max} = W/V_{50}$$

Where $P_{b,\,max}$ = tapped density, W = mass of the powder blend.,V_{50} = volume of powder blend at 50 taps.

4. Carr's consolidation index:

It is defined as:

$$\text{Consolidation Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

5. Hausner's ratio: It is defined as

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

METHOD: Floating matrix tablets containing Famotidine were prepared by direct compression technique using varying concentrations of different grades of polymers with sodium bicarbonate. All the ingredients except magnesium stearate were blended in glass mortar uniformly. After sufficient mixing of drug as well as other components, magnesium stearate was added and further mixed for additional 2-3 minutes. The tablets were compressed with 8mm punch using hydraulic press. The weight of the tablets was kept constant for formulations F1 to F18.

EVALUATION OF TABLETS

Tablet weight variation

Twenty tablets were randomly selected and accurately weighed and their average weight is calculated,such that each tablet weight should within the range of ±5% .Results are expressed as mean values ± SD.

Tablet hardness: The Hardness of tablets was tested using Pfizer hardness tester.

Tablet thickness

A vernier caliper was used to determine thickness of 10 randomly selected tablets. Results are Expressed as mean values

***In Vitro* Buoyancy Studies**

The *in vitro* buoyancy was determined by floating lag time as per the method

described by Rosa et al. Briefly the tablets were placed in a 200-mL of 0.1 N HCl, maintained in a water bath at 37±0.50C. The time required for the tablet to rise to the surface and float was determined as Floating Lag Time (FLT) and the time period up to which the tablet remained buoyant is determined as Total Floating Time (TFT). The *in vitro* buoyancy time for all the formulation were reported.

Drug content uniformity

Ten tablets were individually weighed and crushed. A quantity of powder equivalent to the mass of one tablet (400 mg) was extracted in 100 mL of 0.1N HCl. The solution was centrifuged at 3000 rpm for 15 min. The drug content was analyzed at 314 nm using a UV/ visible spectroscopy after suitable dilution with 0.1 N HCl.

Tablet friability

According to the BP specifications [12] 10 tablets were randomly selected and placed in the

Drum of a tablet friability test apparatus and rotated 100 times in 4 min at 25 Rpm. The percent weight loss was calculated for all formulation and was reported.

Water Uptake Studies

The swelling index of tablet was determined by placing the tablets in 200 ml beaker using 0.1 N HCl. After every one hour up to 12 hours, each tablet was removed and blotted with tissue paper to remove the excess water and weighed on the balance. The swelling index is expressed as a percentage and was calculated from the equation Swelling Index

$$\mathbf{(S.I.) = \{(Wt\text{-}Wo)/Wo\} \times 100}$$

Where, Wt = weight of tablet at time t Wo = weight of tablet before immersion.

***In- vitro* Drug release studies:**

Dissolution test was carried out using USP XXIV rotating paddle method (apparatus 2). The stirring rate was 50 rpm. 0.1 N hydrochloric acid was used as dissolution medium (900ml). It was maintained at 37 ± 1˚C. Samples of 5ml were withdrawn at predetermined time intervals, filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably diluted with dissolution fluid, wherever necessary and were analyzed for the Nizatidine at 314 nm by using a double beam UV spectrophotometer.

RESULTS

Table.1.Formulation of Famotidine floating tablets

Ingredients (in mgs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18
Famotidine	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
HPMC K 4 M	15	-	-	-	22.5	-	-	-	30	-	-	-	15	15	15	-	-	-
HPMC K 15M	-	15	-	-	-	22.5	-	-	-	30	-	-	15	-	-	15	15	-
HPMC K 100M	-	-	15	-	-	-	22.5	-	-	-	30	-	-	15	-	15	-	15
Carbopol 934	-	-	-	15	-	-	-	22.5	-	-	-	30	-	-	15	-	15	15
Sodium bicarbonate	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15
MCC PH 101	97	97	97	97	89.5	89.5	89.5	89.5	82	82	82	82	82	82	82	82	82	82
Mag.steavate	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Total	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150

Table.2.Pre compression parameters

Powder blend	Angle of Repose (°)	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Compressibility Index (%)	Hausner ratio
F1	24°.80±0.45	0.180±0.02	0.155±0.05	16.1±0.09	1.192±0.01
F2	26°.77±0.81	0.110±0.00	0.130±0.01	15.3±0.28	1.181±0.00
F3	25°.28±0.56	0.090±0.08	0.102±0.04	11.7±0.18	1.138±0.09
F4	28°.56±0.48	0.105±0.51	0.126±0.07	16.6±0.12	1.2±0.12
F5	29°.88±0.77	0.129±0.42	0.146±0.25	11.6±0.25	1.131±0.11
F6	25°.80±0.89	0.114±0.21	0.135±0.21	15.5±0.041	1.184±0.21
F7	26°.47±0.77	0.182±0.11	0.148±0.51	10.8±0.00	1.121±0.41
F8	24°.28±0.85	0.135±0.12	0.154±0.82	12.3±0.04	1.140±0.07
F9	26°.56±0.75	0.144±0.09	0.162±0.21	11.1±0.11	1.12±0.45
F10	28°.88±0.98	0.106±0.07	0.120±0.51	11.6±0.06	1.13±0.44
F11	26°.80±0.78	0.129±0.00	0.144±0.05	10.4±0.04	1.116±0.09
F12	25°.41±055	0.121±0.02	0.142±0.14	14.7±0.12	1.17±0.08
F13	26°.12±0.78	0.128±0.05	0.147±0.07	12.9±0.11	1.148±0.04
F14	27°.28±0.65	0.109±082	0.129±0.09	15.5±0.21	1.18±0.02
F15	28°.44±0.78	0.181±0.21	0.154±0.14	14.9±0.08	1.17±0.00
F16	24°.90±0.98	0.121±0.12	0.146±0.45	17.1±0.05	1.20±0.01
F17	27°.41±0.78	0.116±0.07	0.138±0.16	15.9±0.00	1.18±0.05
F18	26°.42±0.87	0.126±0.05	0.151±0.21	16.5±0.01	1.198±0.08

Table.3.Post compression parameters

Batch No.	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight variation (%)	Drug content (%)
F1	5.16 ±0.01	4.5 ±0.47	0.41	0.16 ±1.29	97.01±0.21
F2	5.15 ±0.02	4.4 ±0.1	0.40	0.41 ±1.12	98.85±0.44
F3	5.14 ±0.01	4.4 ±0.82	0.86	0.50 ±1.74	99.50±0.20
F4	5.16 ±0.01	4.8±0.42	0.88	0.05 ±1.37	97.40±0.14
F5	5.15 ±0.08	4.2±0.41	0.87	0.10 ±0.18	99.40±0.54
F6	5.12 ±0.06	4.1±0.54	0.88	0.55 ±0.18	98.01±0.24
F7	5.16 ±5.15	4.2±0.82	0.42	0.85 ±0.65	99.21±0.41
F8	5.15 ±0.02	4.8±0.65	0.88	0.08 ±0.11	98.69±0.87
F9	5.16 ±0.08	4.4±0.41	0.89	0.68 ±0.85	98.98±0.55
F10	5.18 ±0.01	4.5±0.85	0.87	0.65 ±0.49	98.40±0.11
F11	5.12 ±0.06	4.2±0.82	0.86	0.50 ±0.74	99.21±0.05
F12	5.14 ±0.01	4.4±0.41	0.41	0.10 ±0.18	98.85±0.07
F13	5.12 ±0.06	4.8±0.42	0.87	0.41 ±0.12	98.50±0.08
F14	5.16 ±0.01	4.4 ±0.1	0.86	0.65 ±0.29	99.40±0.05
F15	5.14 ±0.01	4.5 ±0.47	0.87	0.85 ±0.65	98.69±0.50
F16	5.16 ±5.15	4.8±0.65	0.88	0.55 ±0.18	98.85±0.12
F17	5.18 ±0.01	4.2±0.41	0.40	0.10 ±0.18	98.01±0.87
F18	5.14 ±0.01	4.2±0.41	0.87	0.05 ±0.37	97.01±0.55

Table.4.Cumulative % Drug Released from Tablet Formulations F1 to F9

Time in hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	25.24±0.51	24.30±0.84	20.14±0.78	26.95±0.21	24.94±0.84	20.12±0.25	22.12±0.47	23.73±0.51	20.40±0.31
2	48.67±0.21	48.63±0.41	49.23±0.41	50.12±0.45	49.57±0.19	43.22±0.28	45.63±0.30	39.47±0.41	32.62±0.27
3	59.43±0.09	60.21±0.12	65.95±0.78	71.23±0.44	63.27±0.76	57.82±0.26	60.55±0.46	59.84±0.20	45.26±0.39
4	67.56±0.75	72.54±0.45	83.12±0.45	83.32±0.74	69.81±0.82	70.23±0.49	75.65±0.26	63.71±0.23	54.23±0.36
5	81.98±0.46	86.11±0.64	94.26±0.21	94.12±0.09	83.53±0.92	84.96±0.48	87.55±0.75	73.59±0.46	61.33±0.87
6	97.24±0.81	95.42±0.78	-	99.32±0.45	91.75±0.73	92.01±0.67	94.86±0.40	79.28±0.49	70.56±0.60
7	-	-	-	-	99.42±0.34	98.46±0.80	-	90.69±050	79.32±0.85
8	-	-	-	-	-	-	-	96.35±0.61	84.65±0.50
9	-	-	-	-	-	-	-	-	90.12±0.20
10	-	-	-	-	-	-	-	-	97.36±0.75
11	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-

*All values are expressed as mean ±S.D., n=3

Table.5.Cumulative % Drug Released from Tablet Formulations F10 to F18

Time in hrs	F10	F11	F12	F13	F14	F15	F16	F17	F18
1	21.53±0.81	18.62±0.87	20.45±0.84	23.41±0.72	22.51±0.43	21.64±0.75	20.70±0.75	21.96±0.79	21.64±0.88
2	31.66±0.25	30.20±0.78	31.52±0.75	38.72±0.71	32.43±0.97	31.97±0.14	31.54±0.04	32.65±0.86	33.34±0.09
3	43.15±0.045	40.65±088	40.28±0.15	57.62±0.25	45.56±0.56	45.35±0.01	46.87±0.15	47.24±0.69	47.72±0.45
4	51.63±0.62	51.23±0.45	46.58±0.52	61.28±0.15	58.53±0.78	50.59±0.41	53.12±0.14	56.57±0.78	56.78±0.75
5	60.42±0.55	61.52±0.81	51.39±0.55	71.17±0.46	70.20±0.55	61.41±0.78	66.14±0.47	65.12±0.26	64.84±0.61
6	68.52±0.75	72.69±0.90	59.47±0.63	77.47±0.91	75.67±0.22	70.28±0.02	73.45±0.56	70.24±0.78	69.38±0.76
7	79.65±0.84	80.55±0.95	66.52±0.82	85.53±0.79	80.12±0.03	75.67±0.78	79.85±0.75	77.98±0.41	76.51±0.31
8	86.52±0.99	87.65±0.45	71.47±0.87	88.26±0.16	85.76±0.81	79.12±0.75	85.34±0.25	80.79±0.96	79.20±0.71
9	92.34±0.85	92.66±0.25	78.91±0.72	92.74±0.05	93.89±0.99	83.43±0.90	91.35±0.76	88.97±0.78	87.36±0.48
10	98.56±0.78	96.44±0.30	81.93±0.15	97.31±0.41	98.65±0.15	86.11±0.82	97.43±0.47	94.64±0.45	91.95±0.39
11		-	85.42±0.84	-	-	89.87±0.87	-	99.09±0.23	95.24±0.37
12	-	-	90.94±0.26	-	-	92.56±0.98	-	-	101.20±0.50

All values are expressed as mean ±S.D., n=3

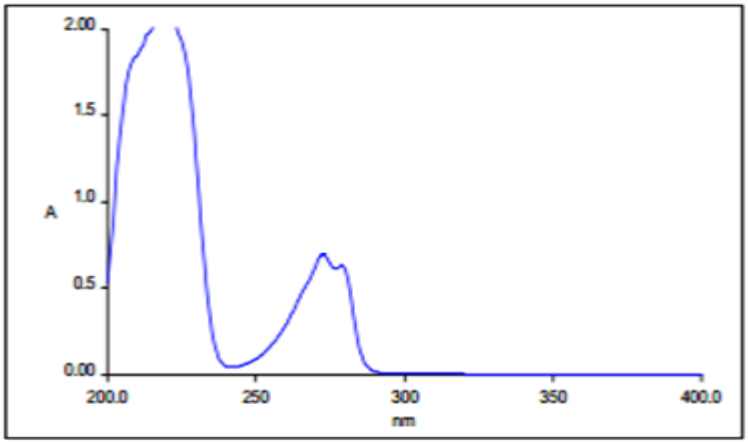

Fig.1.Identification of Famotidine by UV spectra

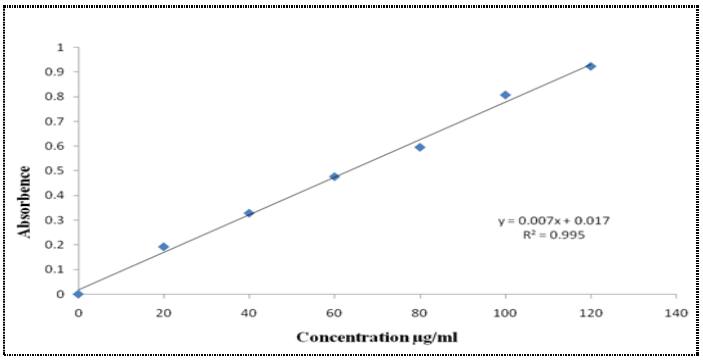

Fig.2.Standard Calibration Curve of Famotidine

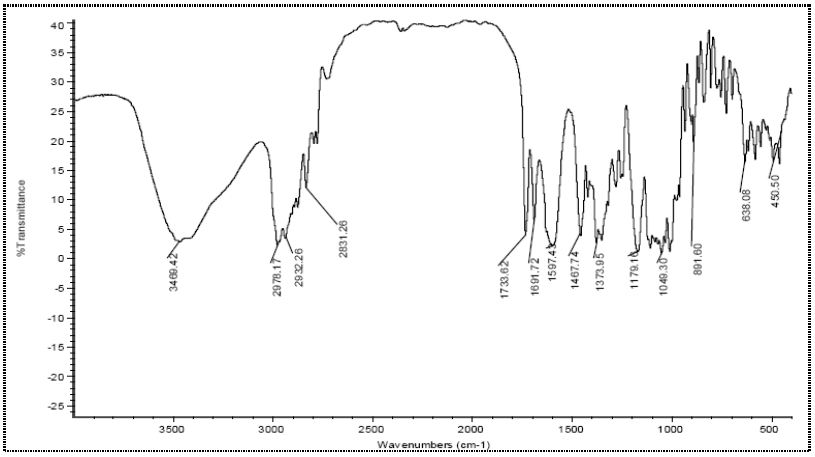

Fig.3. I.R. Spectra for Famotidine

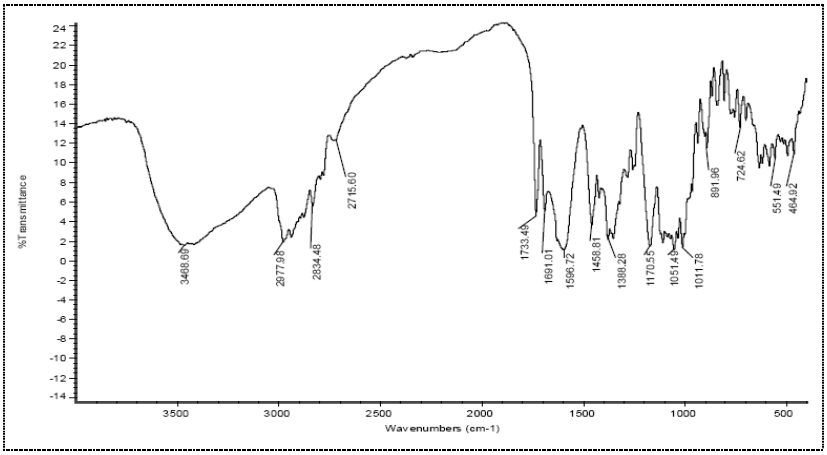

Fig.4.I.R Spectra of HPMC K100M+ Drug

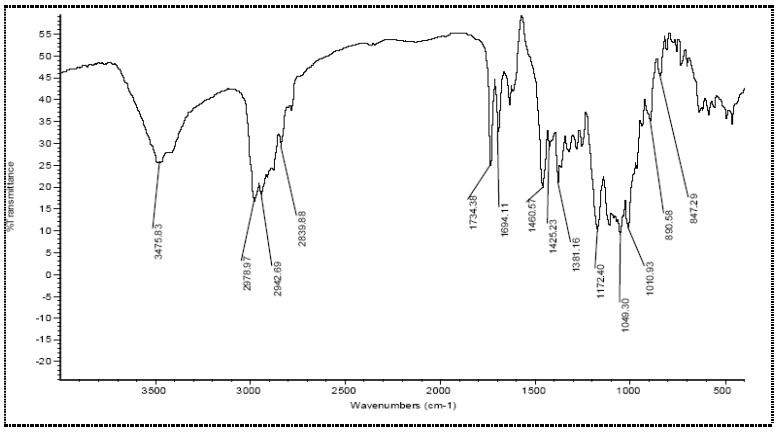

Fig.5. I.R. Interpretation of Physical Mixture

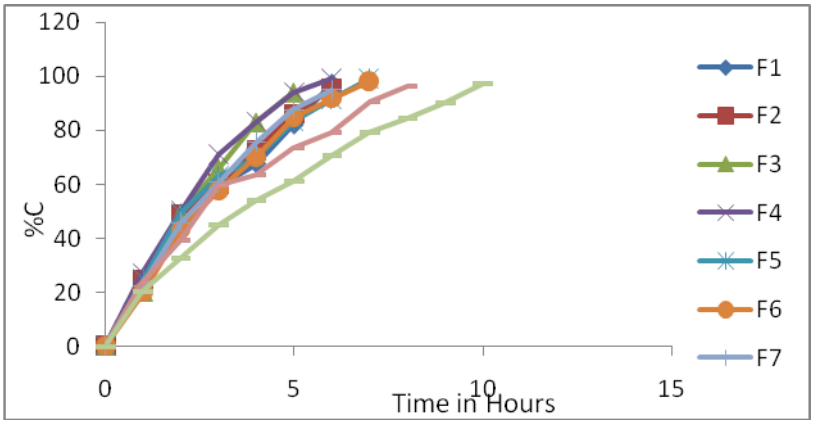

Fig.6.Cummulative drug release for formulations F1-F9

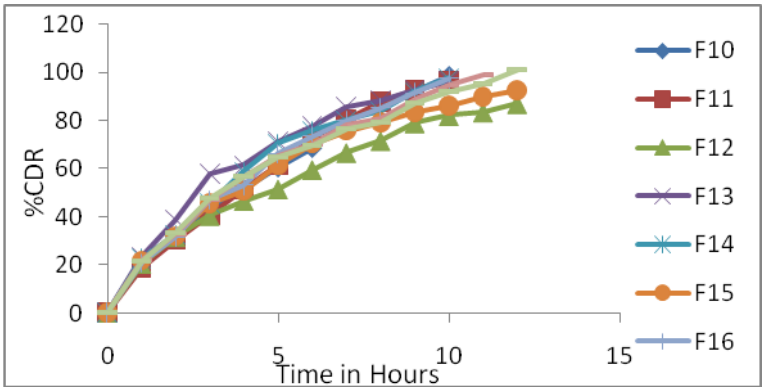

Fig.7.Cummulative drug release for formulations F9-F18

DISCUSSION

The various formulations are prepared by using Hpmc k100m, Hpmck4m, Hpmck15m andcarbopol934p. In the physical evaluation of API the colour was White to off white, odour was characteristic odour and taste was bitter. The solubility of drug was very slightly soluble in distilled water and freely soluble in Dimethyl formamide and in glacial acetic acid and slightly soluble in methanol.Melting point was found to be220^{0}C. Loss on drying is 3% and percentage purity was 100%.

Drug excipient compatibility studies

Drug excipients interaction was checked out by comparing the FTIR spectra of pure drug Famotidine and FTIR spectra of the physical mixture of drug and excipients. The result of FTIR spectra of pure drug famotidine and the physical mixture of drug and excipients were shown in Fig. 2 to Fig. 5 respectively

Pre compression parameter

The values obtained for angle of repose for all formulations are tabulated in table no 2. The values were found to be in the range from 240.88' to 29.30'. This indicates good flow property of the powder blend.Compressibility index value ranges between 12.30% to 16.34% indicating that the powder blend have the required flow property for direct compression**.** Hausner ratio value ranges between 1.13-1.20 indicating flow properties excellent to fair and the results are shown in table no 2.

Post compression study

All the evaluated parameters result obtained from different formulations of tablet is shown in Table.No.5. Hardness of various tablet were in range of 4.1 to 4.5kg/cm2 enabling good mechanical strength. The thickness observed was 5.12 to 5.18mm. The tablets selected from different formulation passed the uniformity of weight test prescribed in IP. The individual tablet weights when compared with average weight were within the official limit (±5%) of % deviation. The friability of tablet formulations were within the acceptable limits and ranged from 0.03 to 0.85%.Tablet formulations containing HPMC K100M,carbopol 934p, (F18) showed less floating lag time than other formulation and a total floating time of >12 hrs as shown in Table No.3.

In-vitro drug release studies

The results acquired from the dissolution study of tablets are shown in Table. No .17 and 18. Tablets were subjected to dissolution in 0.1N Hcl (pH 1.2).Among the 18 formulations, F1 – F4 were prepared using 10% concentration of polymers like HPMC K4M, HPMC K15M, HPMC K100Mand Carbopol 934p which showed sustained action for a period of 5-6 hrs.Formulations F5 – F8 were prepared using 15% concentration of polymers like HPMC K4M, HPMC K15M, HPMC K100Mand Carbopol 934p which showed sustained action for a period of 7-8 hrs.Formulations F9 – F12 were prepared using 20% concentration of polymers like

HPMC K4M, HPMC K15M, HPMC K100Mand Carbopol 934p which showed sustained action for a period of 10 hrs. For formulations F13 to F18 the polymer combination (1:1) of HPMC K4M and HPMC K15M , HPMC K4M and HPMC K100M, HPMC K4M and Carbopol 934p, HPMC K15M and K100M, Carbopol 934p and HPMC K15M, HPMC K100Mand Carbopol 934p were used which showed a sustained drug release for a period of 10 – 12hrs. A drug release of 101.20% at 12th hour was provided by F18 which was considered as best formulation based upon the results obtained from dissolution study performed.

CONCLUSION

The floating tablets of Famotidine were successfully formulated by effervescent technique. The floating tablets containing HPMC K100M and carbopol 934p (F18) showed satisfactory results with respect to floating lag time, total floating duration, swelling ability and sustained drug release properties. The optimized formulation F18 followed zero order kinetic and the mechanism of drug release was found to be Higuchi mechanism.

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