INTERNATIONAL JOURNAL OF DRUG DISCOVERY AND HERBAL RESEARCH (IJDDHR)
ISSN: 2231-6078
14(2): April.-June.: (2024), 57-62

Research Article

FORMULATION AND DEVELOPMENT OF GASTRORETENTIVE MUCOADHESIVE TABLETS USING NATURAL POLYMERS

Brajesh Kumar, Dr. Dharmendra singh rajput and Dr. Naveen Gupta

Madhyanchal Professional University, Bhopal, Madhya Pradesh, India

Abstract

The formulation development of Famotidine mucoadhesive tablets involved a comprehensive assessment of both pre-compression and post-compression properties, as well as the determination of mucoadhesive strength. In the pre-compression phase, the powder blend properties, including bulk density, tapped density, compressibility index, and Hausner ratio, were evaluated for formulations (FI to F6). These parameters are critical indicators of the blend's flowability and compression characteristics. Notably, variations among formulations were observed, reflecting differences in their powder characteristics. Moving to the post-compression properties, parameters such as thickness, hardness, weight variation, friability, and drug content were assessed for Famotidine mucoadhesive tablets. The systematic formulation development and characterization, coupled with the sustained drug release profile and regression analysis results, support the feasibility of Famotidine mucoadhesive tablets for controlled drug delivery applications. Further studies, including in vivo evaluations and stability assessments, are warranted to validate the clinical relevance and long-term performance of these formulations.

Keyword :Famotidine, mucoadhesive tablets, post-compression properties, evaluations.

Introduction :

1.1 Gastro Retentive Drug Delivery System

Oral route of drug administration is the most convenient and commonly used method of drug delivery. However, this route has several physiological problems. Including an unpredictable gastric emptying rate that varies from person to person, a brief gastrointestinal transit time (80-12h), and the existence of an absorption window in the upper small intestine for several drugs These difficulties have prompted researchers to design a drug delivery system which can stay in the stomach for prolonged and predictable period. Attempts are being made to develop a drug delivery system which can provide therapeutically effective plasma drug concentration for a longer period, thereby reducing the dosing frequency and minimizing fluctuation in plasma drug concentration at steady state by delivering the drug in a controlled and reproducible manner .**1.2 Anatomy Of The Gastrointestinal Tract**

The gastrointestinal tract can be divided into three main regions namely

1. Stomach
2. Small intestine- Duodenum, Jejunum and Ileum

Large intestine

Corresponding Author

E.mail: brajeshkumaryadav1998@gmail.com

The GIT is a continuous muscular tube, extending from the mouth to the anus, which functions to take in nutrients and eliminate waste by such physiological processes as secretion, motility, digestion, absorption and excretion. The stomach is a Jshaped enlargement of the GIT which can be divided into four anatomical regions: cardia, fundus, body and antrum. The main function of the stomach is to store and mix food with gastric secretions before emptying its load (chyme) through the pyloric sphincter and into the small intestine at a controlled rate suitable for digestion and absorption. When empty, the stomach occupies a volume of about 50 ml, but this may increase to as much as I litre when full [1-8].

1.3 Mucoadhesive Drug Delivery

Since the early 1980s, the concept of mucoadhesion has gained considerable interest in pharmaceutical technology [221. Adhesion can be defined as the bond produced by contact between a pressure sensitive adhesive and a surface. The American Society of Testing and Materials has defined it as the state in which two surfaces are held together by interfacial forces, which may consist of valence forces, interlocking action or both.

Materials and Methods[9-15]

2.0 PREPARATION AND CHARACTERIZATION

2.1 Method For Preparation Of Famotidine Gastroretentive Mucoadhesive Tablet

Famotidine, polymers, and excipients were mixed thoroughly and passed though sieve 60. The tablets with different composition (Table 7.1) were prepared by direct compression technique on a rotary punch tablet compression machine (Rimek mini press, MT-Il, India). The powder was weighed and individually filled in the die cavity (8 mm diameter), and constant pressure was applied. The tablets were evaluated for various parameters like thickness, average weight, hardness, drug content, swelling index, mucoadhesive strength and in vitro drug release 1841.

Polymers selected for tablets are:

- HPMC K4
- Sodium alginate
- Gum tragacanth

Excipients like Sodium alginate, Gum tragacanth, as mucoadhesive polymers. Steps associated with the manufacture of tablets, required amount of API, polymer and excipients were weighed legitimately and transferred into polyethylene pack and the mix was blended for not less than 15 min. The mix acquired was then lubricated by including Talc and magnesium stearate and again blended for another 5min.

Evaluation of tablets

All the tablets were evaluated for following various parameters which includes;

2.3.1 General Appearance

Five tablets from various batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually. Very good (+++), good (+4), fair (+) poor (-), very poor (- -) [85].

2.3.2Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

2.3.3 Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 10mg of drug was transferred to 10ml standard flask. The powder was dissolved in 5 ml of 0.1 N HCI and made up to volume with of 0.1 N HCI. The sample was mixed thoroughly and filtered through a 0.45g membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at max of 265.0 nm using O. I N HCI blank [861].

2.3.4Hardness

For each formulation the hardness of five tablets was resolved utilizing the Monsanto hardness tester (Cadmach).

2.3.5 Friability

The friability of sample of 10 tablets was estimated utilizing a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated [87].

2.3.6 Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

2.3.7 Swelling Index

Swelling study of individual polymers and combinations was carried out using eight-stage USP type I (basket) Dissolution Test Apparatus (Lab India, DS 8000) at 5() rpm, and 0.1 N HCI was used as medium, and the temperature was maintained at 37 ± 0.5 ^{0}C. Weight of individual tablet was taken prior to the swelling study (WI). The tablet was kept in a basket. The weight of tablet was taken at time interval of 2, 4, 8, 12 hours (W2). Percent hydration
(swelling index) was calculated as shown in Table 7.4 using the following formula:

Swelling index = (W2 - WI) x 100/W2

Where WI is the initial weight of tablet and W2 is the weight of hydrated tablet.

2.3.8 Determination of mucoadhesive strength

The working of a double beam physical balance formed the basis of the bioadhesion test assembly. The left pan was removed and hung with a stainless steel chain. A Teflon block with 1.5 in height and 1.5 in diameter was hung with the stainless steel chain to balance the weight of the other pan.

2.3.9 Dissolution rate studies

In vitro drug release of the sample was done using USP-type Il dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1 N HCI was set into the dissolution flask maintaining the temperature of 37±0.5 ^{0}C and rpm of 75. One Famotidinetablet was set in every container of dissolution apparatus. The mechanical assembly was permitted to keep running for 10 hours. Sample measuring 5 ml were pulled back after each I hour up to 2 hours using pipette. The new disintegration medium (37^{0}C) was supplanted each time with a similar amount of the sample and takes the absorbance at 264.0 nm using spectroscopy.

Results and Discussion

Results Of Post Compression Properties Of Famotidine Mucoadhesive Tablets

The post-compression properties of Famotidine mucoadhesive tablets, as characterized by thickness, hardness, weight variation, friability, and drug content, provide crucial insights into the final product's physical attributes, mechanical strength, uniformity, and drug dosage consistency.

Thickness: The tablet thickness for formulations FI to F6 ranges from 2.1 mm to 2.4 mm. These values indicate reasonable uniformity in tablet dimensions, ensuring consistency in dosing and ease of handling.

Hardness: Tablet hardness, a measure of the tablet's mechanical strength, is reflected in values ranging from 5.3 kg/cm^2 to 5.6 kg/cm^2. These values suggest that the tablets possess adequate hardness, crucial for structural integrity, handling during packaging, and resistance to mechanical stresses during transit and use.

Weight Variation: The weight variation values, ranging from 198 mg to 205 mg, indicate consistency in the tablet weight among different units within each formulation. This is vital for ensuring uniform drug content and therapeutic efficacy across tablets in a batch.

Friability: Friability, calculated as the percentage of weight loss during tablet abrasion, is observed to be low, ranging from 0.744% to 0.856%. These low values suggest minimal tablet abrasion and indicate that the tablets can withstand the mechanical stresses encountered during packaging, transportation, and handling.

Drug Content: The drug content values range from 97.54% to 99.85%, indicating the amount of Famotidine present in each tablet relative to the intended dosage. The high drug content values reflect the accuracy and precision of the formulation process, ensuring that each tablet delivers the desired therapeutic dose.

The post-compression properties collectively suggest that formulations Fl to F6 of Famotidine mucoadhesive tablets exhibit favorable physical charactenstics, mechanical strength, weight uniformity, and drug content consistency. The tablets meet the standard requirements for thickness, hardness, weight variation, friability, and drug content, indicating their potential for reliable clinical performance. The low friability values affirm the tablets' robustness during handling and transportation. These results collectively demonstrate the successful formulation and manufacturing of Famotidine mucoadhesive tablets with the desired attributes for effective drug delivery and patient compliance.

Swelling index

The swelling index results of Famotidine mucoadhesive tablets reveal significant insights into the tablets' mucoadhesive behavior over time. The formulations, denoted as Fl to F6, exhibit a time-dependent increase in the swelling index,

indicating their ability to absorb water and undergo controlled swelling. Notably, all formulations demonstrate a consistent rise in the swelling index from 2 hrs to 12 hrs, with the maximum values reached at the latter time point.

This sustained swelling is essential for mucoadhesive formulations, suggesting prolonged contact with the mucosal surface, which is crucial for achieving prolonged drug release and enhancing therapeutic efficacy. Variability among formulations in terms of swelling characteristics implies differences in composition and formulation parameters, which can influence the tablets' hydration and swelling properties. The observed higher swelling indices may have implications for sustained drug release, making these formulations promising candidates for applications requiring prolonged therapeutic action.

In vitro drug release study of mucoadhesive tablet

In vitro drug release studies were performed by using USP XXIII dissolution test apparatus Il at 50rpm using 900 mL of 1.2 pH buffer maintained at 37±0.5 ^{0}C as the dissolution medium.

The in vitro drug release profiles for the preliminary formulations were tabulated in Table no 8.5. The plot of cumulative percentage drug release v/s time (Hrs) for preliminary formulations were plotted and depicted in Figure.

Conclusion

The overall findings suggest that Famotidine mucoadhesive tablets, especially formulation F5, have the potential for controlled drug release, making them promising candidates for achieving sustained therapeutic effects. The systematic formulation development and characterization, coupled with the sustained drug release profile and regression analysis results, support the feasibility of Famotidine mucoadhesive tablets for controlled drug delivery applications. Further studies, including in vivo evaluations and stability assessments, are warranted to validate the clinical relevance and long-term performance of these formulations.

Reference

1. Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site specific delivery. Int J Pharma. 1996; 136:117-139.
2. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system.
   Expert opin Drug Deliv. 2006; 3 (2): 217-233.
3. Singh BN and Kim. Floating drug delivery systems: an approach to controlled drug delivery via gastric retention. J. Control. Release. 2000; 63: 235-239.
4. Ali J, Arora S, Khar RK. Floating drug delivery System: A Review. AAPS Pharm Sci Tech. 2005; 06(03): E372-E390.
5. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system.
   Expert opin Drug Deliv 2006; 3(2): 217-233.
6. Garg R, Gupta GD. Progress in controlled gastroretentive delivery systems.Trop. J Pharm Res 2008; 7(3): 1055-66.
7. S.J. Hwang, H Park and K Park, "Gastric Retentive Drug Delivery Systems," Critical Reviews in Therapeutic Drug Carrier Systems, 15 (3) (1998), pp. 243284.
8. Chickering DE, Ill, Mathiowitz E. Fundamentals ofbioadhesion. In: Lehr CM, editor. Bioadhesive drug delivery systems-Fundamentals, Novel Approaches and Development. New York: Marcel Dekker; 1999. pp. 1—85.
9. Deepali N. Tapre, Sachin P. Borikar, Shirish P. Jain, Sheelpriya R. Walde, Ganesh G. Tapadiya, Vishal C. Gurumukhi. Development and evaluation of novel famotidine-loaded fast dissolving sublingual film using the quality-by-design approach. Journal of Drug Delivery Science and
   Technology. Volume 85, August 2023, 104581.
10. Filippos-Michail Stavras, Ioannis Partheniadis, Ioannis Nikolakakis.
    Formulation of taste-masked orodispersible famotidine tablets by sequential spray drying and direct compression — Bitterness evaluation. Journal of Drug Delivery Science and Technology. Volume 81, March 2023, 104290.
11. Hrishabh Sharma, Ashutosh Sharma, Saurabh Pandey, Vikas Agarwal, Sunil Sain. Formulation Development and Invitro Evaluation of Famotidine Gastroretentive Tablets. Journal of Biomedical and Pharmaceutical Research 2023;12(3):23.
12. Mohamed, A. 1., Herry, M. 1., Kassem, M. A., EL-Nabarawi, A., & EL Khatib,
    M. M. A. (2023). Preparation and evaluation of once-daily floating gmoalginate microspheres containing famotidine. International Journal of Applied Pharmaceutics, 15(1), 298—307.
13. Hyun Seok Yang, Dong Wuk Kim. Fabrication of Gastro-Floating Famotidine Tablets: Hydroxypropyl Methylcellulose-Based Semisolid Extrusion 3D Printing. Pharmaceutics 2023, /5(2), 316.
14. Thimmaraju MK, Sushma D, Vidhya B, Jyothi A, Gudas GK, Venu K. Formulation and evaluation of mucoadhesive tablets of furosemide by design of experiment. Egyptian Pharmaceutical Journal. 2021 Oct 1;20(4):270.
15. Reddy S, Bijjika S, Rao S. Approaches to gastro retentive drug delivery systems: An overview. International Journal of Research in Phytochemistry and Pharmacology. 2017 Jun 30;7(3):50-63.

Table. 1: Various formulations of Famotidine mucoadhesive tablets

Excipients (mg)						
Famotidine	40	40	40	40	40	40
HPMC K4	25	50	25	50	25	50
Sodium alginate	20	30			30	40
Gum tragacanth			20	30	30	40
MCC	95	60	95	60	55	10
Talc	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10
Total Weight	200	200	200	200	200	200

Table 2. Results Of Post Compression Properties Of Famotidine Mucoadhesive Tablets

Formulation code	**Thickness * (mm)**	**Hardness (kg/cm^2) n=3**	**Weight variation (mg) n=3**	**Friability (%) n=3**	**Drug content (%) n=3**
F1	2.3	5.3	202	0.752	98.65
F2	2.2	5.4	198	0.856	98.85
F3	2.4	5.5	205	0.745	98.12
F4	2.2	5.6	203	0.752	97.85
F5	2.1	5.5	201	0.854	99.85
F6	2.3	5.3	199	O. 744	97.54

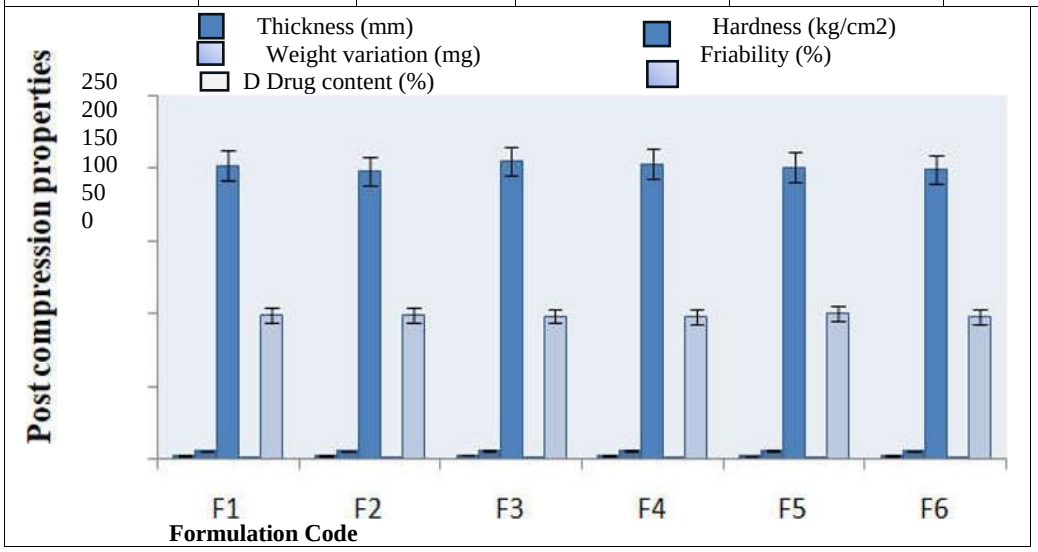

Table 3: Results of Swelling Index of Famotidine mucoadhesive tablets

Formulation Code	% Swelling Index			
	2 hrs.	4 hrs.	8hrs.	12hrs.
F1	45.56	65.58	85.56	99.23
F2	52.32	72.32	92.32	105.65
F3	55.65	69.98	83.35	92.65
F4	64.56	75.65	95.56	105.98
F5	78.89	98.89	102.32	120.32
F6	65.58	83.32	98.87	100.65

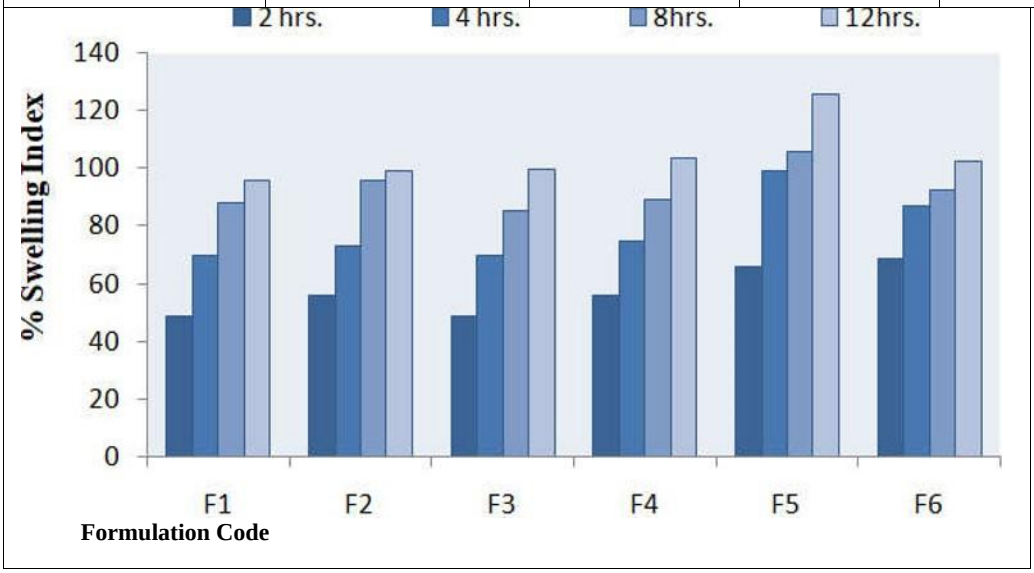

Figure 2: Results of Swelling Index of Famotidine mucoadhesive tablets

Table 4: In-vitro drug release study of mucoadhesive tablets

Time	% Cumulative Drug Release					
(hr)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
0.5	33.45	30.45	28.98	25.65	22.65	12.25
1	55.48	45.58	40.65	39.98	34.85	32.25
1.5	69.98	58.89	50.65	46.65	42.32	40.95
2	98.85	68.78	61.56	58.78	56.65	51.47
3	-	99.12	88.98	73.36	69.98	60.36
4	-	-	98.85	85.65	75.65	69.98
6	-	-	-	92.56	83.65	76.65
8	-	-	-	99.45	91.65	80.65
12	-	-	-	-	99.45	86.65

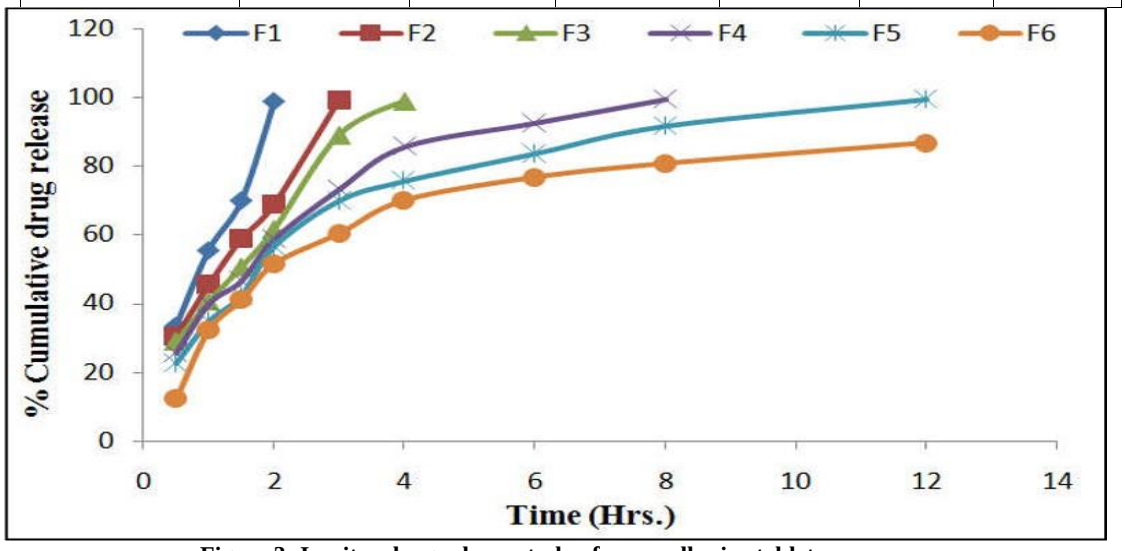

Figure 3: In-vitro drug release study of mucoadhesive tablets