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FORMULATION AND EVALUATION OF GASTRORETENTIVE FLOATING TABLETS OF FAMOTIDINE

Brajendra singh Rajpoot

Shri R.N.S. College of pharmacy, Gormi, Bhind M.P. India

***Corresponding author e-mail:** brajendrap@yahoo.co.in

ABSTRACT

The purpose of this investigation was to prepare a gastro retentive drug delivery system of famotidine. Floating tablets of famotidine were prepared by using two different grades of HPMCK4M and HPMCK100M by effervescent technique; these HPMCK have gel-forming properties. The floating tablets were evaluated for weight variation, hardness, friability, drug content. All prepared tablet showed good *in vitro* buoyancy.

Keywords: Floating tablets, Famotidine, *In vitro* buoyancy

INTRODUCTION

Gastro retentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and resultant improve the bioavailability of the drugs. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability.[1] Drug whose solubility is less in the higher pH of the small intestine than the stomach and the drugs for local action in the stomach can be delivered in the form of dosage forms with gastric retention. Antibiotics, catecholamine, sedative, analgesic, anticonvulsants, muscle relaxants, antihypertensive and vitamins can be administered in Hydrodynamically balanceed System dosage form.[2-4] Several approaches can be used to prolong gastric retention time, including floating drug delivery systems (i.e., hydrodynamically balanced systems), swelling and expanding systems, polymeric bioadhesive systems, modified-shape systems, high-density systems, and other delayed gastric-emptying devices [5–11]. Famotidine is a histamine H2-receptor antagonist. It is widely prescribed in the treatment of gastric ulcers, duodenal ulcers, Zollinger-Ellison syndrome, and gastro esophageal reflux disease in doses ranging from 10 to 80 mg.[12] A dosage form that delivers famotidine in the stomach as a floating drug delivery system is one approach. A floating drug delivery system can be designed by incorporating at least one porous structural element that is less dense than gastric juice. [13] This article describes the development of gastro retentive matrix tablets of famotidine to increase therapeutic efficacy, reduce frequency of administration, and improve patient compliance. The study includes the use of low-density polymers for their high porosity and floating efficiency.

MATERIALS AND METHODS

Materials: Famotidine was received as agift sample from Zydus cadila Pharmaceuticals Ltd, Ahmadabad, India.HPMCK4M and HPMCK 100M, Xanthan gum were received as gift sample from Zydus- cadila Pharmaceuticals Ltd, Ahmadabad, India. Sodium bicarbonate, Citric acid anhydrous (here after referred to as citric acid) were purchased from S.D. Fine-Chem Ltd, Ahmadabad, India Polyvinyl pyrrolidone K-30 (PVP K-30) was purchased from Ottokemi, Mumbai, India. All other ingredients were of laboratory grade.

Preformulation studies of Floating Tablets of famotidine: Various methodologies are adopted while carrying out the present study like determination of melting points, solubility and evaluation of granules.

Evaluation of granules: The flow properties of granules (before compression) were characterized in

terms of angle of repose, Carr index and Hausner ratio.[14] For determination of angle of repose (θ), the granules were poured through the wall of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0cm above hard surface. The granules were poured till the time when upper tip of the pile surface touched the lower tip of the funnel.

The tan-1 of the (height of the pile / radius of its base) gave the angle of repose. Granules were poured gently through a glass funnel into a graduated cylinder cut exactly to 10 ml mark. Excess granules were removed using a spatula and the weight of the cylinder with pellets required for filling the cylinder volume was calculated. The cylinder was then tapped from a height of 2.0cm until the time when there was no more decrease in the volume. Bulk density (ρ_b) and tapped density (ρ_t) were calculated. Hausner ratio (H_R) and Carr index (I_C) were calculated according to the two equations given below:

$H_R = \rho_t/\rho_b$

$Ic = (\rho_t - \rho_b)/ \rho_t$

Praparation of Floating Tablets of Famotidine: The composition of different formulations of famotidine floating tablets is shown in Table 1. The ingredients were weighed accurately and mixed thoroughly. Granulation was done with a solution of PVP K-30 in sufficient isopropyl alcohol. The granules (40 meshes) were dried in conventional hot air oven at 45º C. The dried granules were sized through 40/60 mesh, lubricated with magnesium stearate (0.5%w/w) and purified talc (1.0%w/w) and than compressed on a single punch tablet machine. The tablets were round and flat with an average diameter of 12.0 ±0.1 mm and a thickness of 3.13 ±0.2 mm.

Evaluation of Floating tablets:

Hardness test: Monsanto hardness tester was used for the determination of hardness of tablets.[15]

Friability: Twenty tablets were accurately weighed and placed in the friabilator (Roche's Friabilator) and operated for 100 revolutions. The tablets were dedusted and reweighed. The tablets that loose less than 1% weight were considered to be compliant.

Weight variation: 10 tablets were selected randomly from the lot and weighed individually to check for weight variation.[16]

Drug content uniformity: The drug content in each formulation was determined by triturating 20 tablets and power equivalent to average weight was added in 100ml of 0.1 N HCL, followed by stirring for 30 minutes. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometrically at 265 nm using 0.1 N HCl as blank.

RESULTS AND DISCUSSIONS

In the present study 10 formulations with variable concentration of polymer were prepared and evaluated for physiochemical parameters. The formulated batch composition were show in table no. 1 .The melting point of famotidine was found to be in range of 162-164º C which complied with BP standards, indicating purity of the drug sample. Famotidine was found to be soluble in water, 0.1 N HCL, and insoluble in ethanol, chloroform and ether.

The angle of repose for the formulated bland was carried out and the result were shown in table 2.it concludes all the formulations blend was found to be in the range of 24.263° to 29.796°.Bulk density ranged between 0.090 to 0.135 gm/cm^2 and tapped density ranged between 0.102 to 0.155 gm/cm^2. Carr index was found to be 0.087 to 0.161 and Hausner ratio ranged from 1.095 to 1.192 for granules of different formulations. These values indicate that the prepared granules exhibited good flow properties.

The tablets of 10 formulations were formulated and are examined for different parameters mentioned. Microscopic examinations of tablets from F1 to F10 were found to be circular shape with no cracks. The percentage wt. variations for all formulations were tabulated in table no. 3. All formulated tablets passed weight variation test as par Pharmacopoeia limits. The hardness for different formulations was found to be between 4.05 to 5.32 Kg/cm^2 indicating satisfactory mechanical strength. The friability was below 1% for all the formulations, which is indication of good mechanical resistance of the tablet. The drug content varied between 39.22 to 39.96 mg in different formulations with low coefficient of variation (C.V. < 1.0%), indicating content uniformity in the all prepared batches. 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. The combination of sodium bicarbonate and citric acid provided desired floating ability and therefore this combination was selected for the formulation of floating tablets. The density decreased due to this expansion and upward force of carbon dioxide gas generation. It plays an important role in ensuring the floating capability of the dosage form. To provide good floating behavior in the stomach, the density of the tablets should be less than 1.and tablet becomes buoyant.

Table 1: Composition of Famotidine Floating Tablets

Ingredients (mg per tablets)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Famotidine	40	40	40	40	40	40	40	40	40	40
HPMC K4M	40	-	-	-	-	40	80	40	-	20
HPMC K100M	40	80	40	40	-	-	-	-	-	40
Xanthan gum	-	-	-	40	40	40	-	-	80	20
Sodium bicarbonate	20	20	20	20	20	20	20	20	20	20
Citrc acid	10	10	10	10	10	10	10	10	10	10
PVP K-30	20	20	20	20	20	20	20	20	20	20
Magnesium Stearate	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2

Table 2: Evaluation of granules

Code	Angle of repose (θ)	Bulk density (gm/cm^2)	Tapped density (gm/cm^2)	Hausner ratio (H_R)	Carr Index (I_C)
F1	26.471°	0.132	0.148	1.121	0.108
F2	28.562°	0.115	0.126	1.095	0.087
F3	26.773°	0.110	0.130	1.181	0.153
F4	24.263°	0.135	0.154	1.140	0.123
F5	25.284°	0.090	0.102	1.133	0.117
F6	26.561°	0.144	0.162	1.125	0.111
F7	29.796°	0.129	0.146	1.131	0.116
F8	24.301°	0.130	0.155	1.192	0.161
F9	26.564°	0.114	0.135	1.184	0.155
F10	28.867°	0.106	0.120	1.132	0.116

Table 3: Evaluation of Famotidine floating tablets

Code	Wt. variation (%)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Drug content (mg)
F1	±2.11	4.05±0.15	0.45±0.05	3.15±0.01	39.96±0.42
F2	±1.56	5.01±0.10	0.71±0.02	3.08±0.06	39.78±0.45
F3	±3.54	4.50±0.25	0.72±0.09	3.12±0.03	39.80±0.18
F4	±1.89	5.25±0.10	0.68±0.07	3.11±0.04	39.42±0.20
F5	±2.15	4.20±0.20	0.57±0.06	3.16±0.01	39.22±0.15
F6	±2.56	5.25±0.08	0.63±0.05	3.12±0.03	39.34±0.25
F7	±3.54	5.32±0.19	0.70±0.05	3.20±0.05	39.80±0.12
F8	±1.75	4.23±0.15	0.67±0.05	3.14±0.01	39.30±0.39
F9	±1.12	5.23±0.11	0.61±0.08	3.10±0.03	39.49±0.27
F10	±2.04	5.01±0.07	0.54±0.09	3.16±0.02	39.61±0.35

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