



DEVELOPMENT AND *IN VITRO* EVALUATION OF GASTRORETENTIVE FLOATING TABLETS OF FAMOTIDINE

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Abstract

The present study reports the development and *in vitro* evaluation of gastro retentive floating tablets of Famotidine. The formulations were developed using cellulose derivatives such as HPMC K4M, HPMC K15M and HPMC K100M in different ratios with gas generating agents and other excipients by wet granulation technique. The formulations were subjected to various evaluation parameters *in vitro*, viz., hardness, friability, uniformity of drug content, *in vitro* floating studies, *in vitro* dissolution studies, all the formulations were good in appearance and showed better physical and mechanical properties. Formulation M15 containing HPMC K4M 80 mg, Sodium bicarbonate 40 mg, 30 mg citric acid and PVP K30 10mg was found to be the best formulation in terms of drug release and *in vitro* buoyancy time and was subjected to stability studies and IR spectroscopy. The results indicate that the formulation was stable and there was no chemical interaction between the polymer and the drug.

Key words: Famotidine, HPMC K4M, *In vitro* buoyancy, *In vitro* Dissolution studies, IR Spectroscopy.

Introduction

Gastric emptying is a complex process and is highly variable and results in uncertain absorption of drugs this can be overcome by a proper drug delivery system such as gastro retentive drug delivery system. The GRDDS can be used to retain the drug in the stomach thereby increasing the absorption and bioavailability of the drug. This system is particularly important for the drugs which have higher absorption rate in a particular region of gastrointestinal tract¹. Famotidine is a potent H₂ receptor antagonist used in the treatment of peptic ulcer, reflux esophagitis etc. It is absorbed mainly at a specific absorption site in the GIT. A dosage form which can retain Famotidine at its absorption site for an extended period will increase its absorption and bioavailability².

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So the present study was designed to develop gastro retentive floating tablets of Famotidine using easily available and relatively economical cellulose derivatives viz., HPMC K4M, HPMC K15M and HPMC K100M.

Materials and Methods

Famotidine was obtained as a gift sample from Sreenivasa Pharmaceuticals Pvt. Ltd, Hyd. HPMC K4M, HPMC K15M and HPMC K100M were obtained as a gift sample from Colorcon Asia Pvt. Ltd., Goa. All other chemicals were of analytical grades and were used as procured. Materials and excipients used in GRDDS were of IP grades.

Preparation of Gastro Retentive Floating Tablets of Famotidine

The gastro retentive tablets were prepared by wet granulation method using different ratios of polymers as described in Table No:1 PVP K30 was used as granulating agent and citric acid, sodium bicarbonate were used as gas generating agent, lactose, Micro

crystalline cellulose was used as diluents. All the through sieve no. 60. Drug and the excipients except Magnesium stearate and talc were bended geometrically in mortar and pestle and then granulating agent was added granules were obtained by passing the mass through sieve no 12 the resulting granules were dried at 60°C for 4 hour. The dried granules were passed through sieve no. 18 and lubricated with Magnesium stearate and talc. The granules so obtained were compressed into tablets using tablet compression machine³ (Rimek mini press machinery Co. Pvt. Ltd., India).Seventeen formulations were prepared and coded as M1, M2 and so on.

Evaluation of Gastro Retentive Floating Tablets of Famotidine

The prepared gastro retentive tablets were evaluated for hardness (Monsantotester), friability (Rochetype friabilator), weight variation^{4,5}, drug content estimation, floating lag time and total floating time.

In vitro Buoyancy Studies

In- vitro buoyancy studies were performed for all the eight formulations as per the method described by Rosa *et al*⁶ Randomly selected tablets from each formulation were introduced in a 100ml beaker containing simulated gastric fluid, P^H 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The time for which the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).The results were depicted in Table.No-2

Drug Content Estimation

The drug content in each formulation was estimated by triturating 20 tablets. Powder equivalent to 10 mg of Famotidine was added in 100ml of 0.1N HCl followed by stirring for 10 minutes. The stock solution was diluted suitably and the absorbance of resultant solution was measured at 265 nm by using Elico-UV-Visible Spectrophotometer (SL-159) 0.1N HCl was used as blank⁵.

In vitro Dissolution Studies

The release rate of Famotidine from floating tablets was determined using USP dissolution apparatus II (Lab Hosp India). The dissolution test was performed using

ingredients were accurately weight and passed 900 ml of 0.1N hydrochloric acid, at 37 ± 0.5°C and 50 rpm. Aliquots 5ml was collected at predetermined time intervals and replenished with an equivalent volume of fresh medium. The samples were filtered through a 0.45 µm membrane filter and diluted suitably with 0.1N HCl and were analyzed using Elico UV/Visible spectrophotometer at 265 nm⁷. The results are illustrated in Figure-1.

Short Term Stability Studies

To evaluate the formulation stability ICH guidelines were followed. The best formulation was tested for short term stability for 4 weeks at 25°C ±2 °C/60% RH ±5% and accelerated stability for period of 12 weeks at 40°C ±2°C/75 % RH ± 5%, for their drug content and other parameters⁸.

FTIR Spectroscopy

IR spectra were obtained for A pure drug Famotidine, B HPMC K4M, and C) Famotidine with HPMC K4M. The sample pellet was mounted in IR compartment and scanned at wavelength 40000cm⁻¹-600cm⁻¹.The IR spectrum is depicted in Figure 4A, 4B, and 4C.

Results and Discussion

The prepared tablets were subjected to various evaluation parameters like hardness, friability, weight variation, drug content estimation, floating lag time and total floating time. The hardness of tablets was found to be in the range of 4.36 to 5.06 kg/cm², friability of all the formulations was found to be less than 1% i.e 0.54-0.73%, weight variation, 91.3±5.8 to 223.32±7.8 indicating good physical strength of the formulation. The drug content of the formulations was in the range 96.69 to 100.85 showing the uniform distribution of the drug, total floating time of all the formulations was around 24 hours which may be an efficient parameter for the enhanced gastric retention time of the formulation. *In vitro* buoyancy studies indicated that the formulations containing Sod bicarbonate showed decrease in floating lag time. Addition of MCC along with Sodium bicarbonate further reduced the floating lag time. Faster buoyancy was observed in the formulations containing a combination of Citric acid and sodium bicarbonate may be attributed to immediate formation of CO₂.

Table 01: Composition of Gastro Retentive Floating Tablets of Famotidine

Formulation Code	HPMC K4M	HPMC K15M	HPMC K100M	Lactose	MCC	Sodium bicarbonate	Citric acid	PVP K30
M1	40	-	-	-	-	-	-	08
M2	80	-	-	-	-	-	-	10
M3	100	-	-	-	-	-	-	12
M4	-	40	-	-	-	-	-	08
M5	-	80	-	-	-	-	-	10
M6	-	100	-	-	-	-	-	12
M7	-	-	40	-	-	-	-	08
M8	-	-	80	-	-	-	-	10
M9	-	-	100	-	-	-	-	12
M10	80	-	-	20	-	20	-	10
M11	80	-	-	20	-	40	-	10
M12	80	-	-	-	20	20	-	10
M13	80	-	-	-	20	40	-	10
M14	80	-	-	-	20	20	15	10
M15	80	-	-	-	20	40	30	10
M16	80	-	-	-	20	20	10	10
M17	80	-	-	-	20	20	05	10

Note: All the quantities are expressed in terms of milligrams. Each formulation contains 40 mg of Famotidine, 0.5% of talc and 1% of magnesium stearate.

Table 02: Results of Evaluation Gastro retentive Floating Tablets of Famotidine

Formulation code	Hardness (kg/cm ²)	Friability (%)	Drug content (%)	Average weight (mg)	Buoyancy Lag Time (Sec)	Total Floating Time (hrs)
M1	4.65	0.62	97.62	91.7±2.3	60 Sec	24
M2	4.36	0.63	98.87	113±7.5	90 Sec	24
M3	4.93	0.55	99.37	155.9±4.8	95 Sec	24
M4	4.58	0.58	97.37	91.85±6.8	75 Sec	24
M5	4.45	0.72	99.40	113.35±2.9	100 Sec	24
M6	4.76	0.68	99.62	155.75±5.4	102 Sec	24
M7	4.83	0.62	100.85	91.3±5.8	80 Sec	24
M8	4.98	0.65	99.07	113.25±9.7	105 Sec	24
M9	4.98	0.56	97.45	155.2±4.8	120 Sec	24
M10	5.06	0.54	98.62	173.4±2.8	10 Sec	24
M11	4.86	0.58	99.15	193.05±7.8	07 Sec	24
M12	4.95	0.65	100.42	193.2±3.9	05 Sec	24
M13	5.00	0.61	99.72	213.05±8.8	02 Sec	24
M14	4.98	0.63	99.25	173.25±7.3	01 Sec	24
M15	5.02	0.65	99.50	193±7.5	50 sec	24
M16	4.88	0.59	98.97	188.225±6.7	90 sec	24
M17	4.57	0.73	96.65	223.32±7.8	02 Sec	24

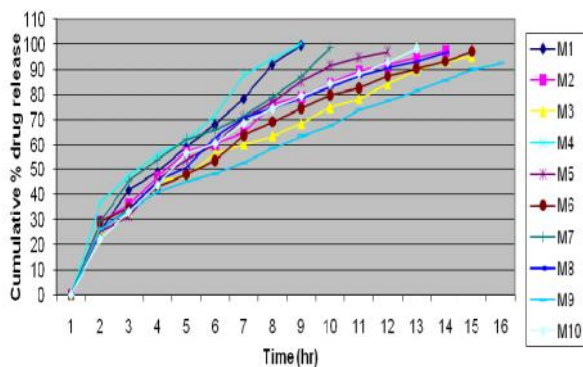


Figure 01: Dissolution Profile of Formulation M1 to M10 Gastro Retentive Floating Tablets of Famotidine

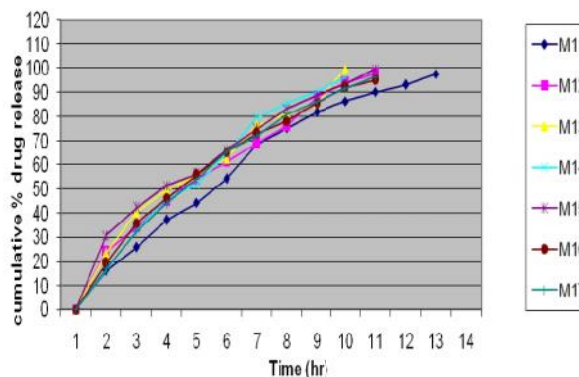


Figure 02: Dissolution Profile of Formulation M11 to M17 Gastro Retentive Floating Tablets of Famotidine

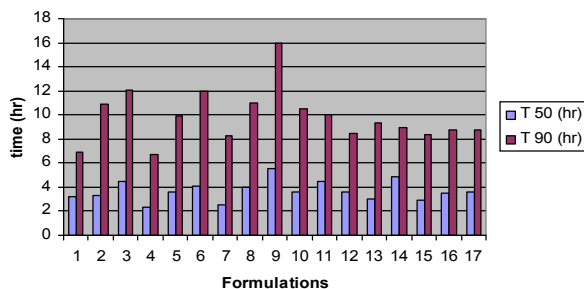


Figure 03: Dissolution T₅₀ and T₉₀ Values of Gastro Retentive Floating Tablets of Famotidine

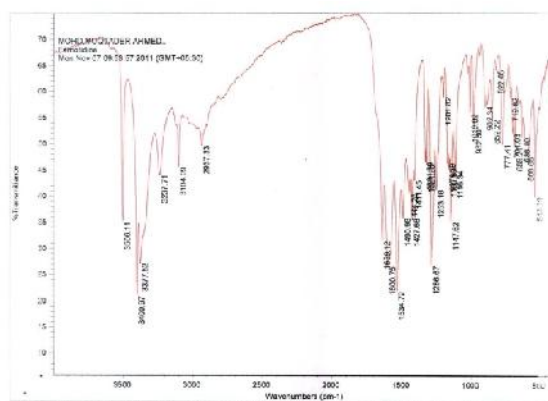


Figure 04(a): Pure Drug Famotidine

Table 03: Stability Study of Formulation M15

Parameters	For 4 weeks at 25 °C ±2 °C/60% RH ±5%	For 12 Week at 40 °C ±2 °C/75 % RH ± 5%
Physical	No change	No change
Average Weight (mg)	193	193
Friability (%)	0.65	0.68
Hardness (kg/cm ²)	5.02	5.00
Drug content (%)	99.15	98.99
Buoyancy Lag Time(Sec)	53 sec	54 sec
Total Floating Time (hrs)	24	24
Cumulative % drug released ± SD 12h	98.82±0.20	97.86±0.42
Buoyancy on disturbing	Float	Float

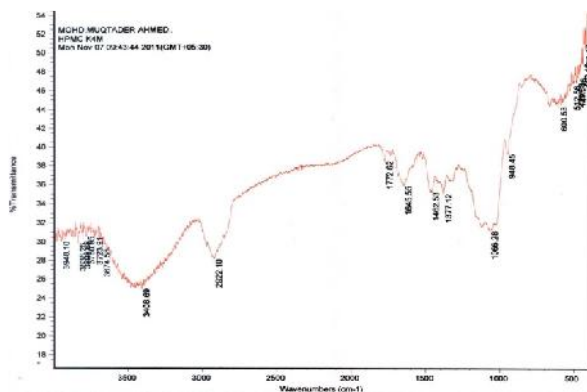


Figure 04(b): HPMC K4M

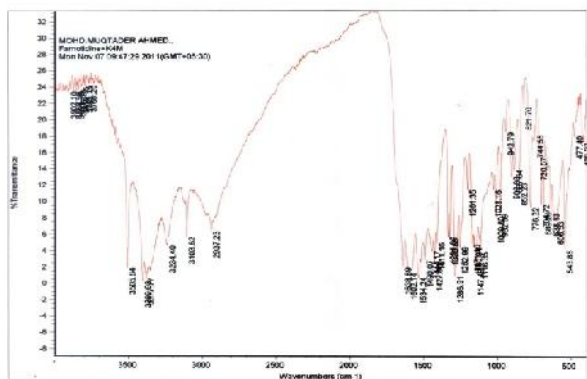


Figure 04(c): Famotidine with HPMC K4M

In vitro drug release studies exhibited a decrease drug release with an increase in polymer concentration which may be due to increase in viscosity of the gel as well as the gel layer with longer diffusional path. Formulations containing high viscosity grade HPMC showed slower drug release compared to formulations containing low viscosity polymers. There was no considerable effect of gas generating agents on the release of the drug.

IR spectroscopy was carried out for the selected formulation to assess any chemical interaction between the drug and the polymers. The spectrum obtained suggests that there was no chemical interaction between the drug and polymers and there was purely physical entrapment of the drug in the polymer matrix.

Conclusion

From the results of the study it is evident that the gastro retentive floating tablets of Famotidine can be successfully developed by using cellulose derivatives in combination with gas generating agents and this would be a feasible alternative to conventional oral dosage form of Famotidine in order to retain the drug at the

site of its absorption and to increase the bioavailability of the drug thereby reducing dose or dosing interval.

References

1. Patel R.P, Baria A.H, Pandya N.B. Stomach-specific drug delivery of famotidine using floating alginate beads. *International Journal of Pharm Tech Research*, 1(2), 2009, 288-291.
2. Shweta Arora, Javed Ali, Alka Ahuja, Roop K Khar, Sanjula Baboota. Floating drug delivery systems: an updated review. *AAPS PharmSciTech*, 6, 2005, E372–E390.
3. Banker GS, Anderson NR; Tablets: Lachman L, Lieberman HA, Kanig JL; *The Theory and Practice of Industrial Pharmacy* 3rded, Varghese Publication House, Bombay, 1987; 296-303.
4. Lachman L, Lieberman A, Herbert K, Joseph L. *The theory and practice of industrial pharmacy*. 3rd ed, Varghese Publishing House, Mumbai, 1991, 293-373.
5. Indian Pharmacopoeia. Publications & information directorate (CSIR). New Delhi, 1996, Vol II, 179-183, 662-663.
6. Rosa M, Zia H, Rhodes T. "Dosing and testing *in vitro* of a bioadhesive and floating drug delivery system for oral application", *Int J Pharm*. 105, 1994, 65-70.
7. Zeenath S, Ramesh Gannu, Suresh Bandari. Development of gastroretentive systems for famotidine: *in vitro* Characterization. *Acta Pharmaceutica Scientia*. 52, 2010, 495-504.
8. "Stability Testing of New Drug Substances and Products" Eur Medicines Agency, 2003, 1-20.
9. Patel Manish P, Patel Madhabhai M, Patel Dipti H, Patel Krisnakumar N. "Formulation Development, Optimization and evaluation of famotidine floating matrix tablets; 1(2), 2009, 85-90.