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RESEARCH ARTICLE

Design and Development, *In vitro* Characterization of Gastro Retentive Floating Tablets of Anti-Ulcer Drug

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Abstract: The objective of this study was to design a delayed release formulation of Famotidine, aimed at sustaining therapeutic drug concentrations for an extended period exceeding 12 hours. Famotidine was administered at a fixed dose of 40 mg, and the total tablet weight was set at 250 mg. Hydroxypropyl methylcellulose (HPMC) derivatives, specifically HPMC K4M and HPMC K15M, were employed as polymer matrices at concentrations of 20, 40, and 80 mg. All formulations successfully met established physicochemical criteria, falling within predetermined limits. Dissolution studies revealed that formulation F6 exhibited superior and desired drug release characteristics, achieving a release rate of 96.33% within the 12-hour timeframe. Furthermore, the release mechanism of this formulation was found to conform to the Higuchi release kinetics model
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Keywords: Famotidine; Floating System; Antiulcer Activity; HPMC K4M; HPMC K15M

1. Introduction

Oral controlled release drug delivery has recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation, Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. The floating drug delivery system (FDDS) also called Hydro dynamically Balanced Drug Delivery System (HBS) [1, 2]. FDDS is an oral dosage forms (capsule or tablet) designed to prolong the residence time of the dosage form within the GIT. It is a formulation of a drug with gel forming hydrocolloids meant to remain buoyant on stomach contents. Drug dissolution and release from dosage retained in the stomach fluids occur at the pH of the stomach under fairly controlled condition. Famotidine belongs to the group of medicines known as histamine H2-receptors antagonists or H2- blockers. It works by decreasing the amount of acid produced by the stomach [3, 4]. The main aim of this work was to design a delayed release formulation of Famotidine, aimed at sustaining therapeutic drug concentrations for an extended period exceeding 12 hours

2. Material and methods

2.1. Materials: Famotidine, Sodium bicarbonate, Magnesium stearate, Hydroxy Propyl Methyl Cellulose (HPMC), Talc all the chemicals were laboratory grade

2.2. Formulation development of tablets: All the formulations were prepared by direct compression. The compressions of different formulations are given in Table 1. The tablets were prepared as per the procedure given below and aim is to prolong the release of Famotidine. Total weight of the tablet was considered as 250 mg. Famotidine and all other ingredients were individually passed through sieve no 60.All the ingredients were mixed thoroughly by triturating up to 15 min. The powder mixture was lubricated with talc. The tablets were then compressed by using direct compression method. Sodium bicarbonate was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of Sodium bicarbonate were employed, floating lag time and floating duration were observed. Based on that the concentration of Sodium bicarbonate was finalized and preceded for further formulations. Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimized [5, 6].

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Table 1 Formulation of famotidine effervescent tablets

Formulation	Famotidine	HPMC K4M	HPMC K15M	Citric Acid	$NaHCO_3$	Mag. Stearate	Talc	Lactose
F1	40	20	-----	7	70	5	3	105
F2	40	40	-----	7	70	5	3	85
F3	40	80	-----	7	70	5	3	65
F4	40	-----	20	7	70	5	3	105
F5	40	-----	40	7	70	5	3	85
F6	40	-----	80	7	70	5	3	65
F7	40	-----	-----	7	70	5	3	105
F8	40	-----	-----	7	70	5	3	85
F9	40	-----	-----	7	70	5	3	65

All the quantities were in mg, Total weight is 250 mg

2.5 Evaluation of post compression parameters: The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content [7-9]]

3. Results and discussion

The present study was aimed to developing gastro retentive floating tablets of famotidinie using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

3.1. Analytical methods: Calibration curves of Famotidine were obtained in Simulated Gastric fluid (pH 1.2). The concentration of the drug is measured using UV spectrophotometer at 297 nm [11]. The analytical method is found to be accurate as evident from the r^2 value (0.9937) of the calibration curve (shown in Figure 1)

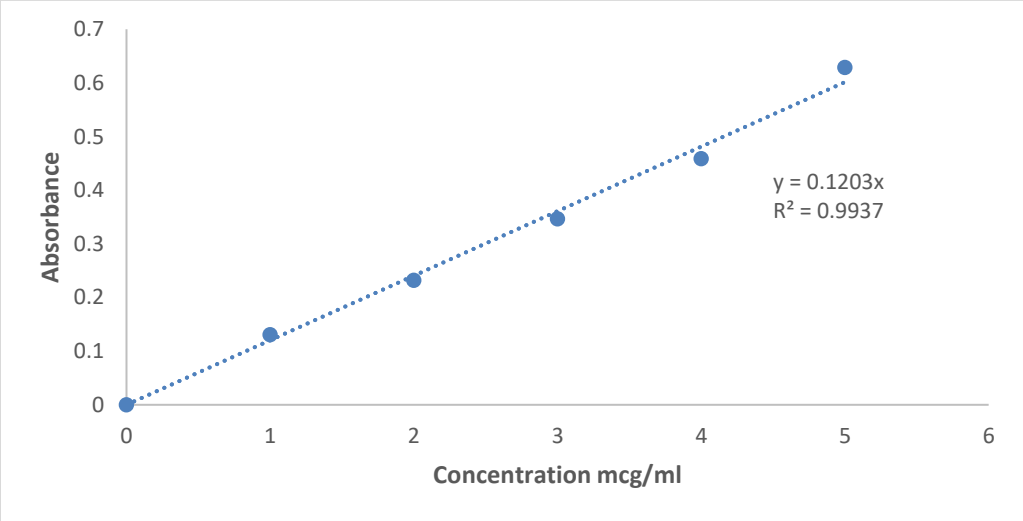

Figure 1 Standard Calibration curve of famotidine in 0.1N HCl

3.2. Pre-formulation parameters: Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values (24.84 ± 0..972 to 29.65 ± 0.784) indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.561±0.03 to 0.634±0.04 (gm/cm^3) while the tapped density of all the formulations was found to be in the range of 0.634±0.04 to 0.679±0.05 showing that the powder has good flow property. The compressibility index of all the formulations was found to be ranging from 8.24 to 15.4 that shows that the powder has good flow property. All the formulations have shown the Hausner's ratio ranging from 1.08 to 1.18 indicating the powder has good flow properties [12]. The results are shown in Table 2.

Table 2 Pre-compression parameters of powder blend

Formulation Code	Angle of Repose	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	27.52±0.235	0.561±0.03	0.634±0.04	11.5	1.130
F2	24.51±0.290	0.567±0.04	0.660±0.05	14.1	1.164
F3	27.21±0.352	0.574±0.05	0.652±0.08	11.9	1.135
F4	27.05±0.252	0.582±0.02	0.674±0.04	13.6	1.158
F5	24.62±0.374	0.575±0.04	0.680±0.06	15.4	1.18
F6	28.56±0.380	0.634±0.04	0.691±0.05	8.24	1.08
F7	24.84±0.972	0.607±0.05	0.667±0.06	8.99	1.09
F8	29.65±0.784	0.605±0.08	0.682±0.04	11.3	1.12
F9	28.46±0.674	0.611±0.04	0.676±0.05	10.01	1.167

* Mean + SEM (n=3 observations)

3.3. Quality control tests for prepared tablets: Tablet quality control tests such as weight variation, hardness, friability and thickness performed on the tablets. All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits [12]. The results are shown in Table 3.

Table 3 Quality control parameters of the prepared tablets

Formulation Code	Weight Variation (mg)*	Hardness (kg/cm^2) *	Friability (%loss) *	Thickness (mm) *	Drug Content (%)*
F1	242.1±0.25	4.25±0.11	0.57±0.06	2.87±0.014	99.26±0.15
F2	244.5±0.20	5.00±0.07	0.54±0.09	2.76±0.011	99.61±0.35
F3	247.6±0.29	4.25±0.19	0.70±0.05	2.94±0.003	99.80±0.12
F4	243.2±0.45	5.25±0.08	0.68±0.07	2.81±0.002	99.42±0.20
F5	241.3±0.55	5.25±0.15	0.45±0.05	2.68±0.012	99.92±0.42
F6	242.5±0.48	4.20±0.20	0.63±0.05	2.97±0.011	99.34±0.25
F7	248.3±0.56	5.25±0.10	0.71±0.02	2.73±0.015	99.78±0.45
F8	247.4±0.43	4.50±0.25	0.67.05	2.85±0.012	99.30±0.39
F9	242.5±0.32	5.01±0.10	0.72±0.09	2.91±0.019	99.80±0.18

* Mean + SEM (n=3 observations)

3.4. *In vitro* drug release studies: From the dissolution data it was evident that the formulations prepared with HPMC K4M as polymer were unable to retard the drug release up to desired time period i.e., 12 hours. Whereas the formulations prepared with HPMC K15M retarded the drug release in the concentration of 80 mg showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.33 % in 12 hours (Formulation F6) with good floating lag time and floating buoyancy time. The formulations prepared with lactose showed more retardation even after 12 hours they were not shown total drug release. Hence, they were not considered [11, 12]. The drug release pattern from all the formulations is shown in Table 4.

3.5. Drug release kinetics: Various models were tested for explaining the kinetics of drug release. To analyse the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model. The results shown in Figure 2 indicate that the best formulation F6 followed first order drug release with Higuchi mechanism as indicated by the higher r^2 values [11, 12].

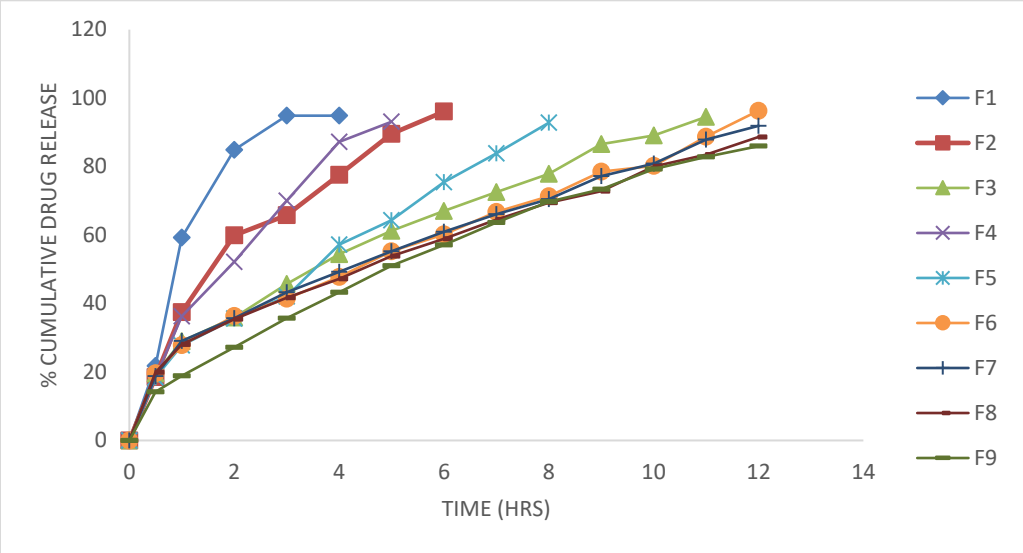

Figure 2 *In vitro* drug release from all the formulations

4. Conclusion

The aim of the present study was to develop delayed release formulation of Famotidine to maintain constant therapeutic levels of the drug for over 12 hrs. HPMC K4M and HPMC K15M are used as polymers. Famotidine dose was fixed as 40 mg. Total weight of the tablet was considered as 250 mg. Polymers were used in the concentration of 20, 40 and 80 mg concentration. All the formulations have passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e., 96.33 % in 12 hours. It followed Higuchi mechanism of drug release.

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