FORMULATION AND EVALUATION OF GASTRORETENTIVE FLOATING TABLETS OF FAMOTIDINE

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ABSTRACT

Gastroretentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs. Different approaches for gastroretentive dosage forms include floating, raft, expanding or swelling, bioadhesive or mucoadhesive and high/low-density systems. Famotidine, an anti-ulcer drug, suffers from poor bioavailability (50%), as Famotidine is very less soluble in alkaline pH. Famotidine used in combination with antacids promotes local delivery of these drugs to the receptor of the parietal cell wall. Local delivery also increases bioavailability at the stomach wall receptor site and increases the efficacy of drugs to reduce acid secretion. Thus, the present work is aimed to formulate floating tablets of famotidine using an effervescent approach for gastroretentive drug delivery system.

Key-Words: Famotidine, Gastric residence time, Formulation. Evaluation

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INTRODUCTION

Floating systems are one of the important categories of drug delivery systems with gastric retentive behavior. Drugs that could take advantage of gastric retention include: furosemide, cyclosporine, allopurinol ciprofloxacin and metformin. Drugs whose solubility is less in the higher pH of the small intestine than the stomach (e.g. chlordiazepoxide and cinnarizine, the drugs prone for degradation in the intestinal pH (e.g. captopril), and the drugs for local action in the stomach (e.g. misoprostol) can be delivered in the form of dosage forms with gastric retention. Antibiotics, catecholamines, sedative, analgesics, anticonvulsants, muscle relaxants, antihypertensive and vitamins can be administered in HBS dosage form.[1,2,3]

Floating tablets were prepared using directly compression technique using polymers like HPMC, K4M and HPMCK100M for their gel-forming properties. The HPMC alone polymer unable to controlled on release rate it release drug >90% in 4-6 hrs while in combination with Xanthan gum it release >90% in 8 hrs. The results indicate that gas powered gastroretentive floating of Famotidine containing 40mg HPMCK100M and Xanthan gum provides a better option for controlled release action and improved bioavailability. [4,5]

OBJECTIVES

1. Preparation and evaluation of floating tablet of Famotidine based on low density polymer that retains the dosage form in the stomach.
2. Provide an increased gastric residence time resulting in prolonged drug delivery in gastrointestinal tract using HPMCK4M, HPMCK100M and Xanthan gum as sustain release polymers.
3. To study the various formulation and process variables that ultimately affects the drug release.

4. Selection and optimization of polymer concentration, type of filler and amount of low density polymer that has pronounced effect on tablet properties and drug release profile as well as buoyant properties of the formulations.

METHODOLOGY

Following methodology are adopted while carrying out the present study

1. Determination of Melting Point
2. Solubility
3. Evaluation of powder blend[6,7,8,9]
    - Angle of repose
    - Bulk density
    - Compressibility Index
    - Total Porosity
5. Preparation of gastro retentive floating tablets
6. Evaluation of tablets[10,11]

- Weight variation test
- Drug content
    - Hardness
    - Thickness
    - Friability Test
    - Tablet Density

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RESULTS AND CONCLUSIONS

In the present study 10 formulations with variable concentration of polymer were prepared and evaluated for physio-chemical parameters. The formulated batches were show in Table:1. The melting point of famotidine was found to be in the range 162-164^{o}c, which complied with BP standards, indicating purity of the drug sample. Famotidine was found to be soluble in water, 0.1NHCL, and practically insoluble in ethanol (95%), chloroform and ether. The angle of repose for the formulated blend was carried out and the results were shown in Table 2. It concludes all the formulations blend was found to be in the range 24^{0}.88' to 29.30'. Compressibility index was found between 12.34% to 16.30% indicating the powder blend have the required flow property for compression. The tablets of 10 formulations were formulated and are examined for different parameters mentioned. Microscopic examinations of tablets from FT1 to FT10 were found to be circular shape with no cracks. The percentage weight variations for all formulations were tabulated in Table no 3.All the formulated (FT1 to FT10) tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values. The measured hardness of tablets of each batch ranged between 4.3 to 6.4kg/cm^2 (Table 3).This ensures good handling characteristics of all batches. The values of friability test were tabulated in Table 3.The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable. When tablet contacts the test medium, tablet expanded (because of swellable polymers) and there was liberation of CO_2 gas (because of effervescent agent, $NaHCO_3$). The density decreased due to this expansion and upward force of CO_2 gas generation. This 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 that of the gastric contents the density below (1.004g/cm^3) than of gastric fluid. For formulation FT1-FT10 density were found to be less than that of the gastric content. The percentage of drug content for FT1 to FT10 was found to be between 97.11% to 99.69% of famotidine, it complies with official specifications (Table 3).

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Table 1 → Composition of Famotidine Floating Tablets

INGREDIENTS	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8	FT9	FT10
Famotidine	40	40	40	40	40	40	40	40	40	40
HPMC K4M	40	-	-	-	80	-	40	-	40	20
HPMC K100M	-	40	-	80	-	-	40	40	-	40
Xanthan gum	-	-	40	-	-	80	-	40	40	20
Sodium bicarbonate	20	20	20	20	20	20	20	20	20	20
Citric acid (anhydrous)	10	10	10	10	10	10	10	10	10	10
PVP-K-30	20	20	20	20	20	20	20	20	20	20
Avicel PH-102	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Magnesium Stearate	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2

All quantities were in milligrams.
All the batches contained 1% w/w talc and 0.5% w/w magnesium stearate

Table 2 → Micromeritic properties of powder blend

Powder blend	Angle of Repose (^{0})	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Compressibility Index (%)	Total Porosity (%)
FT1	24°.30'	0.130	0.155	16.13	15.78
FT2	26°.77'	0.110	0.130	15.67	20.00
FT3	25°.28'	0.090	0.102	14.48	37.50
FT4	28°.56'	0.105	0.126	16.30	26.31
FT5	29°.88'	0.129	0.146	15.41	27.77
FT6	25°.30'	0.114	0.135	14.30	12.50
FT7	26°.47'	0.132	0.148	12.76	35.00
FT8	24°.28'	0.135	0.154	13.47	13.04
FT9	26°.56'	0.144	0.162	12.34	20.83
FT10	28°.88'	0.106	0.120	15.91	10.00

Table 3 → Evaluation of Physical Parameters of Floating Tablets

Tablets Batch	Weight variation test (%)	Friability (%)	Hardness (kg/cm^2)	Thickness (mm)	Drug content (%)
FT1	± 1.75	0.92	5.6 ±0.47	3.08 ± 0.2	98.02
FT2	±3.52	0.72	4.5 ±0.63	3.16 ±0.010	97.01
FT3	±2.15	0.91	6.4 ±1.27	3.14 ±0.012	99.53
FT4	±1.56	0.86	5.1 ±0.03	3.12 ±0.06	98.01
FT5	±3.54	0.79	4.3 ±0.83	3.16 ±0.011	97.04
FT6	±1.42	0.86	5.1±0.03	3.18 ±0.012	98.40
FT7	±2.11.	0.78	4.3 ±0.83	3.15 ±0.010	97.11
FT8	±1.89	0.81	6.4 ±1.27	3.10 ±0.012	99.55
FT9	±2. 56	0.96	5.1 ±0.03	3.11 ±0.06	99.01
FT10	±2.04	0.75	4.3 ±0.83	3.20±0.011	99.69

All the values are expressed as mean ± SE.