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Research Article

Formulation and evaluation of matrix floating tablet of Famotidine

Sumit R. Rathi*[1], Dr. V. R. Patil[2], Dr. M. M. Patel[3], Amol B. Patil, Gaurav A.Shankhpal and S. D. Barhate.

*[1]Dept. of Pharmaceutics, Smt. S. S. Patil College of Pharmacy, Chopda- 425107. Maharashtra.

[2]Principal, College of Pharmacy, Faizpur, Maharashtra.

[3] Principal, Kalol Institute of Pharmacy, Kalol -382721. Gujarat.

For correspondence: Sumit R. Rathi, Dept. of Pharmaceutics, Smt. S. S. Patil College of Pharmacy, Chopda- 425107. Maharashtra

E-mail: sumeet_rathi007@rediffmail.com

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ABSTRACT

The objective of the present study was to develop single unit gastroretentive drug delivery system of Famotidine. Famotidine is histamine H_2 receptor antagonist. It is widely for duodenal ulcers, gastric ulcers, gastro esophageal reflux disease and erosive esophagitis. Famotidine is having a short biological half-life of 2.5-3.5 hrs. The gastroretentive drug delivery system can be retained in the stomach and assist in improving the oral sustained delivery of drugs. The floating matrix drug delivery system of famotidine was prepared by using sodium alginate, HPMC K15M, sodium bicarbonate and citric acid. The formulated formulations showed good buoyancy, in vitro sustained release of famotidine and good stability at short term accelerated stability study.

Key words: Formulation ,evaluation , floating tablet ; Famotidine

INTRODUCTION

The gastroretentive drug delivery system can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastro-intestinal tract. The system helps in ensuring optimal bioavailability. It is also reported that the oral treatment of gastric disorders with an H_2 antagonist like famotidine, if used in combination with antacids promotes local delivery of these drugs, and increases stomach wall receptor site bioavailability which improves the efficacy of such drugs to reduced acid secretion. Several approaches are currently used to prolong gastric retention time. Among them the principle of buoyant preparations offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release.

Famotidine is histamine H_2 receptor antagonist. It is widely used for duodenal ulcers, gastric ulcers, gastro esophageal reflux disease and erosive esophagitis. Famotidine is having a short biological half-life of 2.5-3.5 hrs. Famotidine has 40–45% absolute bioavailability on oral administration. In contest of the above principle, a strong need was recognized for the development of a dosage form to deliver sustained release gastroretentive delivery system of famotidine.

MATERIALS AND METHODS

Famotidine was received as generous gift from Zydus-Cadila, Ahmedabad India. HPMCK15M were received from Colorcorn Asia, Ltd, Goa, India. Sodium bicabonate, sodium alginate, dicalcium phosphate and magnesium stearate were received from S.D. Fine Chemicals Ltd. Mumbai. All other chemicals used were of analytical reagent grade, available commercially and used as such without further processing.

Formulation of famotidine floating tablet

The matrix floating tablets of famotidine were prepared by wet granulation technique. All the powders were passed though 80 mesh sieve. The required quantity of drug, polymer and filler were mixed thoroughly, and granules were prepared by using isopropyl alcohol. The granules were dried at 60 ^{0}C in a tray dryer. Talc and magnesium stearate were finally added and the granules were compressed on rotary tablet machine with 12 mm flat punches.

Table 1: Composition of matrix floating tablets of famotidine

Composition	O1	O2	O3	O4
Famotidine	20	20	20	20
Sodium Alginate	20	40	80	120
Sodium bicarbonate	50	50	50	50
Lactose	152	132	92	52
Magnesium stearate	5	5	5	5
Talc	3	3	3	3

All the quantities in mg * Weight of tablet is 250 mg

Physical evaluation, drug content and floating properties

The formulated matrix floating tablets of famotidine were evaluated for average weight, hardness, thickness, friability, floating lag time, buoyancy and drug content.

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Table 2: Results of in vitro dissolution studies of matrix floating tablets of famotidine

Time (h)	Cumulative percentage drug release				
	O1	O2	O3	O4	Theoretical Release
0	00.00	00.00	00.00	00.00	00.00
1	27.12	25.43	23.00	21.66	22.65
2	39.27	37.35	35.76	32.18	33.71
3	58.99	56.49	49.26	44.16	44.77
4	72.32	71.36	66.17	54.21	55.83
5	83.14	77.50	69.00	65.47	66.89
6	97.41	84.04	86.42	73.82	77.95
7	100	98.39	92.65	83.52	89.01
8	-	100	100	90.18	100

Table 3: Floating lag time and buoyancy of formulation O1-O4

Formulation	Floating lag time (Sec)	Buoyancy (h)
O1	242	10.5
O2	260	11.00
O3	335	10.45
O4	342	10.40

Table 4: Curve fitting of dissolution data

Formulation	Higuchi (R^2)	Zero order (R^2)	Krosmeyer Peppas (R^2)	Hixson Crowel (R^2
O1	0.9991	0.6678	0.9264	0.7231
O2	0.9994	0.6724	0.9342	0.7342
O3	0.9992	0.6754	0.9382	0.7568
O4	0.9997	0.7239	0.9241	0.7611

In vitro dissolution study and release kinetics

The *in vitro* dissolution studies were carried out using USP XXIV dissolution test apparatus by using paddles. The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5 ^{0}C and 50 rpm. The samples were withdrawn at fixed intervals. The removed samples were filtered through a 0.45 µ membrane filter and z analyzed at 265 nm using Shimadzu1601A spectrophotometer. The in vitro release data was fitted in Higuchi matrix, Zero order, Krosmeyers peppas and Hixson Crowel models to find out release kinetics and mechanism of drug release.

Accelerated stability study

The formulated tablets were packed in aluminum pouch and subjected to short term stability at 25^0 C/60% RH and 40^0 C/75% RH for a period of three months to find out the effect of aging on drug content and floating behavior.

RESULTS AND DISCUSSION

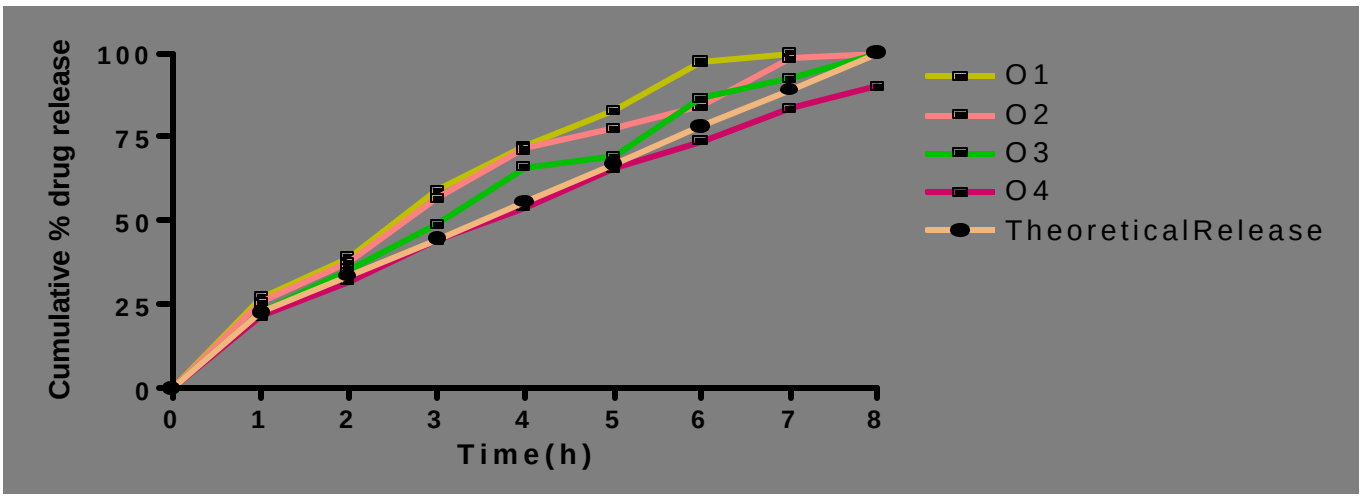
Physical evaluation, drug content and floating properties

The results of physical evaluation showed that the weights of tablets varies between 249.56 mg to 251.06 mg (average weight 250.31 mg), hardness between 3.6 and 4.4 kg/cm (average 4.0 kg/cm), thickness between 3.25 and 4.10 mm and friability ranged from 0.38 % and 0.65 % (average 0.51 %). Thus all the physical parameters are practically within

Table 5: Results of short term accelerated stability study

Month	Parameter	25^{0}C/60% RH				40^{0}C/75% RH			
		O1	O2	O3	O4	O1	O2	O3	O4
1	Drug content	99.98	99.96	99.98	99.95	99.98	99.96	99.98	99.95
	Floating lag time	242	260	335	342	240	260	335	340
	Buoyancy	10.5	11.00	10.45	10.40	10.50	11.00	10.45	10.40
2	Drug content	99.96	99.92	99.96	99.90	99.93	99.92	99.96	99.91
	Floating lag time	240	260	335	340	240	260	335	340
	Buoyancy	10.5	11.00	10.45	10.40	10.50	11.00	10.45	10.40
3	Drug content	99.96	99.90	99.95	99.90	99.93	99.91	99.95	99.90
	Floating lag time	240	260	330	340	240	260	335	340
	Buoyancy	10.5	11.00	10.45	10.40	10.50	11.00	10.45	10.40

Figure no.1 *In vitro* dissolution studies of matrix floating tablets of famotidine



control. The drug content of the prepared tablets was found between 99.25 to 99.98 %. The floating lag time varies between 220 and 342 seconds and the buoyancy over 10 h.

In vitro dissolution study and release kinetics

The *in vitro* dissolution study revealed that the formulation O1 and O2 released the drug faster as compared to formulation O3 and O4. This variation in vitro dissolution profiles was due to the content of sodium alginate. The formulation O1 and O2 contains 20 and 40 mg of sodium alginate. During dissolution weak gel layer was developed around the tablet that results in 100 % release of drug at the end of 7h and 8h receptively in case of O1 and O2. Where as, in case of formulation O3 and O4, as the content of sodium alginate was 80 mg and 120 mg, the drug dissolution was delayed due to formation of dense layer of sodium alginate around the tablet. This swollen layer controls the diffusion of famotidine in to the surrounding solution. Hence sustained release behavior of famotidine was observed up to 8h. The curve fitting results of the in vitro release data of formulations indicated that Higuchi model is the best-fit model to describe the release of the drug from matrix floating tablets and the mechanism of drug release was diffusion.

Accelerated stability study

The results of short term accelerated stability study at 25^0 C/ 60% RH and 40^0 C/75% RH for a period of three month showed no significant alteration in drug content, floating lag time and buoyancy of matrix floating tablets of famotidine.

CONCLUSION

From the results it can be concluded that sodium alginate can be successfully used to modify release rates in hydrophilic matrix floating tablets. The sustained release of famotidine was observed in formulated floating tablets for the period of 8h and Higuchi was the best-fit model to describe the drug release. The probable mechanism of drug release was diffusion. The short term accelerated stability showed no significant alteration in drug content and floating properties.

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