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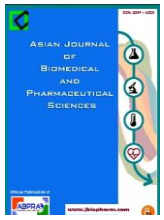

RESEARCH ARTICLE

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Formulation and Characterization of Effervescent Floating Matrix Tablets of Famotidine Hydrochloride

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Abstract

Gastro retentive drug delivery systems are the dosage forms which are retained in the stomach for a prolonged period of time and hence improve the bioavailability of drugs. Famotidine, an anti-ulcer drug, have less oral bioavailability (50%) because of its poor solubility in alkaline pH. Therefore, the main objective of present work is to develop floating effervescent tablets of famotidine. The tablets were prepared with polymers like HPMC K4M and HPMC K100M using directly compression technique. The floating tablets were evaluated for uniformity of weight, hardness, friability, drug content, *In vitro* buoyancy and dissolution studies All the prepared batches showed good *In vitro* buoyancy. The tablet remained buoyant for 6-10 hours. The tablets with HPMC K100M were found to float for longer duration as compared with formulations containing HPMC K4M. The In vitro dissolution studies confirmed the sustained and non fickian drug release from tablets. Stability studies showed that tablets can be stored at room temperatue.

Keywords: Famotidine, HPMC K4M, HPMC K100M, Gastric residence time, Swelling index.

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1. INTRODUCTION

Over the last two decades, various gastroretentive dosage forms have been developed to prolong gastric residence time [1,2,3]. Such dosage form enables oral administration of drugs having a narrow absorption window in the upper part of the gastrointestinal tract or drugs with a poor stability in the colon. Furthermore, the drug can act locally within the stomach and prolonged intimate contact with the absorbing membrane increases efficacy [4].

Floating drug delivery systems (FDDS) are oral dosage forms (capsule or tablet) that are designed to prolong the residence time of the dosage form within the GI tract [5]. It is formulation of a drug and gel forming hydrocolloids meant to remain buoyant in stomach. This not only prolongs gastric residence time but also does so in an area of the gastrointestinal tract that would maximize drug reaching its absorption site in solution and hence, ready for absorption [6].

Famotidine (3-[[[2-[(aminoiminomethyl)am- ino]-4-thiazolyl]methyl]thio]-N-(aminosulfonyl) propionamide) is a relatively new and potent histamine-2 receptor antagonist [7]. It has been found to be effective for acute treatment of duodenal ulcer (dose: 20 or 40 mg per day), maintenance therapy in duodenal ulcer and treatment of pathological hypersecretory conditions like Zollinger Ellison syndrome. Famotidine is incompletely absorbed from GI tract and hence have low bioavailability (40-45%). It has short biological half-life (2.5-3.5 h) [8].

In the present study, a floating sustained release dosage form was developed to enhance oral bioavailability, to deliver drug at the site of action (mucosa) and to improve patient compliance.

2. MATERIALS AND METHODS

Famotidine and Xanthan gum was given as gift sample by Intas Pharmaceuticals, Ahmadabad. Color con Asia Pvt. Ltd., Goa gifted HPMC K4 and HPMC K100. Chitosan was purchased from Himedia lab. Pvt. Ltd., Mumbai.

Preparation of gastro retentive floating tablets

The tablets were prepared by direct compression technique. The composition of different tablet batches is given in Table 1. All the ingredients were weighed, co-grounded and mixed in a glass pestle motor. The resulting blend was evaluated for mass-volume relationship (bulk density, tapped density, Hausners ratio and compressibility index) and flow properties (angle of repose) [9] [10]. The mixture was compressed using a Lab press-I rotary tablet punching machine (Shakti rotary SLP-1) to produce convex shape tablets.

S. No	MF1	MF2	MF3	MF4	MF5	MF6
Famotidine	40	40	40	40	40	40
Xanthan gum	10	10	10	10	10	10
Sodium bicarbonate	70	70	70	70	70	70
Chitosan	40	20	40	20	10	10
HPMC K100M	50	0	40	0	0	60
HPMC K4M	0	50	0	60	40	0
Citric acid	5	5	7.5	2.5	7.5	2.5
Lactose	72.5	72.5	72.5	72.5	72.5	72.5
Magnesium stearate	5	5	5	5	5	5

Table 1: Composition of Famotidine Floating Matrix Tablets

Evaluation of tablets

Thickness

The thickness of tablet was recorded using Vernier caliper. For each formulation, average of six tablets was calculated.

Hardness

For each batch, the hardness of 6 tablets was determined using Monsanto hardness tester.

Uniformity of Weight

Twenty tablets were weighed individually and the percent deviation of each tablet from average weight was calculated using equation:

$$Percent\ deviaion = \frac{Average\ weight\ of\ tablet - individual\ weight\ of\ tablet}{Average\ weight\ of\ tablet} X\ 100$$

Drug content

Ten tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in 0.1 N HCl, the drug content was determined measuring the absorbance at 265 nm after suitable dilution using a Shimadzu UV-1800UV/V spectrophotometer [11].

Friability Test

Friability of the tablets was determined using Roche Friability apparatus. The weighed amount of tablets was placed in the fibrilator which was then operated for 100rpm. The tablets were dusted and reweighed. The % friability is calculated using equation:

$$\%\ F = \frac{(W_o - W) \times 100}{W_o}$$

where, W_0 is initial weight of the tablets before the test and W is the weight of the tablets after test.

In vitro buoyancy studies

The method described by Dave *et. al.,* 2004 was used to carry out *In vitro* buoyancy studies. The tablets were placed in a beaker containing 0.1 N HCl. The time taken for dosage form to emerge on surface of medium is taken as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is noted as Total Floating Time (TFT) [11].

Swelling index

The swelling index of tablets was determined in 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablets was determined after predefined time

intervals. The swelling index was calculated with the help of equation [13]:

Swelling index WU = $(W_t - W_0)$ X $100/W_0$

Where, W_t = Weight of tablet at time t.

W_0 = Initial weight of tablet

In vitro dissolution studies

The dissolution studies were carried out using USP apparatus II (paddle method). The 900 mL of dissolution medium 0.1 N HCl was stirred with paddle rotating at speed 75 rpm. The temperature was maintained at 37 ± 0.5°C. After suitable time intervals, the samples were withdrawn and analyzed at 265 nm using a Shimadzu UV-1800 UV/V spectrophotometer [11].

Accelerated Stability Studies

In order to access the long term stability and shelf life, the optimized tablets of drug were packed in wide mouth air tight glass container and stored at (40± 2°C/75±5% RH) for a period of 3 months. The samples were withdrawn at predetermined time intervals (0, 30, 60 and 90 days) and characterized for parameters like physical appearance, drug content and dissolution profile.

[14].

3. RESULTS AND DISCUSSION

Preparation of FDT

The drug and excipients were mixed and evaluated for flow characterstics. Table 2 enlisted the result of evaluation of different formulation blends. The bulk density for all formulation blends varied between 0.291±0.001 - 0.396±0.002 g/cc. The tapped density was found in the range of 0.373±0.001 - 0.520±0.002 g/cc. The calculated Hausner's ratio for all blends was less than 1.20. So, the blends had good flow characteristics [9] [10]. Similarly, the values of compressibility index (less than 16%) and angle of repose (22º- 29º) revealed free flow behavior of mixture [15].

Parameter→ / Formulation ↓	Bulk Density (g/cc) (Mean ± SD)*	Tapped Density (g/cc) (Mean ± SD)*	Hausners Ratio (Mean ± SD)	Compressibility Index (%) (Mean ± SD)*	Angle of Repose (θ) (Mean ± SD)*
MF1	0.341±0.001	0.520±0.002	1.17±0.002	10.60±0.001	22.67±1.124
MF2	0.362±0.001	0.407±0.001	1.16±0.001	12.01±0.001	28.22±0.717
MF3	0.396±0.002	0.483±0.002	1.15±0.001	10.91±0.002	22.07±0.152
MF4	0.362±0.002	0.506±0.002	1.16±0.002	11.62±0.001	29.21±0.866
MF5	0.366±0.001	0.400±0.001	1.17±0.001	12.3±0.001	23.84±0.111
MF6	0.291±0.001	0.373±0.001	1.16±0.002	11.02±0.002	24.53±0.415

Table 2: Characterization of blends of different formulations

Parameters → / Formulation ↓	Thickness (mm) (Mean ± SD)*	Weight (mg) (Mean ± SD)*	Friability (%) (Mean ± SD)*	Hardness (kg/cm²) (Mean ± SD)*
MF1	2.87±0.014	291.61±0.11	0.58±0.002	3.88±0.103
MF2	2.76±0.011	269.03±0.25	0.54±0.002	3.75±0.131
MF3	2.94±0.003	281.50±0.95	0.51±0.001	3.49±0.190
MF4	2.81±0.002	276.96±1.20	0.67±0.001	3.45±0.147
MF5	2.68±0.012	253.02±0.72	0.39±0.002	3.56±0.110
MF6	2.97±0.011	286.47±1.51	0.60±0.002	3.29±0.125

Table 3: Results of evaluation of tablets

Evaluation of tablets

The evaluation result of different tablet batches was listed in table 3. The thickness of tablets varied between 2.68- 2.97 mm. The weight of all tablets varied between 253mg and 301mg with low standard deviation. The hardness of tablet ranges from 3.29 to 3.88 Kg/cm³. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable. The amount of famotidine was found to be more than 96% in all the batches.

***In vitro* Buoyancy Study**

Sodium bicarbonate generated CO_2 in the presence of dissolution medium (0.1N HCl). The gas generated is trapped and protected within the gel, formed by hydration of polymer, thus decreasing the density of the tablet. As the density of the tablet falls below 1, the tablet becomes buoyant. Whitehead et al have demonstrated good correlation between In vitro and in vivo buoyancy of floating dosage forms [16]. The BLT and TFT of tablets were shown in table 4. The tablets of MF3 batch showed the minimum floating lag time and

maximum duration of flotation. The tablets with low viscosity grade HPMC exhibited short FLT and prolonged TFT. The increase in citric acid concentration decreased the floatation lag time and tablets were found to float for short duration. Thus, the MF6 batch was found to achieve optimum In vitro buoyancy.

Batch	Buoyancy Lag Time (s)	Total Floating time (h)
MF1	95.02±1.05	7.83±.02
MF2	53.42±2.45	9.02±0.05
MF3	76±2.01	8.15±0.10
MF4	**35±1.27**	**10.07±.01**
MF5	61±1.73	9.26±0.41
MF6	118±1.52	6.50±0.15

Table 4: BLT and TFT of different tablets

Swelling Study

The tablets of batch MF4 had the highest swelling index. The viscosity of the polymer had major influence on swelling process, matrix integrity, as well as floating capability, hence from the above results it can be concluded that linear relationship exists between swelling process and viscosity of polymer.

In-vitro Dissolution Studies

It is evident from the *In vitro* dissolution studies that viscosity as well as amount of polymer and It is evident from the *In vitro* dissolution studies that viscosity as well as amount of polymer and concentration of citric acid influenced the drug release from the tablet. The plot of percent cumulative drug released and time was shown in figure 1. The tablets of all batches sustained the drug release for 10 hours. The tablets with low grade HPMC showed better sustained effect than high viscosity grade HPMC. The data obtained was fitted into zero order, first order and Higuhci equation [17, 18]. The results were shown in table 5. The high values of regression coefficient for zero order plots indicated good linearity.

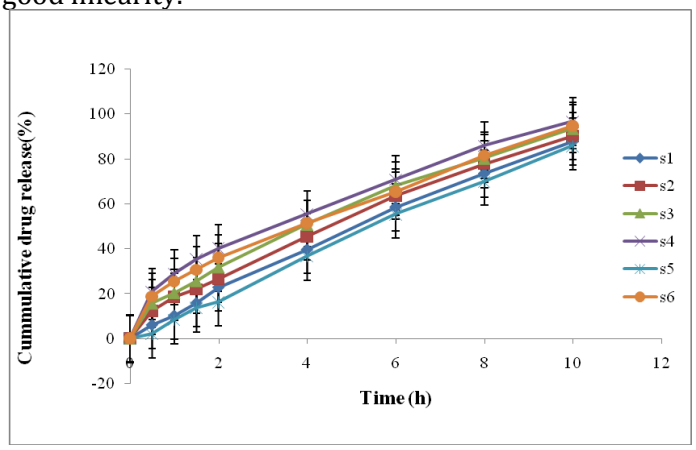

Fig 1: *In vitro* dissolution profile of tablets of different batches

Batch	First order		Zero order		Higuchi release	
	R^2	K	R^2	K	R^2	K
MF1	0.784	7.981	0.902	1.452	0.605	0.651
MF2	0.815	8.025	0.945	1.023	0.689	0.602
MF3	0.694	6.253	0.946	1.486	0.785	0.712
MF4	0.789	7.456	**0.997**	**1.311**	0.852	0.703
MF5	0.649	6.845	0.986	1.256	0.645	0.636
MF6	0.725	7.857	0.912	1.458	0.610	0.812

Table 5: Coefficient of correlation and slope for different release model

Time interval (Days)	Weight variation (mg) (Mean ± SD)*	Friability (%) (Mean ± SD)*	Hardness (kg/cm^2) (Mean ± SD)*	Drug Release (%) (Mean ± SD)*
0	276.96±1.20	0.61±0.01	3.45±0.147	98.11±0.25
15	251.08±0.93	0.62 ±0.26	3.49±0.01	97.23±0.20
30	251.14±0.92	0.61±0.10	3.49±0.02	98.15±0.73
45	251.41±0.86	0.63±0.21	3.40±0.02	97.19±0.43
60	251.48±0.75	0.66±0.20	3.45±0.02	98.12±0.19
75	251.73±1.03	0.68±0.10	3.36±0.02	98.10±0.58
90	251.91±1.05	0.61±0.20	3.42±0.01	97.13±0.59

Table 6: Effect of Storage Condition on tablets of MF4 batch at accelerated storage condition (40+2ºC/75 ± 5% RH)

Accelerated Stability Studies

The results of accelerated stability studies were shown in table 6. There was no significant change in percent friability and tablet weight. There was insignificant change in disintegration time and drug content. The dissolution studies had revealed that storage condition had little effect on the drug release. Thus, the tablet can be stored at room temperature.

4. CONCLUSION

The floating tablets prepared on effervescent technique were a promising approach to achieve *In vitro* buoyancy. The gel-forming polymer and gas-generating agent sodium bicarbonate along with citric acid was essential to achieve buoyancy. The tablets showed sustained and zero order drug release. The accelerated stability studies revealed that the tablets can be stored at room temperature.

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