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**Research paper**

# FORMULATION AND IN-VITRO EVALUATION OF MUCOADHESIVE TABLETS OF FAMOTIDINE

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Famotidine is a histamine H2-receptor antagonist. It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis. The effective treatment of erosive esophagitis requires administration of 20 mg of Famotidine 4 times a day. a conventional dose of 20 mg can inhibit gastric acid secretion up to 5 hours but not up to 10 hours. An alternative dose of 40 mg leads to plasma fluctuations; thus a sustained release dosage form of famotidine is desirable. The short biological half-life of drug (2.5-4 hours) also favors development of a sustained release formulation. The present study aims to reduce the dosing frequency by using single and combinations of synthetic and natural polymers for preparation of mucoadhesive tablets. Various approaches to combine synthetic (HPMC-100, sodium bicarbonate) and natural (xanthum gum) hydrophilic polymers have been made to prepare total eight formulations. Further, these formulations were subjected to different evaluation studies like friability, content uniformity, surface *pH*, wash-off and dissolution tests. All the tests were performed using standard methods. Results for *in vitro* drug release and wash-off studies suggest that the formulation (FHT) containing HPMC-100 and xanthum gum has shown better mucoadhesive property. Other studies have shown satisfactory results in all eight formulations. Thus, the present investigation suggests the combination of HPMC-100 and xanthum gum, as hydrophilic polymers for preparation of famotidine mucoadhesive tablets.

***Key words:*** Famotidine , Mucoadhesive tablets..

## INTRODUCTION

Famotidine is a histamine H2-receptor antagonist. In gastroesophageal reflux disease the recommended dose is 20 mg by mouth twice daily for 6 to 12 weeks. In the Zollinger-Ellision syndrome the initial dose by mouth is 20mg every 6 hours, increased as necessary; dose up to 80 mg daily have been employed[1].The low bioavailability (40-45%) and short biological halflife (2.5-4.0 hours) of famotidine following oral administration favors development of a sustained release formulation[2]. Famotidine provides protection against NSAIDS-associated gastric and duodenal ulcers[3]. Controlled release formulation describes sustained action along with its predictability and reproducibility of release of drug ingredients from the drug delivery system[4]. Out of drug delivery systems, the mucoadhesive drug delivery system is more reliable than traditional drug delivery systems. Mucoadhesion, an interfacial phenomenon, is based on two materials, one of which is mucus layer of mucosal tissue to which the drug is held together by means of interfacial forces for prolonged period of time. Control release system ensures localization of drug in a particular site to improve and increase the bioavailability. The contact time is also enhanced due to interaction between polymers and mucus lining of tissue for sustained action[5]. Advance polymer systems in controlled delivery systems maintain the release rate as well as the

concentration in the biological system by increasing its localization and avoiding first pass metabolism[6].mucoadhesion as a means of influencing the duration of contact of medicinal formulations with mucous membranes immediately became a subject of interest to technologists[7].

**Materials and Methods:**

Famotidine (Balaji drug supplier,Surat,Gujarat), HPMC-100, Sodium carbonate, Magnesium striate,(Subham pharma chem. Mumbai. Steric acid,Xanthum gum,,Citric acid,Talc (Pragati chem..impact pvt.ltd. Mumbai.) were employed in the present study. All other chemicals were of analytical grade and were freshly prepared.

**Method of preparation of famotidine mucoadhesive tablet**: -

Mucoadhesive tablets each containing 20 mg of Famotidine were prepared by conventional wet granulation method employing HPMC-100, Lactose, sodium bi carbonate, Citric acid, Xanthum gum as mucoadhesive materials.

A batch of 100 tablets was prepared in each case a blend of 2 gm of famotidine with required amount of polymers and required amount of diluents which were then granulated along with alcoholic solution of HPMC-100(1% w/v)used as a granulating agents . At first the required quantity of drug, diluent taken in a motor and pestle for trituration. Then the solvent is added drop wise with continuous stirring until the wet mass is formed. Then the wet masses were passed through 12 mesh sieve and wet granules were dried at 60º C for 4 hours. The dried granules (20 mesh) after blending with talc (0.1 gm) and magnesium stearate (0.1 gm) in a laboratory cube blender for 5 mins were compressed into 300 mg tablets of hardness 4 kg/sq.cm on a tablet compression machine. The tablets were then considered for further study[8].

**Evaluation of mucoadhesive formulation:**

The physical evaluation tests for the mucoadhesive tablets of all the formulations were performed and mean values were calculated. Weight variation analysis was done by weighing 20 tablets individually, the average weight was calculated and % variation of each tablet from the average weight of tablets was calculated. Hardness and friability of the mucoadhesive tablet formulations were evaluated using Monsanto hardness tester and Roche friabilator respectively.

**Drug Content uniformity:**

The tablets were kept in 100 ml volumetric flask containing upto 100 ml with 0.1 N Hcl for 2 hr. When tablets were completely dissolved the solution was centrifuged. After centrifuged the supernatant was collected. Absorbance was measured spetrophotometrically at 284 nm. Dilution was made using as per requirement[9].

**Surface pH:**

The surface *pH* was determined to investigate the possible *in vivo* side effects of the formulation. An acidic or alkaline formulation causes irritation of the mucosal membrane and hence, this is an important parameter in developing a mucoadhesive dosage form. A combined glass

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electrode was used for determination of surface *pH*. The tablets were kept in contact with 5 ml distilled water pH 6.5 ± 0.5 for 2 h in 10 ml beakers. The tablets swell up and *pH* was noted by bringing the electrode near the surface of the formulation after equilibrating for 1 min.[10].

**Wash-off test:**

The mucoadhesive properties of the tablets were evaluated by an *in vitro*, wash-off method. Pieces of intestinal mucosa of goat were mounted on the glass slides provided with suitable support. After fixing of 2 tablets to this glass slide, it was tied to the arm of USP tablet disintegration test apparatus and was run at 37°C. Time of detachment of both tablets was noted down[11].

**In vitro drug release study:**

The in vitro drug release study was performed using USP dissolution rate test apparatus (paddle type; 50 rpm). Dissolution study was carried out for 12 h. 0.1 n Hcl (900 ml) was used as dissolution media. Samples of each 5 ml were withdrawn at intervals of 1,2,3,6,9,12 hr. Volume in dissolution vessel was kept constant by equal replacement with fresh media. The samples were collected in test tubes after filtration through Watt Mann filter paper. The amount of the drug in the aliquots was quantified by taking the absorbance of the sample at 286 nm spectrophotometrically, using 0.1 N Hcl (dissolution media) as the blank.

**Results and Discussion:**

The prepared mucoadhesive tablets were evaluated for various physical parameters such as weight variation, hardness, friability and drug content. All the batches were produced under conditions to avoiding processing variables. Hardness of tablets ranged from 3.5-4.5 kg/cm$^2$ and the percentage friability was between 0.4-0.5% as shown in table no 2, is with in limit of IP. The values of hardness test and percentage friability indicates good handling property of prepared mucoadhesive tablets. The drug content uniformity in the mucoadhesive tablets was within the range from 92.18 -98.37% as shown in **table no 2**. The surface pH study in the mucoadhesive tablets was within the range from 6.7-7.4 as shown in **table no 3**.

**Table 1: Formulation codes of different famotidine mucoadhesive tablets**

| Ingredients (mg/tab) | Formulation Code | | | |
|---|---|---|---|---|
| | F1 | F2 | F3 | F4 |
| Famotidine | 20 | 20 | 20 | 20 |
| HPMC-100 | ---- | 80 | 100 | 80 |
| Xanthum gum | 100 | --- | 20 | 40 |
| Sodium bicarbonate | 60 | 60 | 50 | 50 |
| Lactose | 45 | 65 | 45 | 45 |
| Steric acid | 30 | 30 | 30 | 30 |
| Magnesium Stearate | 03 | 03 | 03 | 03 |
| Citric acid | 40 | 40 | 30 | 30 |
| Talc | 02 | 02 | 02 | 02 |

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**Table 2: Percentage loss in weight, % drug content and hardness exhibited by fam mucoadhesive tablets**

| S.No. | Formulation Code | % Loss in weight | % Drug content | Hardness (Kg/cm²) |
|---|---|---|---|---|
| 1 | F1 | 0.46 | 92.18 | 3.5 |
| 2 | F2 | 0.61 | 95.45 | 3.67 |
| 3 | F3 | 0.43 | 97.31 | 4.50 |
| 4 | F4 | 0.66 | 98.37 | 4.00 |

**Table 3: Surface pH and detachment time exhibited by famotidine mucoadhesive tablets**

| Formulation Code | Surface *pH* | Average detachment time (min) |
|---|---|---|
| F1 | 7.2 | 465 |
| F2 | 7.3 | 401 |
| F3 | 6.7 | 366 |
| F4 | 7.1 | 435 |

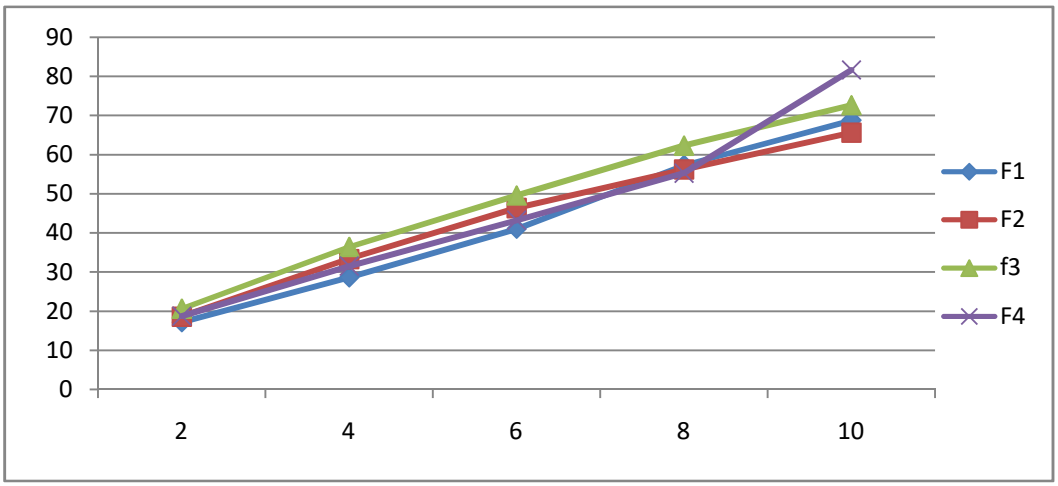


**Fig. 1: Comparative dissolution profiles of F1, F2, F3, F4, formulations**

The release of famotidine from the prepared formulations was analyzed by plotting cumulative percentage drug release vs time as shown in **fig. 1**. From all formulations, over 20% of the famotidine was release within the first hour of dissolution study. In the present study the formulation F4 (HPMC-100 and Xanthum gum) has shown cumulative percent drug release of about 81.65% in 10 h as shown in **fig. 1**.

## CONCLUSION

The present study concludes that formulation containing famotidine with HPMC-K4M and tragacanth (FHT) has given better drug release property than the other seven formulations and the wash-off test has shown that this formulation (FHT) has better mucoadhesive property as shown in **table no 3**.

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