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Advances in Bioresearch

## ORIGINAL ARTICLE

# Formulation Optimization and Characterization of Rabeprazole Sodium Core Tablets for Enteric Coating

**Ashish Srivastava*[1], Sanjay Bhawar[2]**
[1]Research Scholar, Department of Pharmaceutical Sciences Bhagwant University, Ajmer, Rajasthan, India.
[2]Research Guide, Department of Pharmaceutical Sciences Bhagwant University, Ajmer, Rajasthan, India.
**For Correspondence :** sbbhawar@gmail.com

**ABSTRACT**
*The present research paper outlines the development of Rabeprazole Sodium core tablets with the intention of subsequently applying an enteric coating. Rabeprazole Sodium is categorized as a proton pump inhibitor medication, primarily used for conditions that require protection against stomach acid or prevent stomach lining irritation. In order to create a stable, risk-free, and efficacious formulation, the preformulation research sought to analyze the pharmacological molecule's physicochemical features that may impact its performance. A number of properties were examined in the designed core pellets. Studies were conducted in simulated gastric fluid for in vitro release and in simulated intestinal fluid for acid-resistance. tablets from all batches exhibit similar appearances and meet the weight variation and hardness specifications. However, there is some variation in tablet thickness among the different batches, which may require addressing to ensure consistent tablet performance. Based on the obtained results, it is concluded that effective Rabeprazole Sodium core tablets were achieved and successfully evaluated.*
***Keywords:****Rabeprazole sodium, proton pump inhibitors, micromeritic properties, powder blend*

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## INTRODUCTION

Rabeprazole sodium is classified as a proton pump inhibitor (PPI) medication used for treating gastroesophageal reflux disease (GERD), ulcers, and other digestive problems. PPIs function by inhibiting the production of acid in the stomach. Regurgitation, chest pain, and heartburn are symptoms of gastroesophageal reflux disease (GERD), which is caused by acid from the stomach flowing back into the oesophagus. Ulcers are sores that form in the stomach or small intestine, causing discomfort, nausea, and other digestive issues. [1]

Administration of rabeprazole sodium is usually oral and once daily, with or without food, with dosage and duration dependent on the condition being treated and the patient's health profile.[2,3]

A significant benefit of rabeprazole sodium is its long-lasting symptom relief, particularly in reducing inflammation and irritation in the digestive system. While it is an effective medication, it has potential side effects such as headache, nausea, diarrhea, and stomach pain, while serious side effects are infrequent but may include allergic reactions, kidney problems, and bone fractures.[4,5]

"Core Tablets" with enteric coating refer to a type of tablet where the medication is contained in a central core surrounded by a protective coating that is resistant to the acidic environment of stomach. This allows the medication to pass through stomach and release in intestines, where it can be absorbed into bloodstream [6]

The medication is usually provided in the form of core tablets with an enteric coating to protect the medication from stomach acid, prevent irritation to the stomach lining, and improve absorption in the intestines. The core tablets contain the active ingredient(s) while the enteric coating is typically composed of cellulose acetate phthalate or methacrylic acid copolymers [7-8]

## MATERIAL AND METHODS

### Material

The chemicals and reagents utilized were of analytical grade, and the kind gift sample of Rabeprazole Sodium came from Cadila healthcare Ltd.

### Rabeprazole Sodium powder preparation

Weigh the required amount of *Rabeprazole Sodium* powder using a calibrated analytical balance. The amount of powder to be weighed depends on the intended use and the desired concentration of the drug. Transfer the weighed *Rabeprazole Sodium* powder into a clean, dry, and labeled container. Store in a cool, dry, and dark place.

### Preformulation studies

The purpose of the preformulation studies was to investigate the drug molecule's physical properties that could affect its overall performance as well as the stability, effectiveness, and safety of the formulation.

### Organoleptic Properties

The sensory qualities of a substance, such as its smell, texture, color, taste, and appearance, are known as organoleptic features. These properties are typically used to assess product quality and can influence consumer acceptance.

### Drug identification by IR

Rabeprazole Sodium is proton pump inhibitor employed in management of gastrointestinal ailments, including acid reflux and ulcers. Identification of Rabeprazole Sodium may be accomplished through the application of IR spectroscopy.

### Solubility

A solubility investigation can be undertaken to ascertain the solubility characteristics of Rabeprazole Sodium in diverse solvents and at variable temperatures. This is typically achieved by introducing a precise quantity of Rabeprazole Sodium to a predetermined volume of the solvent and agitating the mixture until the drug is entirely dissolved.

### Standard Curve of Rabeprazole Sodium

To generate a standard curve for Rabeprazole Sodium, a sequence of standard solutions with predetermined concentrations of drug can be synthesized. These solutions should encompass a spectrum of concentrations that are appropriate for the intended analysis. UV spectroscopy can be employed to quantify the response of the drug in the standard solutions.

### Preparation of Stock Solution

A stock solution is a highly concentrated solution of a drug that serves as a reference point for the preparation of solutions with known concentrations for analytical purposes. In order to prepare a Rabeprazole Sodium standard stock solution, a precise quantity of 10mg of Rabeprazole Sodium should be added to 10 ml of ethanol, resulting in a concentration of 1000 µg/ml. To make stock II with a concentration of 100 µg/ml, take 1 ml of this stock solution and dilute it further with ethanol as a solvent until it reaches a final volume of 10 ml.

### Preparation of Calibration Curve

A series of dilutions were prepared from the stock solution (100 µg/ml) of Rabeprazole Sodium, with concentrations ranging from 2 µg/ml to 14 µg/ml. At the absorption maximum, the dilutions' absorbance was measured. After that, a calibration curve was produced by comparing the absorbance readings with the dilution concentrations.

### Evaluation of powder blend

### Angle of repose

An approach to evaluating a powder's flow characteristics is the angle of repose. The static angle of repose, a specialized measurement tool included in the funnel method, is used for this purpose. A precise adjustment is made to the height of the funnel such that its tip meets the peak of the powder mixture. The next step is to release the powder mixture onto a surface by letting it run freely through the funnel. The formula is used to determine the angle of repose after measuring the diameter of the powder cone that is produced. [9]

$\tan \theta = h/r$

$\theta$ = angle of repose, h = height of powder cone, and r =radius of powder cone.

### Bulk density and tapped density

After shaking the mixture to remove any clumps, 2 grams of powder from each recipe was added to a 10-milliliter measuring cylinder. Following the measurement of the starting volume, the cylinder was allowed to descend to a hard surface at 2.5 cm intervals until it fell under its own weight. The tapping was kept up until the volume did not change any further. In order to determine the bulk density ($\rho B$) and the tapped density ($\rho T$), the following equations were used:[10]

 

ρB= Weight of powder blend/Untapped Volume of packing
ρT=Weight of powder blend/Tapped Volume of packing

**Compressibility Index**

In order to find the powder blend's compressibility index, one uses Carr's formula:.[11]
Carr's index (%) = $(\rho T - \rho B)/\rho T \times 100$

**Hausner's ratio**

One numerical measure of a material's flowability is Hausner's ratio, which is applicable to both powders and granules. The following formula is used to compute it: tapped density/bulk density.[11]

$$H = \frac{\rho T}{\rho B}$$

**Preparation of Granules**

1. The preparation of granules of Rabeprazole Sodium involves a multistep process, including wet granulation and drying.
2. The procedure can be summarized as follows:
3. Accurately weigh the required amounts of Rabeprazole Sodium and other excipients, such as binders, disintegrants, and lubricants, as per the formulation.
4. Thoroughly mix the Rabeprazole Sodium powder and the excipients in a suitable mixer, for example a tumble or planetary mixer, to ensure even distribution.
5. Slowly add a suitable binder solution, such as HPMC, to the powder mixture while continuously mixing. The amount of binder solution used depends on desired granule size and properties of excipients.
6. Mix powder mixture with the binder solution until a uniform wet mass is obtained, which should be suitable for granulation.
7. To get the granules of the right size, run the moist mixture through a granulator, like a high-shear mixer or a fluidized bed granulator.
8. Dry granules in an appropriate dryer, such as a fluidized bed or tray dryer, at a suitable temperature and for a specified time, depending on the excipients used. It is essential to monitor the drying process to avoid over-drying, which may cause drug degradation.
9. After drying, the granules can be further processed as per the formulation requirements, such as coating or tableting [12].

**Table 2.1. Composition of various core tablet formulations**

| Ingredients (mg) | F-1 | F-2 | F-3 | F-4 | F-5 |
|---|---|---|---|---|---|
| Rabeprazole Sodium | 20 | 20 | 20 | 20 | 20 |
| Lactose | 35 | 40 | 30 | 35 | 30 |
| Microcrystalline cellulose | 45 | 40 | 45 | 40 | 50 |
| Sodium starch glycolate | 1 | 10 | 10 | 15 | 11 |
| Crospovidone | 7 | 8 | 6 | 7.5 | 6.5 |
| Magnesium stearate | 3 | 2.5 | 3.0 | 2.5 | 3.0 |
| Total | 120 | 120 | 120 | 120 | 120 |

**Evaluation of core tablets [9-15]**

**Weight variation test**

To perform the weight variation test, a sample of tablets from each formulation would need to be selected. The number of tablets to be tested would depend on the weight of each tablet, as determined by a preliminary test. Assuming that the weight of each tablet is around 200 mg, which is the sum of the weights of all the ingredients in the formulations, the weight variation test can be performed on 20 tablets for each formulation, as per the USP guidelines for tablets weighing less than or equal to 300 mg.
Calculate % deviation of each tablet weight from average weight using formula:
Weight variation = (individual tablet weight - average weight) / average weight x 100.

**Hardness**

A Monsanto hardness tester was used to measure the tablets' hardness. The hardness tester had ten tablets chosen at random from the batch, and each one was set between the anvils. We measured the hardness of the pill as the force needed to smash it.

**Friability Test**

Twenty tablets were chosen at random and their weights recorded. After that, the pills were spun at 100 revolutions per minute for five minutes in a friabilator. Following the rotation, the tablets were brushed with a dusting brush, weighed again, and the friability, a measure of weight loss, was computed.

 

**Uniformity of weight**

Twenty tablets were weighed in a single pan balance, both separately and all at once. We calculated the standard deviation and recorded the average weight.

**Disintegration time**

At a temperature of 37 ± 2°C, the disintegration equipment USP was used to measure the time it took for the substance to dissolve in 0.1N HCl for 2 hours, followed by phosphate buffer pH 6.8.

## RESULT AND DISCUSSION

**Identification of Drug**

The powder looked good, which was an acceptable result. The patches that were made were smooth, bendable, uniform, opaque, and didn't stick together.

**Table 3.1 Physical properties**

| Parameters | Remarks |
|---|---|
| Colour | White To Slightly Yellowish |
| Taste | Slightly bitter |
| Odour | Characteristic |

**3.2 Solubility Study :( Solubility of Rabeprazole Sodium in Surfactant)**

Before beginning formulation development, a solubility study on the drug is conducted to determine the best excipients that can solubilize and deliver drug to site of action.

**Table 3.2** Solubility **Study**

| Surfactant | Wavelength(nm) | Solubility |
|---|---|---|
| Lactose | 237 | Insoluble |
| Microcrystalline cellulose | 237 | Insoluble |
| Sodium starch glycolate | 237 | Slightly soluble |
| Crospovidone | 237 | Insoluble |
| Calcium hydroxide | 237 | Slightly soluble |
| Magnesium stearate | 237 | Insoluble |

**Calibration of pure drug**

The pure drug absorbed with their respective concentrations is mentioned in below table Absorbance values for Rabeprazole Sodium at different concentrations using UV-Vis spectroscopy at a wavelength of 283 nm in 0.1 M HCl:

**Table 3.3 Absorbance values for Rabeprazole Sodium**

| Concentration µg/ml | Absorbance |
|---|---|
| 5.0 | 0.054 |
| 10.0 | 0.108 |
| 15.0 | 0.162 |
| 20.0 | 0.217 |
| 25.0 | 0.271 |
| 30.0 | 0.326 |
| 35.0 | 0.379 |

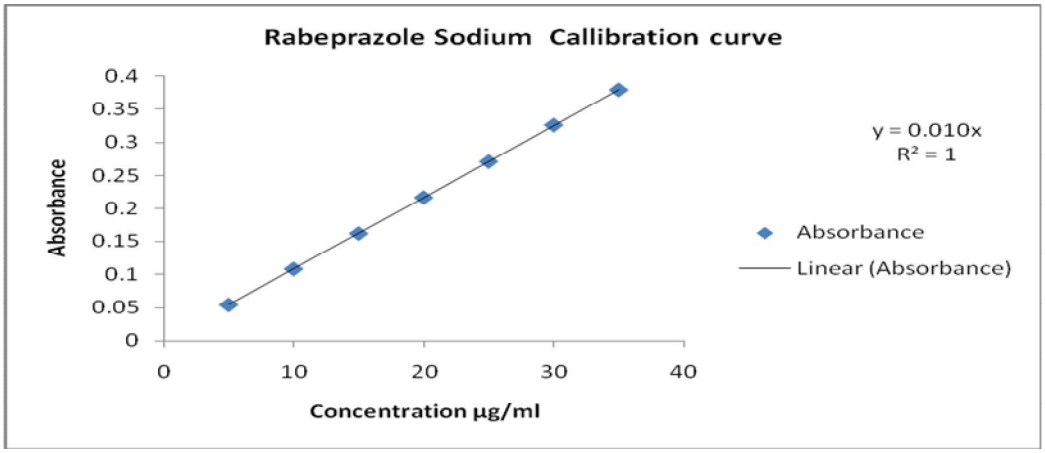


**Fig 3.1 Rabeprazole Sodium Callibration curve**

 

**Micromeritic properties batches F1-F5.**

Table 3.1 shows the micromeritic properties of six distinct powder blend batches, numbered F-1 through F-5.

**Table 3.4 Micromeritic properties of powder blends of batches F1-F5.**

| Powder Blend | Angle of Repose (°) | Bulk density (g/cc) | Tapped density (g/cc) | Carr's Index (%) | Hausner's Ratio |
|---|---|---|---|---|---|
| F-1 | 24±.20 | 0.45±.07 | 0.56±.03 | 19.6±.1 | 1.24±.03 |
| F-2 | 23±.13 | 0.42±.07 | 0.51±.18 | 17.6±.3 | 1.21±.04 |
| F-3 | 24±.10 | 0.46±.05 | 0.55±.16 | 16.36±.1 | 1.19±.01 |
| F-4 | 23±.30 | 0.50±.06 | 0.60±.47 | 16.66±.2 | 1.22±.02 |
| F-5 | 25±.41 | 0.45±.-1 | 0.52±.42 | 13.46±.5 | 1.15±.05 |

**Angle of repose**

The angle of repose, which refers to slope formed by surface of a heap of powder when it is poured onto a flat surface, is often used as a quantitative indicator of powder flow ability. angle of repose of examined powder blends was determined to be in range of 23 to 25 degrees, suggesting that they possess a good to moderate level of flow ability.

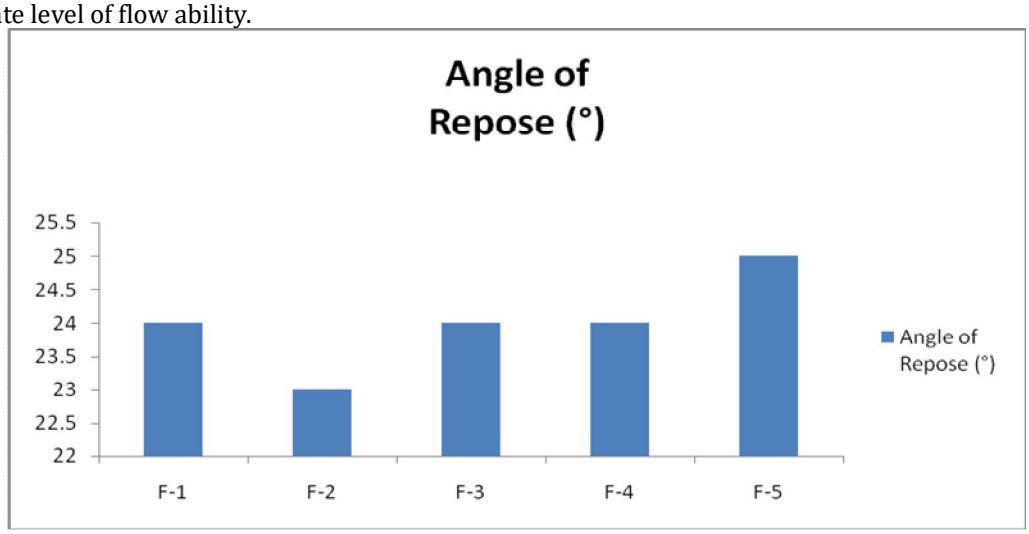


**Fig 3.2 angle of repose of batches F1-F5**

**Bulk density**

Powder blends have different densities while they are in a loose form (bulk density) and when they have been tapped to settle the particles (tapped density). Bulk density values are between 0.42 and 0.50 g/cc, and tapped density values are between 0.51 and 0.60 g/cc. The capacity of the powder to settle is indicated by the difference between its bulk and tapped densities; a smaller difference indicates better settling ability.

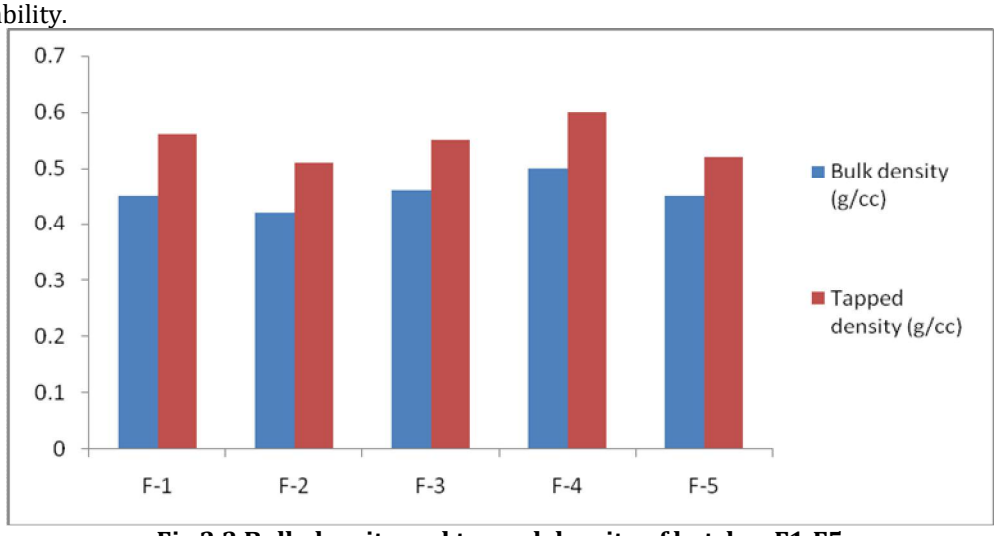


**Fig 3.3 Bulk density and tapped density of batches F1-F5**

 

**Carr's index**

To find the powder's compressibility, one can use the formula (tapped density - bulk density) / tapped density * 100, which gives the Carr's index. The powders have a moderate compressibility, as shown by Carr's index values ranging from 13.46% to 19.6%.

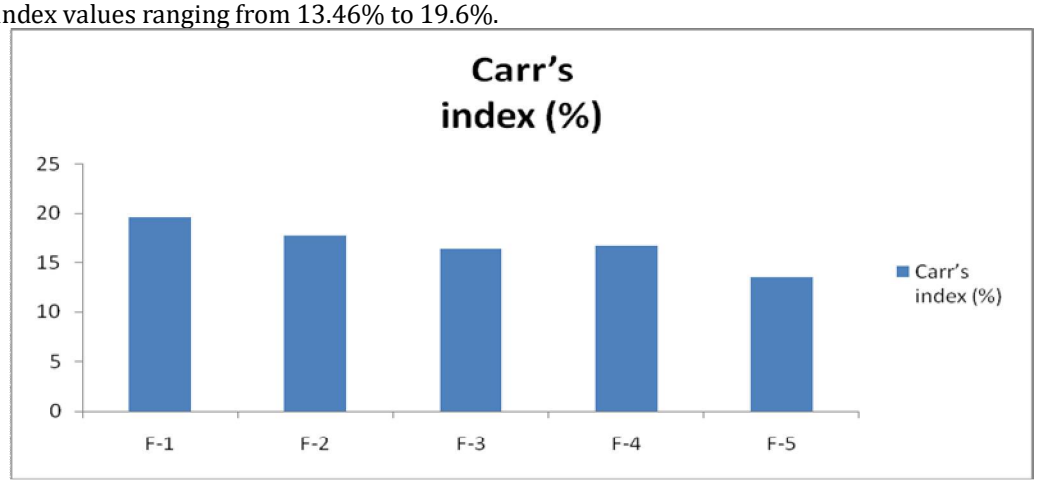


**Fig 3.4 The Carr's index of batches F1-F5**

**Hausner's ratio**

The values for Hausner's ratio range from 1.15 to 1.24, with higher values indicating higher cohesiveness and lower flowability.

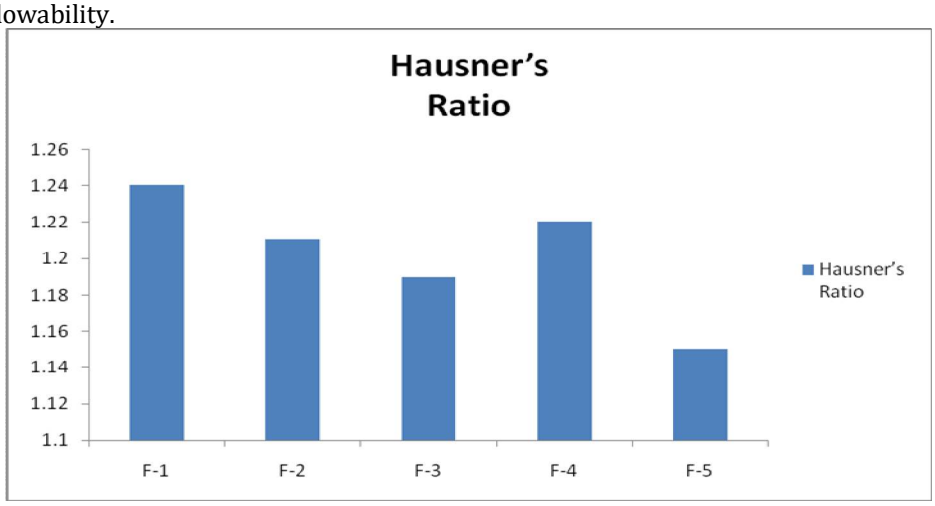


**Fig 3.3 The Hausner's ratio of batches F1-F5**

**Evaluation parameters of core tablet**

The data presented in the table represents the evaluation parameters of 5 different batches of tablets labeled F-1 through F-5. The parameters evaluated include appearance, weight variation, thickness, and hardness.The tablets in all batches have a white to off-white appearance, indicating that they have a similar color and visual appearance.

**Table 3.5 Evaluation Parameters of 5 different batches of tablets labeled F-1 through F-5**

| Evaluation Parameters | Appearance | Wt. variation (mg) % | Thickness (mm) | Hardness (kg/cm2) |
|---|---|---|---|---|
| F-1 | White to off | 1.0±.30 | 4.20±.40 | 5.5±.19 |
| F-2 | White to off | 2.0±.15 | 4.57±.03 | 5.2±.25 |
| F-3 | White to off | 1.01±.12 | 4.65±.12 | 5.7±.13 |
| F-4 | White to off | 1.02±.31 | 4.25±.21 | 5.4±.37 |
| F-5 | White to off | 1.1±.26 | 4.75±.15 | 5.8±.10 |

Weight variation is an important parameter to evaluate as it ensures that the tablets contain correct amount of active pharmaceutical ingredient (API) and other excipients. The values for weight variation range from 1.0% to 2.0%, indicating that the tablets are within the acceptable limits set by USPor EP.

 

Tablet thickness is another important parameter to evaluate as it can affect the tablet's dissolution profile and disintegration time. The values for tablet thickness range from 4.20 to 4.75 mm, indicating that there is some variation in tablet thickness between the different batches.
The hardness of a tablet indicates its mechanical strength and its ability to withstand handling and transportation without breaking. The tablets fall within the permissible range for pharmaceutical tablets, with hardness values ranging from 5.2 to 5.8 kg/cm2.

**Table 3.6 Evaluation Parameters of 5 different batches of tablets labeled F-1 through F-5**

| Evaluation Parameters | Content uniformity (%) | Disintegration time (min) | Friability (%) |
|---|---|---|---|
| F-1 | 92.13±0.11 | 4±0.19 | 0.45±0.11 |
| F-2 | 96.37±0.33 | 3±0.10 | 0.35±0.14 |
| F-3 | 96.74±0.10 | 4±0.18 | 0.33±0.20 |
| F-4 | 93.88±0.13 | 3±0.16 | 0.37±0.10 |
| F-5 | 96.55±0.17 | 4±0.13 | 0.47±0.15 |

Results shown in form of ± standard deviation.
Overall, the data suggests that the tablets from all batches have a similar appearance and meet the weight variation and hardness specifications. However, there is some variation in tablet thickness between the different batches, which may need to be addressed to ensure consistent performance of the tablets.

## CONCLUSION

The present analysis includes data on the preformulation and micromeritic properties of five distinct powder blend batches as well as evaluation parameters of five distinct tablet batches. Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio results show that all five batches of the powder mixes have identical micromeritic properties and hence similar flow characteristics. These results imply that powder blends are suitable for compression into tablets and exhibit consistent flow properties. Evaluation of the tablet batches reveals that all five batches have a white to off-white appearance and satisfy the acceptable weight variation and hardness specifications. The hardness values vary between 5.2 to 5.8 kg/cm2, suggesting that the tablets meet the acceptable range for pharmaceutical tablets. However, the tablet thickness values range from 4.20 to 4.75 mm, indicating that there is some variation in tablet thickness between the different batches. The weight variation values range from 1.0% to 2.0%, suggesting that the tablets are within the acceptable limits. Nevertheless, the observed variation in tablet thickness between the different batches may require attention to ensure consistent tablet performance. In conclusion, the results indicate that all five powder blend batches have appropriate flow properties for tablet compression, and all five tablet batches exhibit similar appearances and meet acceptable weight variation and hardness specifications. However, addressing the variation in tablet thickness between the different batches may be necessary to ensure consistent tablet performance. Overall, this analysis provides valuable information for quality control and formulation optimization of enteric-coated tablets.

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## CONFLICT OF INTEREST

No Conflict of interests.

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