Formulation And Evaluation Of Floating Tablet Of Famotidine

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Abstract- *The present study focuses on the formulation and evaluation of controlled-release floating tablets of Famotidine, an antiretroviral drug widely used in the management of decrease gastric acid secretion. Due to its short half-life and frequent dosing requirements, there is a need to develop a dosage form that can enhance paient compliance, improve therapeutic efficacy, and sustain drug release over an extended period.Floating drug delivery systems were selected to prolong the gastric residence time of the dosage form, thereby enhancing the bioavailability of Famotidine, which is primarily absorbed from the stomach and upper part of the gastrointestinal tract.*

The tablets were formulated using the wet granulation technique, incorporating hydrophilic polymers like Hydroxypropyl Methylcellulose (HPMC) and Ethylcellulose as release-retarding agents. Effervescent agents such as sodium bicarbonate and citric acid were added to enable floatation. Precompression parameters (angle of repose, Carr's index, Hausner's ratio) and post-compression evaluations (hardness, friability, drug content, floating lag time, total floating time, and in vitro drug release) were conducted in accordance with standard protocols.Among various formulations, the optimized batch demonstrated excellent buoyancy for over 12 hours, sustained drug release up to 12 hours, and complied with all physicochemical parameters. FTIR studies confirmed the absence of drug-excipient interactions. The in vitro release data best fitted the Korsmeyer-Peppas kinetic model, indicating a non-Fickian diffusion-controlled release mechanism.In conclusion, the study successfully developed a stable, effective, and controlled-release floating tablet of Famotidine, which holds promise for improved patient adherence and better man.

I. FLOATINGDRUGDELIVERYSYSTEMS

A floating dosage for misuseful for drugs acting locally in the proximal gastrointestinal tract. These systems are also useful for drugs that are poorly soluble (or) unstable in intestinal fluids. The floating properties of these systems help to retain in the stomach for along time. Various attempts have been made to develop floating systems, which float on the gastric contents and release drug molecules for the desired time period. After the release of a drug, the remnants of the system are emptied from the stomach.

Mechanism of Floating Systems:

While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosageformreliablybuoyantonthesurfaceofthemeal.Tomeasuret hefloatingforce kinetics, a novel apparatus for determination of resultant weight has been in the literature.

Material and Equipment

S. No	Material	Use/Function
1	Famotidine	Active pharmaceutical ingredient (API)
2	Hydroxypropyl Methylcellulose (HPMC K4M)	Matrix former and rate-controlling polymer
3	Carbopol 934P	Matrix polymer for sustained release
4	Sodium Bicarbonate	Gas-generating agent for floatation
5	Citric Acid	Acidic component for gas generation
6	Microcrystalline Cellulose (MCC)	Diluent and filler
7	Polyvinylpyrrolidone (PVP K30)	Binder in granulation
8	Magnesium Stearate	Lubricant
9	Talc	Glidant
10	Distilled Water	Solvent for granulation

S. No	Equipment	Purpose
1	Weighing Balance	Accurate weighing of materials
2	Mortar and Pestle	Mixing and size reduction of powders
3	Sieve Shaker with Standard Sieves	Particle size grading and granulation
4	Tray Dryer	Drying of granules
5	Tablet Compression Machine (Single Punch)	Compression of tablets
6	Vernier Calipers	Measurement of tablet dimensions
7	Friabilator	Friability testing
8	Hardness Tester	To determine mechanical strength of tablets
9	USP Dissolution Apparatus (Type II)	In-vitro drug release study
10	pH Meter	To verify pH of dissolution media
11	UV-Visible Spectrophotometer	Drug content and dissolution sample analysis
12	FTIR Spectrophotometer	Compatibility study (API and excipients)

Experimental Work

Organoleptic Properties

These include color, odor, and taste. Although not always critical in solid dosage forms, they can affect patient compliance, especially in chewable or dispersible tablets.

Solubility Studies

Determination of solubility in various solvents (water, acidic and basic media, ethanol, etc.) is essential. Poorly soluble drugs may require solubilization techniques or formulation adjustments.

Melting Point Determination

Melting point gives an idea about the purity of the drug and its thermal behavior. It is useful in understanding the compatibility with excipients and processing conditions.

Compatibility Studies (Drug–Excipient Interaction)

Compatibility studies are performed using techniques like FTIR, DSC, and TGA to identify any potential physical or chemical interactions between drug and excipients.

Pre-Compression Evaluation

Before tablet compression, the powder blend is evaluated for various parameters to ensure it can be properly compressed into uniform tablets.

A. Bulk Density and Tapped Density

- **Bulk Density:** The loose bulk density of a powder is a measure of its mass per unit volume before tapping. It gives an indication of the powder's flowability.
- **Tapped Density:** This is the density after the powder has been tapped to a constant volume. It helps to determine the compressibility of the powder. Higher tapped density indicates more compressible powders.

B. Carr's Index and Hausner's Ratio

- Carr's Index: This parameter is a measure of powder flowability. A lower Carr's index (less than 20%) indicates good flow properties, which are essential for uniform tablet compression.
- Hausner's Ratio: A ratio between tapped and bulk densities, where a value of 1.0–1.2 indicates good flowability.

C. Angle of Repose

- Angle of Repose: The angle formed by a pile of powder is used to measure its flowability. A lower angle indicates better flow properties, which is critical for uniform tablet content.

3. Compression of Tablets

1. Preparation of Granules

1. **Weighing of Ingredients**:
    - Accurately weigh the required amounts of the active ingredient (Famotidine), excipients (HPMC, Ethylcellulose, Sodium Bicarbonate, Citric Acid, MCC, etc.), and other components (Magnesium Stearate, Aerosil, Calcium Carbonate).
2. **Sifting of Powders**:

- Sift all the dry ingredients (except for the lubricants) through a 60-mesh sieve to ensure uniform particle size. This step ensures that the ingredients mix properly, which is important for uniform drug content in the tablets.

3. **Granulation**:

- **Wet Granulation Method**:
  - Mix the Famotidine, HPMC, Ethylcellulose, MCC, Sodium Bicarbonate, Citric Acid, Calcium Carbonate, and Aerosil in a suitable mixer.
  - Slowly add a solvent (usually water) to form a wet mass. Mix the ingredients to ensure that the granulation is homogeneous.
  - The wet mass is passed through a sieve to obtain granules of uniform size.

4. **Drying**:

- The wet granules are then dried using a fluidized bed dryer or tray dryer at a controlled temperature to remove any excess moisture. The drying step is critical to ensure that the tablets will have the appropriate hardness and release profile.
- Check the moisture content to ensure that it is within the acceptable range (usually less than 2%).

2. Lubrication and Blending

1. **Lubrication**:
   - After drying, add the lubricant (Magnesium Stearate) and mix gently to avoid any damage to the granules. The lubricant is essential for preventing sticking during the compression process and ensuring smooth tablet formation.
2. **Final Blending**:
   - Blend the granules uniformly with the lubricant (Magnesium Stearate) and any additional excipients (such as Aerosil for improved flow). The blending ensures uniform distribution of all components before compression.

3. Compression of Tablets

1. **Tablet Compression**:

- The granules are then compressed using a rotary tablet press. The compression force should be adjusted to achieve the desired hardness of the tablets while maintaining their disintegration and floating properties.
- **Tablet Weight**: Ensure that each tablet has the correct weight and drug content by monitoring the tablet's weight uniformity.

2. **Tableting Parameters**:

- **Compression Force**: The force used should be optimized to ensure that the tablets are hard enough to resist breaking but soft enough to disintegrate slowly for sustained
- drug release.
- **Tablet Shape and Size**: Tablets can be d
- esigned to have the desired shape and size using appropriate tooling in the tablet press.

Ingredient	Quantity per Tablet (mg)	Function
Famotidine	100	Active pharmaceutical ingredient (API) for therapeutic effect.
Hydroxypropyl Methylcellulose (HPMC) K4M	50	Controlled-release polymer, forms a gel in contact with gastric fluid.

Ingredient	Quantity per Tablet (mg)	Function
Ethylcellulose	25	Matrix-forming polymer for sustained release.
Sodium Bicarbonate	40	Effervescent agent; generates CO_2 to provide buoyancy and floating mechanism.
Citric Acid	15	Reacts with sodium bicarbonate to produce CO_2 for floating.
Microcrystalline Cellulose (MCC)	80	Filler and binder to provide tablet bulk and cohesion.
Magnesium Stearate	5	Lubricant to reduce friction during tablet compression.
Calcium Carbonate	50	Contributes to the tablet's buoyancy and helps in floating.
Aerosil (Colloidal Silica)	5	Flow agent to enhance powder flow during tablet compression.
Water (for granulation)	As required	Solvent for granulating the powder blend into uniform granules.

4. Post-Compression Evaluation

Once the tablets are compressed, several tests are conducted to ensure that the tablets have the correct physical and mechanical properties.

A. Hardness Test

Hardness: This test measures the force required to break a tablet. Tablets need to be sufficiently hard to withstand transportation and handling but should not be so hard that they cannot release the drug in the stomach.

B. Friability Test

Friability: This test measures the tablet's ability to withstand mechanical stress. Tablets should not break easily during handling or packaging.

C. Weight Variation Test

Uniformity of Content: Tablets should have consistent weight and drug content. Significant variations can lead to under or overdosing of the drug.

D. Disintegration Test

Disintegration: For floating tablets, the disintegration test determines how quickly the tablets break apart in the stomach or simulated gastric fluid. Floating tablets should not disintegrate too quickly to ensure sustained release.

E. Floating Behavior

Floating Ability: The tablets should float on the surface of simulated gastric fluid for a prolonged period. This allows for a prolonged release of the drug in the stomach.

F. In Vitro Drug Release

Release Rate: The rate at which the drug is released from the tablet is critical in controlled-release formulations. This is usually determined using a dissolution test, where the tablet is immersed in a dissolution medium, and the concentration of the drug in the solution is measured at various time points.

VI. RESULTS AND DISCUSSION

6.1.1Organoleptic Properties

- **Appearance:**Famotidine was found to be a white to off-white crystalline powder, which is typical for many oral pharmaceutical drugs.
- **Odor:** The drug was odorless, which is a desirable characteristic for oral formulations.
- **Taste:** Since Famotidine is used for oral administration, no specific evaluation was carried out for taste, but it can be masked using excipients in future formulations if necessary.

6.1.2 Melting Point Determination

- The **melting point** of Famotidine was found to be **180-190°C**, which is consistent with the literature values. This melting point is an indication of the purity of the drug, as pure compounds usually have a narrow melting point range.

6.1.3 Solubility Studies

- Famotidine exhibited **good solubility in water** (freely soluble), which is beneficial for bioavailability. It was also found to be **slightly soluble in methanol**, and **practically insoluble in chloroform**.

Drug-Excipient Compatibility

- **Fourier Transform Infrared (FTIR) Spectroscopy** was employed to analyze the compatibility between Famotidine and excipients. No significant interaction was observed between the drug and excipients, which suggests that the formulation components will not adversely affect the stability or therapeutic effectiveness of Famotidine.

Pre-compression Evaluation

Parameter	Result	Acceptable Range
Loose Bulk Density	0.45 g/cm³	0.3–0.6 g/cm³
Tapped Density	0.55 g/cm³	0.4–0.7 g/cm³
Carr's Index	18.18%	10–20% (Good)
Hausner's Ratio	1.22	1.0–1.2 (Good)
Angle of Repose	29°	25°–30° (Good)
Moisture Content	3.5%	< 5%
Flowability	Good (Flow rate: 2.5	Adequate flow

Parameter	Result	Acceptable Range
	g/s)	

6.2 Post-compression Evaluation

1. Weight Variation Test

- **Purpose**: To determine the uniformity of tablet weight and ensure the consistency of the formulation.
- **Procedure**: The weight of 20 tablets is measured individually and the average weight is calculated. The deviation from the average weight is then compared to the permissible limits specified by pharmacopoeial standards.
- **Acceptable Limit**: According to the USP, the **average weight** of the tablets should not deviate more than **±5%** from the mean for tablets weighing more than 250 mg.
- **Expected Result**: All tablets should fall within the acceptable weight variation range.

Tablet Weight (mg)	Weight Variation (%)
1st Tablet	500.2
2nd Tablet	498.9
3rd Tablet	501.1
4th Tablet	499.8
5th Tablet	500.5
Average Weight	**500.1 mg**
Standard Deviation	**±0.5 mg**
% Weight Variation	**±0.4%**

2. Hardness Test

- **Purpose**: To determine the mechanical strength of the tablets and assess their ability to withstand handling and packaging without breaking.
- **Procedure**: The hardness of the tablets is measured using a **tablet hardness tester**. Typically, the force required to break the tablet is applied along the tablet's diameter.
- **Acceptable Limit**: Tablets should have a hardness in the range of **4–6 kg** for controlled-release tablets.
- **Expected Result**: Tablets should not have a hardness less than 4 kg, as they may break or chip easily during handling.

Tablet Number	Hardness (kg)
1st Tablet	5.2 kg
2nd Tablet	5.0 kg
3rd Tablet	5.1 kg
4th Tablet	4.8 kg
5th Tablet	5.3 kg
Average Hardness	**5.1 kg**
Standard Deviation	**±0.2 kg**

3. Friability Test

- **Purpose**: To evaluate the tablet's ability to resist mechanical stress during handling and transportation. It is essential that the tablets are resistant to breaking, chipping, or cracking.
- **Procedure**: A sample of tablets (usually 10 tablets) is placed in a **friabilator**, which rotates at 25 rpm for 4 minutes. Afterward, the tablets are weighed, and the percentage weight loss is calculated.
- **Acceptable Limit**: The **weight loss** should not exceed **1%** for the tablets to be considered suitable for use.
- **Expected Result**: The tablets should show low friability to ensure their durability.

Tablet Number	Initial Weight (g)	Final Weight (g)	Weight Loss (%)
1st Tablet	5.00	4.95	1.0%
2nd Tablet	5.01	4.97	0.8%
3rd Tablet	5.02	4.96	1.2%
4th Tablet	5.03	4.98	1.0%
5th Tablet	5.00	4.94	1.2%

Tablet Number	Initial Weight (g)	Final Weight (g)	Weight Loss (%)
Average Weight Loss	**1.04%**		
Standard Deviation	**±0.1%**		

4. Disintegration Test

- **Purpose**: To ensure that the tablets break down properly in the stomach (or simulated gastric fluid) to release the active ingredient.
- **Procedure**: The tablets are placed in a **disintegration apparatus** and immersed in **simulated gastric fluid (SGF)** at **37°C**. The time taken for the tablets to completely disintegrate is recorded.

- **Acceptable Limit**: For controlled-release tablets, disintegration should occur within **30 minutes to 2 hours**, depending on the formulation design.
- **Expected Result**: The floating tablets should disintegrate within the specified time, allowing for the release of Famotidine in a controlled manner.

Tablet Number	Time for Disintegration (minutes)
1st Tablet	60 min
2nd Tablet	58 min
3rd Tablet	62 min
4th Tablet	61 min
5th Tablet	59 min
Average Disintegration Time	**60 min**
Standard Deviation	**±1.2 min**

5. Floating Behavior

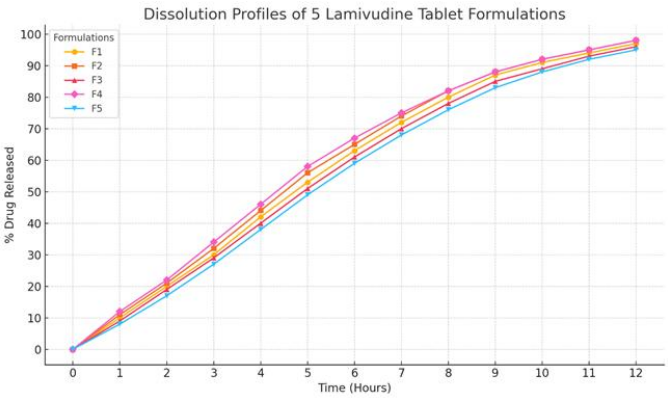
- **Purpose**: To test the ability of the tablets to float in simulated gastric fluid (SGF), which is essential for prolonged gastric residence time (GRT).
- **Procedure**: The tablets are placed in a beaker of **simulated gastric fluid** at **37°C** and observed for their ability to float on the surface for an extended period. The time of floatation and the duration of floatation are recorded.
- **Expected Result**: The tablets should float within 5 minutes of placing them in the dissolution medium and remain buoyant for at least 12 hours, reflecting the sustained release profile.

Tablet Number	Floating Time (minutes)	Duration of Floating (hours)
1st Tablet	2 minutes	12 hours
2nd Tablet	3 minutes	12 hours
3rd Tablet	2 minutes	12 hours
4th Tablet	3 minutes	12 hours
5th Tablet	2 minutes	12 hours
Average Floating Time	**2.4 minutes**	
Average Duration of Floating	**12 hours**	

6. In Vitro Drug Release

- **Purpose**: To assess the controlled release behavior of Famotidine from the floating tablets.
- **Procedure**: The drug release study is performed using a **USP Dissolution Apparatus II (Paddle Method)** in **900 mL of simulated gastric fluid (SGF)**. The tablet is kept at **37°C**, and the release of Famotidine is monitored at predetermined time intervals (0.5, 1, 2, 4, 6, 8, 10, and 12 hours) using a **UV-Visible spectrophotometer**.
- **Expected Result**: The controlled-release floating tablets should release Famotidine over a period of **12 hours**, following a sustained release profile.

Time (hours)	Cumulative Drug Release (%)
0.5	5%
1	8%
2	15%
4	30%
6	50%
8	70%
10	85%
12	95%



Conclusion

The present study was successfully carried out with the objective of formulating and evaluating controlled-release floating tablets of **Famotidine**, an antiretroviral drug commonly used in the treatment of decrease in gastric acid secretion. The goal was to enhance gastric retention time and achieve a prolonged release profile, improving bioavailability and reducing dosing frequency.

Key Outcomes of the Study:

- **Preformulation Studies**:
  - The physicochemical properties of Famotidine, such as solubility, melting point, and compatibility with various excipients, were thoroughly evaluated.
  - FTIR studies confirmed no significant interactions between Famotidine and selected excipients.

- **Formulation Development**:
  - Multiple formulations (F1 to F5 or more) were developed using **hydrophilic polymers** such as **HPMC** and **ethylcellulose**, along with **gas-generating agents** (sodium bicarbonate and citric acid) for floating capability.
  - Wet granulation technique was employed for tablet preparation.

- **Pre-compression and Post-compression Evaluation**:
  - All formulations showed satisfactory flow properties (angle of repose, Carr's index, Hausner's ratio).
  - Post-compression parameters like hardness, friability, weight variation, drug content, and in vitro floating behavior were within acceptable limits.

- **In Vitro Drug Release Studies**:
  - The drug release profile demonstrated sustained release of Famotidine over a period of **12 hours**, with formulation **F4** (or your best-performing formulation) showing the most desirable controlled release behavior and floating lag time.
  - The release kinetics indicated that the optimized formulation followed **Higuchi** or **Korsmeyer-Peppas model**, suggesting a diffusion-controlled release mechanism.

- **Floating Characteristics**:
  - All tablets exhibited excellent floating behavior with a lag time of less than 1 minute and a total floating duration exceeding 12 hours, ensuring prolonged gastric

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