Formulation and Optimization of Floating Matrix Tablets of Famotidine

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***Abstract*—Famotidine, a histamine H_2-receptor antagonist, is widely used in the treatment of peptic ulcer disease and gastroesophageal reflux disease. Due to its short biological half-life and preferential absorption in the stomach, the drug requires frequent administration, which may reduce patient compliance. The present study was aimed at the formulation and optimization of floating matrix tablets of famotidine to enhance gastric residence time and achieve sustained drug release. Floating tablets were prepared by the direct compression method using hydrophilic polymers such as HPMC K4M and HPMC K15M as matrix formers, along with sodium bicarbonate as a gas-generating agent. Various formulations were developed by varying polymer concentrations and evaluated for pre-compression and post-compression parameters. The prepared tablets were further assessed for floating lag time, total floating time, and in-vitro drug release studies in 0.1 N HCl. Drug release data were fitted to different kinetic models to understand the release mechanism. The optimized formulation exhibited a short floating lag time, prolonged buoyancy for more than 12 hours, and controlled drug release, following Higuchi kinetics with non-Fickian diffusion. The study concludes that floating matrix tablets of famotidine are a promising gastroretentive drug delivery system for improved therapeutic efficacy and patient compliance.**

***Index Terms*—Famotidine; Floating matrix tablets; Gastroretentive drug delivery system; HPMC; Sustained drug release**

I. INTRODUCTION

Oral drug delivery systems are the most commonly used and preferred route of administration due to their convenience, safety, and patient compliance. However, conventional oral dosage forms often fail to achieve optimal therapeutic efficacy for drugs that have a short biological half-life, narrow absorption window, or are unstable in the intestinal environment. Such limitations necessitate the development of advanced drug delivery systems capable of improving bioavailability and sustaining drug release.

Famotidine is a histamine H_2-receptor antagonist widely prescribed for the treatment of peptic ulcer disease, Zollinger–Ellison syndrome, and gastroesophageal reflux disease (GERD). It exhibits a short biological half-life of approximately 2.5–4 hours and requires multiple daily dosing to maintain effective plasma concentrations. Additionally, famotidine is primarily absorbed from the stomach and upper part of the small intestine and shows reduced stability at higher pH levels, making it a suitable candidate for a gastroretentive drug delivery system.

Gastroretentive drug delivery systems (GRDDS) are designed to prolong the residence time of dosage forms in the stomach, thereby enhancing drug absorption and improving therapeutic outcomes. Among the various GRDDS approaches, floating drug delivery systems have gained considerable attention due to their simplicity and effectiveness. These systems are formulated to have a lower density than gastric fluid, enabling them to remain buoyant in the stomach for an extended period without affecting gastric emptying.

Floating matrix tablets are commonly prepared using hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), which swell upon contact with gastric fluid and form a gel barrier that controls drug release. The incorporation of gas-generating agents like sodium bicarbonate further aids in achieving buoyancy by producing carbon dioxide in acidic conditions. By optimizing the type and concentration of polymers and effervescent agents, floating matrix tablets can provide prolonged gastric retention and sustained drug release.

The present study focuses on the formulation and optimization of floating matrix tablets of famotidine using hydrophilic polymers. The objective is to develop a gastroretentive system capable of improving drug bioavailability, reducing dosing frequency, and enhancing patient compliance through controlled drug release and prolonged gastric residence time.

Materials And Methods

Materials

- Famotidine – Active pharmaceutical ingredient
- Hydroxypropyl Methylcellulose (HPMC K4M, HPMC K15M) – Matrix-forming polymers
- Sodium bicarbonate – Gas-generating agent
- Citric acid – Acidifying agent (to enhance CO_2 generation)
- Microcrystalline cellulose (MCC) / Lactose – Diluent
- Magnesium stearate – Lubricant
- Talc – Glidant
- Hydrochloric acid (0.1 N HCl) – Dissolution medium

All materials used were of pharmaceutical grade.

Methods

1. Formulation of Floating Matrix Tablets

Floating matrix tablets of famotidine were prepared by the direct compression method. Different formulations were developed by varying the concentration and type of polymer while keeping the drug and other excipients constant.

Procedure:

1. Famotidine, polymer (HPMC K4M or HPMC K15M), diluent, sodium bicarbonate, and citric acid were accurately weighed.
2. All ingredients were passed through sieve No. 60.
3. The drug was mixed with polymer and diluent uniformly.
4. Sodium bicarbonate and citric acid were added and blended gently.
5. Magnesium stearate and talc were finally added and mixed for 2–3 minutes.
6. The blend was compressed into tablets using a single-punch tablet compression machine.

2. Pre-Compression Evaluation

The powder blends were evaluated for flow properties:

- Angle of repose
- Bulk density
- Tapped density
- Carr's index
- Hausner's ratio

3. Post-Compression Evaluation

The compressed tablets were evaluated for:

- Weight variation
- Thickness
- Hardness
- Friability
- Drug content uniformity

4. Evaluation of Floating Properties

Floating behavior was studied in 0.1 N HCl (pH 1.2):

- Floating lag time (FLT): Time required for the tablet to rise to the surface
- Total floating time (TFT): Duration for which the tablet remained buoyant

5. In-Vitro Drug Release Study

In-vitro dissolution studies were carried out using USP Type II (paddle apparatus) at 50 rpm in 900 mL of 0.1 N HCl maintained at 37 ± 0.5 °C. Samples were withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically at the λmax of famotidine. An equal volume of fresh dissolution medium was replaced after each sampling.

6. Drug Release Kinetics

The dissolution data of optimized formulations were fitted into various kinetic models:

- Zero-order model
- First-order model
- Higuchi model
- Korsmeyer–Peppas model

Results And Discussion

FTIR analysis:

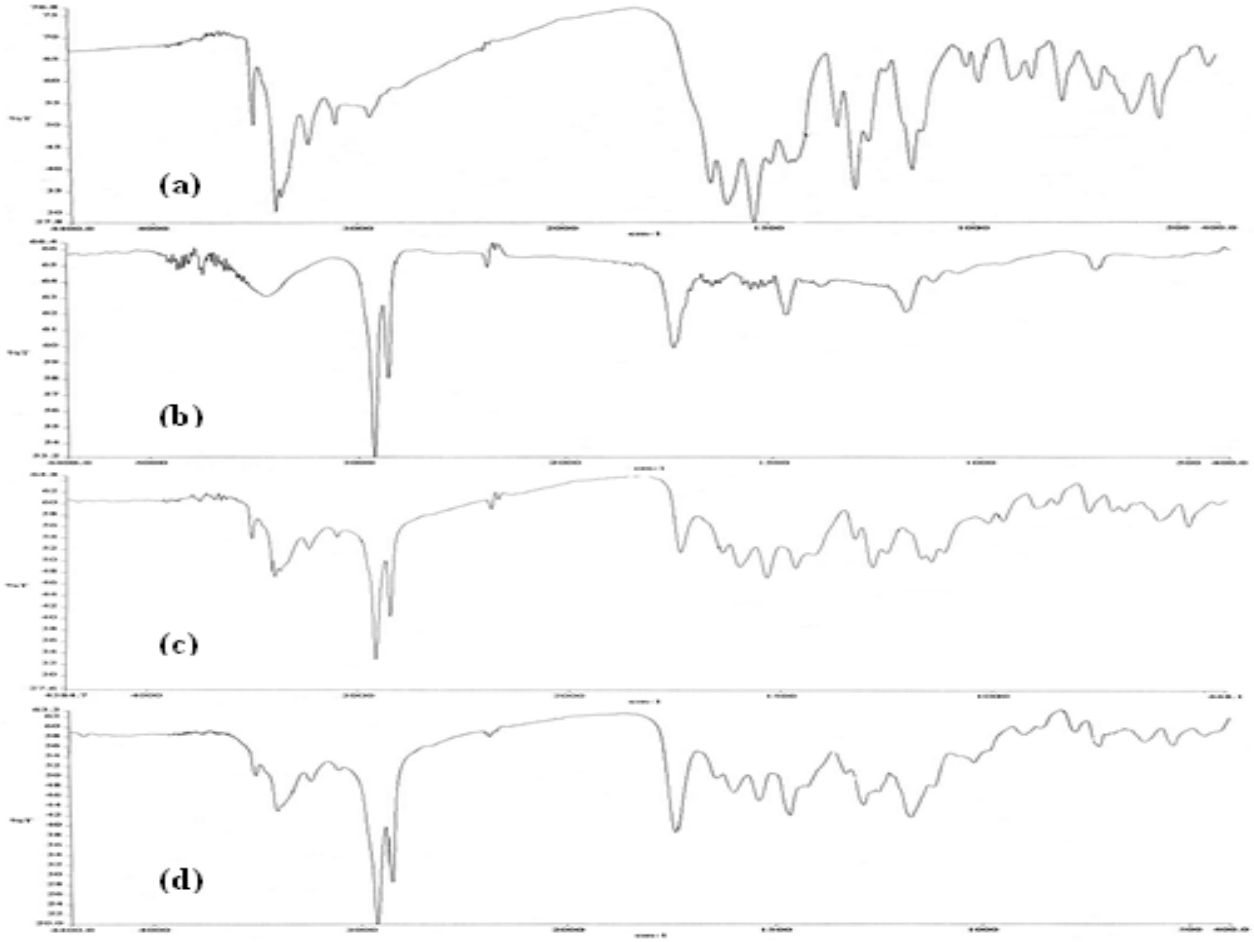

Fig.1.1: FTIRspectraofa)Famotidine,b)GB,c)FPMoptandd)FMGopt

The FTIR spectra of pure famotidine, glyceryl behenate (GB), optimized physical mixture formulation (FPMopt), and optimized melt granulated formulation (FMGopt) are shown in Figure 4.16. The FTIR spectrum of famotidine showed characteristic peaks at 3503.74 cm^{-1} (–OH stretching), 3399.82–3372.73 cm^{-1} and 3236.89 cm^{-1} (–NH_2 and –NH stretching), 1446.39–1599.98 cm^{-1} (C=N stretching), 694.88–608.86 cm^{-1} (C–S stretching), and 1326.12 cm^{-1} and 1144.28 cm^{-1} (asymmetric and symmetric $S(=O)_2$ stretching), confirming the drug structure.

Glyceryl behenate showed characteristic peaks at 3439.24 cm^{-1} (–OH stretching), 1739.85 cm^{-1} (C=O stretching), 1179.57 cm^{-1} (O–C=C stretching), and 1051.53 cm^{-1} (C–O–C stretching).

The FTIR spectra of FPMopt and FMGopt showed all the characteristic peaks of famotidine with minor shifts, indicating that the drug remained chemically intact in both formulations. No new peaks or significant peak disappearance was observed, confirming the compatibility of famotidine with excipients and the stability of the optimized formulations.

DSC analysis: Thermograms of pure drug famotidine, GB and optimized formulations, $FPM_{opt}$and $FMG_{opt}$are shown in Fig. 1.2.

A single sharp endothermic peak at 170.08° C was obtained for famotidine corresponding to its melting point. GB showed broad endothermic peaks at 80.11° C. Characteristic peak of famotidine was slightly shifted to left for FPM_{opt}(166.39° C) and FMG_{opt}(168.95° C).

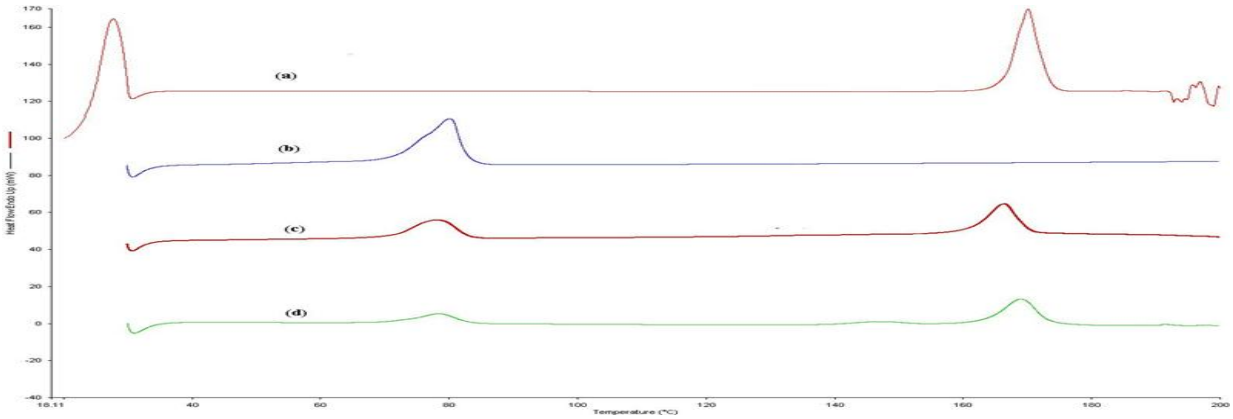

Fig.1.2:DSCthermogramsofa)Famotidine,b)GB, c)FPMoptandd)FMGopt

XRD studies: X-ray diffractograms of pure drug famotidine, GB and optimized formulations FPMoptand FMGoptwere shown in Fig.4.18.The XRD results were in good agreement with the thermal analysis data. X-ray diffraction patterns revealed that pure famotidine was clearly in crystall in estate a sit showed sharp distinct peaks notablyat2θ diffractionanglesof5.8,11.5,15.8,17.5,18.1,19.2,19.5, 20.0,20.5, 21.0,22.4,22.8,23.2,24.0,24.5,26.2,26.6,27.2,30.2and 32.2°(2θ).

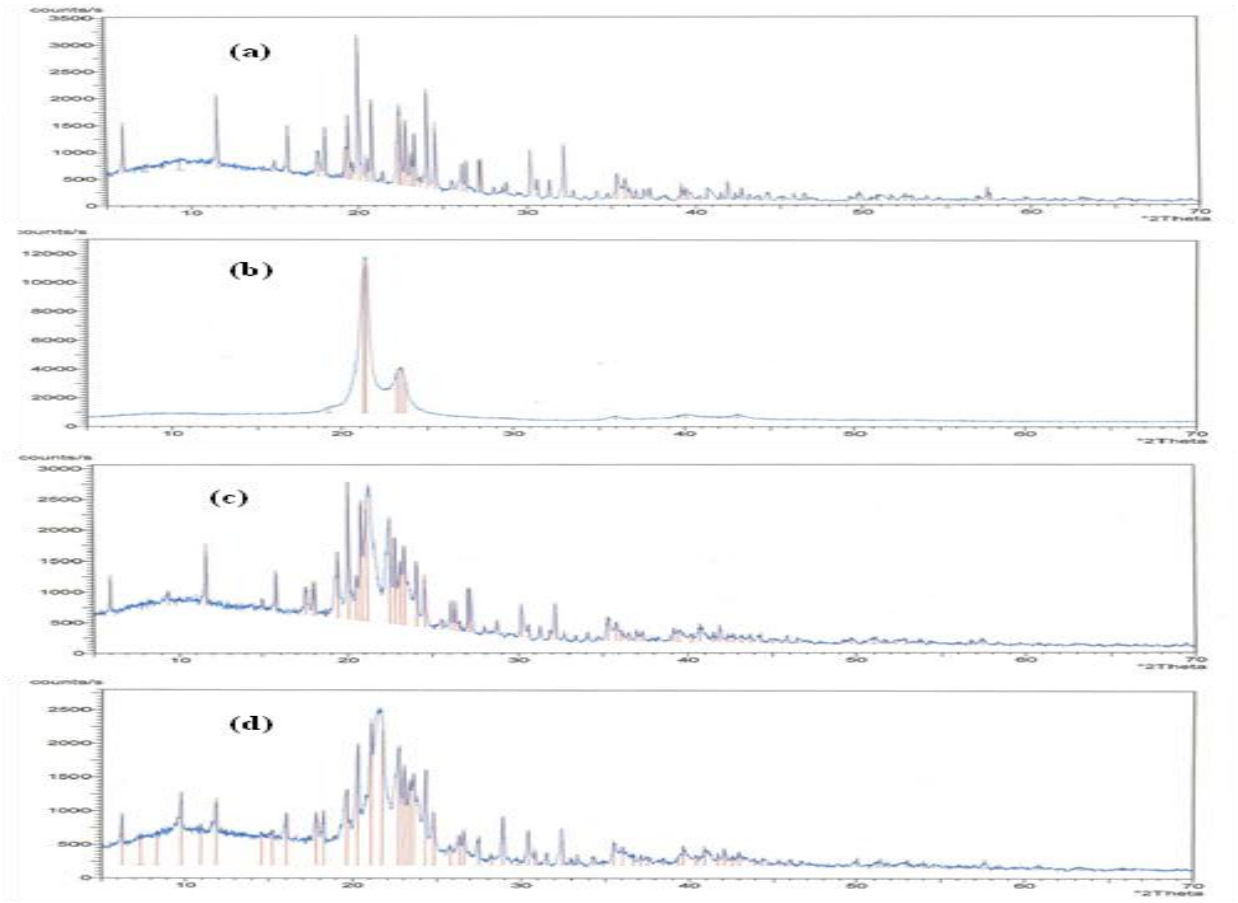

Fig.1.3: X-ray diffract to grams of a) Famotidine, b) GB, c) FPMoptand d) FMGopt

II. CONCLUSION

he present study demonstrated the suitability of glyceryl behenate (GB) for the design of non-effervescent gastric floating matrix tablets (NEGFMT), as the formulations exhibited immediate floating without lag time. Statistical optimization effectively reduced the number of experimental runs required to optimize GB concentration. Since GB is a hydrophobic material, drug release occurred mainly through drug dissolution followed by diffusion. The incorporation of lactose as a channeling agent facilitated consistent drug release by creating pores within the hydrophobic matrix. Optimized formulations contained approximately 8–10% lactose, which was essential to achieve the desired release profile. Among the two preparation methods, melt granulation was more effective than physical mixing due to better drug distribution, requiring significantly lower GB concentration while still meeting the theoretical release profile.

REFERENCES

[1] Ghimire M, McInnes FJ, Watson DG, Mullen AB and Stevens HNE: In-vitro/in-vivo correlation of pulsatile drug release from press-coated tablet formulations: A pharma coscinti graphic study in the beagle dog. Eur J Pharm Biopharm. 67: 515-523, 2007.

[2] Barthelemy P, Laforêt JP, Farah N and Joachim J: Compritol® 888 ATO:aninnovativehot-meltcoatingagent for prolonged-release drug formulations. Eur J Pharm Biopharm. 47: 87-90, 1999.

[3] Obaidat AA and Obaidat RM: Controlled release of tramadol hydrochloride frommatrices prepare dusing glyceryl behenate. Eur J Pharm Biopharm. 52: 231-5, 2001.

[4] KhuriAIandCornellJA:Responsesurfacedesigna ndanalysis.MarcelDekkerInc.,NewYork,1987.

[5] Prakobvaitayakit M and Nimmannit U: Optimization of polylactic-co- glycolic acid nanoparticles containing itraconazole using 32 factorial design. AAPS Pharm Sci Tech. 4: 565-573, 2003.

[6] Akhnazarova S and Kafaro V: Experiment optimization in chemistryand chemical engineering. Mir House Publication, Moscow, Russia, 1982.

[7] ICH Harmonized Tripartite guide line on “Stability Testing of New Drug Substances and Products Q1A (R2)", 6 February, 2003.