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Formulation and evaluation of effervescent floating tablet of famotidine with natural polymer chitosan

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ABSTRACT

A Novel floating controlled release drug delivery system of famotidine was formulated in an effort to increase the gastric retention time of the dosage form and to control drug release. The present work investigates the approach using two different polymers HPMC K100 M and natural polymer Chitosan **.** A floating drug delivery system (FDDS) was developed using gas-forming agents, like sodium bicarbonate, citric acid and hydrocolloids, like hydroxyl propyl methylcellulose (HPMC), MCC, PvP k30 and chitosan. The prepared tablets were evaluated in terms of their precompression parameters, physical characteristics, *in vitro* release, buoyancy and buoyancy lag-time. Famotidine effervescent floating tablets were developed by direct compression technique. F5 formulation showed maximum floating time of 17 hours and gave controlled and maximum drug release of over 17h.Therefore the formulation F5 found to be optimized, to achieve the goal of formulation and evaluation of effervescent floating tablet of famotidine. The effect of citric acid on a floating properties and drug release profile was also investigated. A combination of sodium bicarbonate and citric acid was found to achieve required *in-vitro* buoyancy.

Keywords: Famotidine, Chitosan, Effervescent floating tablet, Direct compression, Buoyancy studies

Introduction

Floating tablets are used to increase the gastric residence time of active pharmaceutical ingredients. To overcome the limitations of conventional drug delivery system the floating tablets were developed. 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 advantages in prolonging the gastric emptying time.

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The uniform distribution of these multiple unit dosage forms along the GIT, could result in more reproducible drug absorption and reduced risk of local irritation; this gave birth to oral controlled drug delivery and led to development of Gastro-retentive floating systems. Floating drug delivery systems were first described by Davis in 1968[1].

Famotidine is histamine [H_2-receptor] antagonist and is widely prescribed in gastric ulcers, duodenal ulcers, Zollinger Ellision syndrome and gastro esophageal reflux disease. They also find use in the management of benign gastric and duodenal ulceration. The standard therapeutic dose is 40 mg daily, orally at bed time, for duration of 4 to 8 weeks [3]. In gastro esophageal reflux disease, the recommended dose is 20 mg orally, twice a day, for a period of 6 to 12 weeks. In case of gastro esophageal reflux, which is associated with esophageal ulceration; the recommended dose is 40 mg twice a day, for similar period [2]. The low bioavailability (40 – 45%) and short biological half life (2.5 - 4.0 hours) [2].

It has been reported that the oral treatment of gastric disorders with an H_2 receptor antagonist, like Famotidine or Ranitidine, used in combination with antacids, promotes local delivery of these drugs to the receptors of parietal cell wall. Local delivery also increases the stomach wall receptor site bioavailability and increases efficacy of these drugs to reduce acid secretion. Hence this principle may be applied for improving systemic, as well as local delivery of famotidine, which would efficiently reduce gastric acid secretion[2].

In the present investigation floating tablets of Famotidine were prepared by effervescent approach using two different polymers HPMC K100 M and natural polymer Chitosan. The aim of the work was, to evaluate the effect of gel-forming polymer HPMC K100M on floating properties and release characteristics of Famotidine tablets.

Materials and Method

Materials

Famotidine was received as a gift sample from Tirupati Medicare Limited Paonta sahib. Chitosan, HPMC K100 M and MCC from Colorcon Asia Pvt. Ltd, Sodium bicarbonate, Citric acid, poly vinyl pyrrolidine (PVP k30), aerosil and Talc were obtained from Loba chemicals.

Methods

Preparation of floating tablets of famotidine

Effervescent Floating tablets containing Famotidine were prepared by direct compression technique, using varying concentrations of HPMC K100M, MCC and Chitosan polymers, along with Sodium bicarbonate and citric acid. All the ingredients were accurately weighed and passed through different mesh sieves(size-40)accordingly. Then, except for Magnesium stearate, aerosil and talc all other ingredients were blended uniformly in glass mortar to get rid of all the lumps. After sufficient mixing of drug as well as excipients, Magnesium stearate was added, as post lubricant along with aerosil and talc, as a glidant and were mixed further for additional 2-3 minutes. The tablets were directly compressed using rotary tablet machine (RIMEK Mini Press1).The weights of the tablets were kept constant for all formulations, that is, 200mg [1].

Table 1: Formulations of famotidine floating tablets

Ingredients	F1	F2	F3	F4	F5
Famotidine	20	20	20	20	20
HPMC K100 M	45	40	40	35	45
Chitosan	30	30	45	45	45
MCC	35	40	25	20	10
Citric acid	25	25	25	25	25
Sodium bicarbonate	30	30	30	30	30
Pvp k-30	5	5	5	5	5
Magnesium Stearate	5	5	5	5	5
Talc	3	3	3	3	3
Aerosil	2	2	2	2	2
Total	200	200	200	200	200

***All the quantities are in mg**

Evaluation of floating tablets [1,6]

Pre-compression parameter

Prior to the compression, the formulations of powder blends were evaluated for their bulk and tapped densities, respectively, and from these values, compressibility indices and Hausner's ratio were calculated. While the flow properties of the powder blend was determined by calculating the angle of repose.

Angle of repose

The angle of repose of powder blend was determined by the funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely to the surface until a cone was obtained, with its apex just touching the tip of the funnel. The diameter of the powder cone

was measured and angle of repose was calculated using the following equation.

Tan θ = h/r

Where, **θ**=$\tan^{-1}$ (h/r) **h** = height of pile **r** = radius of the base of pile

Different ranges of flow ability in terms of angle of repose are given below in Table 2.

Table 2: Effect of Angle of repose (θ) on Flow property

Angle of repose (θ)	Type of flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Bulk density was determined by pouring mass of powder into 25ml graduated measuring cylinder and the bulk volume was noted down. The method was repeated three times and the mean of the values exhibited as final volume was calculated as a result of bulk volume. Bulk density of the powder was determined by applying following formula:

Bulk density: Weight of the powder
Bulk volume of powder

Tapped density

Tapped density was determined by pouring mass of complex and excipients, into 25ml graduated measuring cylinder and graduated cylinder was then to 10tapings, using tapped density apparatus, until the change in the volume approached constant value. The method was repeated three times and the mean of the values exhibited, was calculated as a result of tapped volume. Tapped density of the powder was determined by applying following formula:

Tapped density: Weight of powder
Bulk volume of powder

The simplest way of measurement of free flow property of powder is compressibility, an indication of ease, with which a material can be induced to flow. Given by % compressibility index (% CI) which was calculated as follows:

Tapped density- Bulk density×100
Taped density

Hausner's ratio

Hausner's ratio is an index of ease with which powder flows, it is related to inter particulate friction, which could be used to predict powder flow properties. It is calculated by following formula:

Hausner's ratio: Tapped density
Bulk density

Post- compression parameters [1,7]

Appearance

The surface of the tablet was smooth, free from cracks, depressions and pinholes. The colour of the tablet was buff white.

Weight variation

The weight of the tablets was routinely determined to ensure that the tablets contain proper amount of drug. The USP weight variation tests were done by weighing 20 tablets individually, and then calculating the average weights and comparing the individual weights to that of average. The tablets met the USP specification, according to which no more than 2 tablets were outside the percentage limits and no tablet differed by more than 2 times the percentage limit.

Tablet hardness

The resistance of tablets to chipping or breakage under condition of storage, transportation and handling before usage depends on its hardness. The hardness of each batch of tablet was checked by using Monsanto hardness tester. The hardness was measured in terms of kg/cm^2 six tablets were chosen randomly and tested for hardness. The average hardness of six tablets was recorded.

Friability

Friability determines the resistance of tablets to chipping or breakage under conditions of storage, transportation and handling before usage. Friability generally refers to loss in weight of tablets in the

containers due to removal of fines from the tablet surface. Friability reflects poor cohesion of tablet ingredients. Hence the batch was tested for chipping, capping, cracking or breaking.

$$\%F = (1 - W/W_o \times 100)$$

Where, W_o = weight of tablet before test, W = weight of tablet after test

Method

20 tablets were weighed and the initial weight of these tablets were recorded and placed in Roche friabilator, and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the friabilator, dusted off the fines and again weighed and recorded.

Dimensions

The dimensions of the tablets were determined by thickness and diameter which were measured using Vernier caliper. These values were checked and used to adjust the initial stages of compression.

***In vitro* buoyancy studies**

The *in vitro* buoyancy was determined by floating lag time. The tablets were placed in a 100 ml beaker containing 0.1N hydrochloric acid (pH 1.2, temp.37±0.5°C).The time between introduction of the dosage form and its buoyancy in the medium and the floating durations of tablets was calculated for the determination of lag time and total buoyancy time by visual observation. The Time taken for dosage form to emerge on surface of medium called as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and it is the total duration of time by which dosage form remain buoyant.

***In-vitro* Dissolution studies**

The release rate of Famotidine from floating tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus 2 (paddle method; Veego Scientific, Mumbai, India). The dissolution test was performed using 900 ml of 0.1N hydrochloric acid, at 37 ± 0.5°C and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter and diluted to a suitable concentration with 0.1N hydrochloric acid. Absorbance of these solutions was measured at 265 nm using a Thermospectronic-1 UV/Vis double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve.

Results and discussion[11]

Evaluation of Floating Tablets

The formulations prepared for direct compression of floating tablets were evaluated for their flow properties (table 3). The range of Angle of repose for formulations F5 to F1 varied between 38.65° to 35.09°, maximum being F5 38.65° and minimum being F2 38.09°.Results of the physico-chemical characterization are as follows: The bulk density of the formulations F5 to F1 ranged between 0.47gm/cm^3 to 0.52gm/cm^3, maximum being F4 0.56gm/cm^3 and minimum being F5 0.47gm/cm^3. Tapped density of formulations F5 to F1 ranged between 0.58gm/cm^3 to 0.71gm/cm^3, maximum being F4 0.73gm/cm^3 and minimum being F5 0.58gm/cm^3. Carr's Index of the formulations F5 to F1 varied between 18.96% to 26.7%, maximum being F1 26.7% and minimum being F5 18.96%. Hausner's ratio of the formulations F5 to F1 varied between 1.23 to 1.36, maximum being F1 1.36 and minimum being F5 1.23. These values show that the prepared formulations have good flow properties.

The weight of the tablets varied between 0.190 ± 0.006 g to 0.210 ± 0.004 g for different formulations, with low standard deviation values, indicating uniformity of weight. The variation in weight was within the range of ±5% complying with pharmacopoeial specifications. The hardness for different formulations was found to be between 4.02±0.03 to 5.48±0.01 kg/cm^2 indicating satisfactory mechanical strength. The friability was observed to be below 2.02% for all the formulations, which was an indication of good mechanical resistance of the tablet.

All the tablets were prepared by effervescent approach. Sodium bicarbonate was added as a gas-generating agent. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N hydrochloric acid). The combination of sodium bicarbonate and citric acid provided desired floating ability and therefore this combination was selected for the formulation of the floating tablets. It was observed that the gas generated was trapped and protected within the gel, formed by hydration of polymers (HPMC K100M and Chitosan), thus decreasing the density of the tablet below one and hence making the tablet buoyant. The tablet was observed to swell radially and axially during *in vitro* buoyancy studies.

The *in vitro* studies showed that the Buoyancy lag time varied between 19 to 24 seconds, maximum of that being of F3 24 seconds and minimum of that being F2 19 seconds and Floating lag time varied between 10 to 17 hours, with F5 having more than 17hours showed maximum floating lag time, out of all the five formulations(Table 4).

Table 3: Pre- compression parameters of direct compressed Famotidine floating tablet

Formulations	Angle of repose (θ)	Type of flow
F1	38.09	Passable
F2	35.80	Passable
F3	37.73	Passable
F4	36.24	Passable
F5	38.65	Passable

Batch	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's Ratio	Angle of repose*
F1	0.52	0.71	26.7	1.36	38.09
F2	0.49	0.65	24.6	1.32	35.80
F3	0.53	0.72	26.3	1.35	37.73
F4	0.56	0.73	23.2	1.30	36.24
F5	0.47	0.58	18.96	1.23	38.65

Batch	Weight Variation (g)	Hardness Kg/cm^2	Thickness (mm)	Diameter (mm)	Friability (%)
F1	**0.190 ± 0.006**	**4.02±0.03**	**2.92 ± 0.112**	**10.08 ± 0.02**	**2.02**
F2	**0.210 ± 0.004**	**5.45±0.02**	**2.83 ± 0.115**	**10.08 ± 0.01**	**1.13**
F3	**0.200 ± 0.003**	**4.57±0. 03**	**3.04 ± 0.085**	**10.07 ± 0.01**	**1.65**
F4	**0.206 ± 0.006**	**4.63±0.02**	**3.00 ± 0.117**	**10.08 ± 0.02**	**1.32**
F5	**0.199 ± 0.004**	**5.48±0.01**	**3.54 ± 0.078**	**10.06 ± 0.02**	**1.11**

Table 4: In-*Vitro* buoyancy studies of Famotidine floating tablets

Formulation	Buoyancy lag time (sec)	Total floating time (Hours)
F1	22	11
F2	19	10
F3	24	13
F4	23	12
F5	20	>17

(Initial) (After 20 sec) (After 17 hrs)

Figure 1: *In-vitro* buoyancy studies of F5 batch of Famotidine floating tablets

Table 6: Cumulative % drug release

Time (in hr	F1	F2	F3	F4	F5
0.25	07.01 ±1.0	6.01±0.10	5.68±0.20	3.02±0.10	2.51±0.20
1.00	25.68±1.20	23.38±1.20	22.93±1.40	19.01±0.70	18.90±0.30
2.00	37.48 ±1.40	33.30±1.40	33.81±0.90	32.01±0.70	25.91±0.60
3.00	45.01 ±1.40	37.68±1.30	39.06±10	36.90±10	32.01±0.50
4.00	51.32±0.70	47.29±0.50	47.49±1.20	44.49±0.50	38.03±10
5.00	61.61±2.2	52.09±0.10	58.61± 10	51.33±0.90	47.68±1.20
6.00	72.8±0.20	60.90±0.80	60.77±1.20	56.01±0.30	50.01±0.60

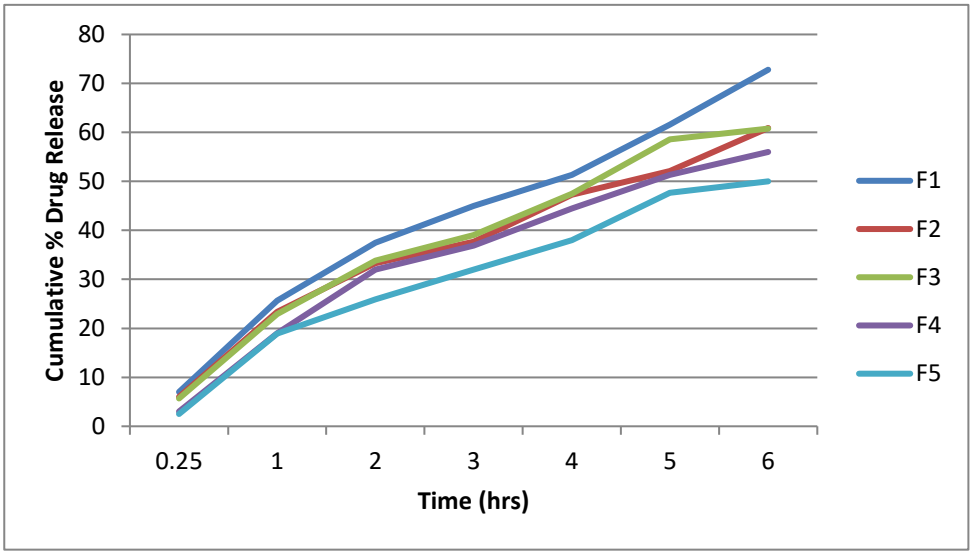

Figure 2: *In-vitro* dissolution profile formulations

Conclusion

Hence it could be concluded that, the effervescent-based floating drug delivery system, was a promising approach to achieve *in vitro* buoyancy of the tablet. The addition of gel-forming polymer HPMC K100M, along with natural polymer Chitosan and gas-generating agents, sodium bicarbonate with citric acid, were crucial in achieving *in vitro* buoyancy. The drug release from the tablets was sufficiently sustained and non-Fickian transport of the drug from tablets was confirmed. Hence, F5 formulation showed maximum floating time of more than 17 hours and gave slow and maximum drug release. So the composition of the batch 5 should be optimized, to achieve the goal of formulation and evaluation of effervescent floating tablet of famotidine.

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Reference

1. Dubey Vivek, Arora Vandana, Formulation and evaluation of effervescent Floating tablet of Amlodipine besilate with natural polymer chitosan. *JPSI* 2012;4(1): 13-18.
2. Ichikawa M, Watanake S, Yake YM. A new multiple unit oral floating dosage systems: Preparation and *in-vitro* evaluation of floating and sustained release characteristics. *J. Pharm. Sci.* 1991; 80:1062-6.
3. Coffin, M; Parr, A. US Patent 5 407 687, April 18, 1995.
4. Reynolds, J. E. F. Martindale: The Extra Pharmacopoeia, The Royal Pharmaceutical Society: London, 1996: 1218-1220.2.Singh BN, Kim KH. "Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention", *J Control Release*, 2000; 63; 235-259.
5. Banker GS, Anderson NR; the Theory and Practice of Industrial Pharmacy, Lachman L,

Lieberman HA, Kanig JL 3rd edition, Varghese Publication House, Bombay, 1987; 296-303.

6. Indian Pharmacopoeia. Publications & information directorate (CSIR). New Delhi, 1996; II: 179-183,662-663.

7. Yeole PG, khan S. Shah K, Floating drug delivery systems: Need and development, *Int.J.Pharma Sci*.2005; 67:265-72.

8. Barar FSK, Essential of Pharmacotherapeutics; 3rd S Chand and Company Ltd. New Delhi. 246.

9. Ali, Arora S, Khar RK, Floating drug delivery system:A Review. *Aaps pharm sci tech.* 2005;06(03):E372-e390.

10. Inouye K.Machide Y.Sannan T.Nagai T. Buoyant sustained release tablets based on chitosan. *Drug Des Deliv.*1988; 2:165-175.

11. M. Jaimini, A.C. Rana and Y.S. Tanwar. Formulation and Evaluation of Famotidine Floating Tablets, *Curr Drug Deliv.* 2007; 4(1) :51-5.

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