

Original article

## In vitro Evaluation of Different Brands of Pantoprazole Tablets Marketed in Sebha City, Libya

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### Abstract

Pantoprazole, a substituted benzimidazole, proton pump inhibitor, is widely used to treat acid-related disorders. This study analyzed five brands of pantoprazole tablets (P1-P5) obtained from local pharmacies in Sebha, Libya, examining each brand's general appearance, weight uniformity, hardness, friability, and disintegration in both acidic and phosphate buffer medium. The tests were conducted according to procedures outlined in the United States Pharmacopeia. All tablets appeared uniform in color, undamaged, and odorless. The average tablet weights ranged from 103 mg to 204 mg, and all brands met USP standards for weight variation. Hardness testing showed the highest crushing strength in brand P1 (16.6 kg) and the lowest in P4 (7 kg), with all brands meeting USP hardness requirements. Friability testing indicated robust resistance to abrasion, with no significant weight loss observed across brands, suggesting high coating durability. All brands except P4 showed no disintegration in acidic conditions (0.1M HCl). However, in phosphate buffer 0.05M (pH 6.8), the disintegration times ranged from 2 to 20 minutes, meeting the USP criteria for enteric-coated tablets. The study concluded that most pantoprazole brands available in Sabha met the required quality standards. Brand P4 showed complete disintegration in an acidic medium, indicating potential issues with its enteric coating. Ensuring the consistency and quality of pharmaceutical products is critical for patient safety and treatment effectiveness

**Keywords.** Pantoprazole Sodium, Weight variation, Hardness, Friability.

### Introduction

Proton pump inhibitors (PPIs) represent a vital class of medications extensively used in the management of various acid-related disorders affecting the upper gastrointestinal (GI) tract. These disorders encompass a range of conditions, including gastric and duodenal ulcers, as well as gastroesophageal reflux disease (GERD), which often presents with esophagitis [1]. PPIs work by inhibiting the hydrogen-potassium ATPase enzyme system of the gastric parietal cells, effectively reducing gastric acid secretion. Among the various PPIs available, pantoprazole has emerged as a notable compound due to its unique pharmacological properties and clinical applications [1]. Chemically, pantoprazole is characterized as 6-(difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzimidazole. This white to off-white crystalline substance has a molecular weight of 383.4 g/mol [1]. One of the defining features of pantoprazole is its formulation as an enteric-coated tablet, a crucial consideration due to its susceptibility to degradation by stomach acid [2]. The enteric coating ensures that the drug is protected from the acidic environment of the stomach, allowing for its release and absorption in the more alkaline pH of the intestines [2].

Upon oral administration, pantoprazole is rapidly absorbed, achieving maximum plasma concentration within 2 to 3 hours. Its bioavailability is notably high, averaging 77% even after multiple doses, which is significant for maintaining therapeutic effects [3]. The elimination of pantoprazole occurs primarily through renal pathways, with approximately 80% excreted as metabolites in urine [2]. The half-life of pantoprazole is influenced by metabolic factors, averaging about 1.3 hours in normal metabolizers and extending to around 6 hours in those classified as poor metabolizers [4]. Quality control in the production of pantoprazole tablets is paramount to ensure safety and efficacy. Various tests, as outlined by pharmacopoeia standards, are conducted to assess parameters such as weight variation, content uniformity, disintegration, dissolution, thickness, hardness, friability, and organoleptic properties. These tests are essential for confirming that each batch of medication meets established quality standards before reaching consumers [5].

In Sebha, Libya, pantoprazole is available in various brands and formulations. However, the quality and efficacy of these products may vary significantly among different manufacturers. Therefore, a thorough evaluation of the various brands of pantoprazole tablets available in the local market is essential to ensure compliance with safety and effectiveness standards. The objective of this study is to evaluate the in vitro quality of different brands of pantoprazole tablets marketed in Sebha City, Libya. Specifically, we will assess parameters such as weight variation, disintegration time, hardness, and friability profile to determine the overall quality of these products.

### Methods

#### Sample collection

Five brands of marketed pantoprazole sodium 20 mg enteric-coated tablets were purchased from various local pharmacists in Sabha City. The samples were properly checked for their manufacturer's name,

physical appearance, batch number, date of manufacturing, and expiry date before purchasing. They were coded as brand P1, P2, P3, P4, and P5, (Table 1). These tablets were tested for identification, weight uniformity, friability, hardness, and disintegration time according to procedures described in the USP.

**Table 1: Detailed description of pantoprazole sodium 20mg enteric-coated tablet products included in the study**

| Brand code | Brands Name  | Country of origin | Batch Number | Expiry date |
|------------|--------------|-------------------|--------------|-------------|
| P1         | Controloc    | Germany           | 534290       | 05/2025     |
| P2         | Sandoz       | United Kingdom    | MR3900       | 08/2025     |
| P3         | Pantoprazole | Jordan            | 1104         | 10/2025     |
| P4         | Pantoronak   | India             | T-9849       | 05/2024     |
| P5         | Pantoprazole | Italy             | 302021       | 02/2027     |

### **Instruments used in the study**

Laboratory instruments such as disintegration test apparatus (USP Single Basket Tablet Disintegration Tester, PTZ-S, Germany), friability tester (Single Drum Tablet, PTF 100, Germany), Electronic balance (0.001g analytical balance-FA-S, China), and hardness tester (ERWEKA, PTB 111EP, Germany), were used for the study.

### **Reagents used in the study**

Phosphate buffer (sodium phosphate, 0.05M, PH 6.8), hydrochloric acid (0.1M, 37%), and deionized water were supplied by the laboratories of the College of Science at Sebha University. All chemicals used were analytical grade and used as received.

### **Evaluation of general appearance**

The general appearance of the tablets was visually examined for defects such as chips, stains, cracks, or any other form of physical defect. The colour and odour were also observed.

### **Weight variation test**

A weight uniformity test is performed to check that the manufactured tablets have a uniform weight. The weight variation test was done by taking twenty tablets from each of the five brands and weighing them individually with an analytical balance. The average weights for each brand, as well as the standard deviation from the mean value, were calculated. The percentage deviation of each tablet from the mean was evaluated according to the USP.

The weight variation of 20 tablets was calculated using the formula:

$$\text{Weight Variation} = \frac{IW - AW}{IW} \times 100\%$$

Where,

Iw = Individual weight of the tablet.

Aw = Average weight of the tablet.

### **Hardness test**

Tablet hardness measures a tablet's ability to withstand mechanical shocks during manufacturing and packaging. To assess hardness, ten tablets from each brand are tested using a hardness tester. A tablet was placed between the spindle of the hardness tester instrument, and pressure was applied gradually until the tablet broke. The average hardness is recorded. The acceptable limit of hardness of a tablet is less than 4 kg. The force required to crush each tablet was measured in Newton (N) and is converted into a kilogram (kg) by dividing it by 9.8, and SD was calculated.

### **Friability test**

Tablet strength was tested by the Roche friabilator. Twenty tablets were randomly taken from each brand and then accurately weighed. Then the tablets were placed in the drum, which was adjusted to rotate at 25 rpm for 4 minutes. After completing the rotation, the drum was stopped, and tablets were removed from it. The loose dust from the tablets was removed with the aid of a soft brush, and the percentage weight loss was calculated by reweighing the tablets.

Friability test was carried out as per USP, and the % friability of each brand was calculated. The percentage of friability for each brand was calculated using the formula:

$$\text{Friability} = \frac{IW - AW}{IW} \times 100\%$$

Where,

Iw = Individual weight of the tablet.

Aw = Average weight of the tablet

### Disintegration test

Disintegration time was determined using the disintegration. First, the disintegration tester was filled with 0.1M HCl, and the temperature of the medium was maintained at  $37 \pm 2^\circ\text{C}$  (1000 mL deionized water). Then, it was run for 1 hr after placing the randomly selected six tablets of each pantoprazole sodium brand in the disintegration tester. Tablets were examined for signs of disintegration within 1 hr running period. By changing the acidic fluid with phosphate buffer of pH 6.8 immediately after 1 hr, the apparatus was operated for an additional 30 minutes at  $37 \pm 2^\circ\text{C}$ , and the disintegration time was noted. The tablets were considered completely disintegrated when all the particles were passed through the wire mesh.

## Results

### Evaluation of general appearance

The general appearance of the studied tablet batches showed that all of them had a uniform colour, were undamaged, and did not have any odour.

### Weight variation

This parameter is crucial because it directly relates to the content uniformity of solid dosage forms. Consequently, the weight variation of individual tablets serves as a valid indicator of the corresponding variation in drug content. The results for the weight parameter are presented as the mean and relative standard deviation in (Table 2). All products exhibited different average weights, ranging from 103 mg to 204 mg.

**Table 2. Average weight of different brands of pantoprazole**

| Brands | Average weight (mg) $\pm$ SD | Weight variation% |
|--------|------------------------------|-------------------|
| P1     | 103 $\pm$ 8                  | 7.8               |
| P2     | 120 $\pm$ 3.9                | 3.3               |
| P3     | 162 $\pm$ 8.9                | 5.5               |
| P4     | 204 $\pm$ 2.9                | 1.4               |
| P5     | 107 $\pm$ 7.8                | 7.3               |

### Hardness

The hardness test is essential for ensuring tablet quality, as it measures the ability of tablets to withstand handling forces during packaging and to resist breakage during storage and transportation. The results indicated that brand P1 exhibited the highest hardness at  $16.6 \pm 4.8$ , while brand P4 had the lowest hardness at  $7 \pm 0.58$ . The observed results are shown in (Table 3).

**Table 3: Hardness variation of different brands of pantoprazole**

| Brand Code | Hardness (Kg) $\pm$ SD |
|------------|------------------------|
| P1         | 16.2 $\pm$ 4,8         |
| P2         | 14.7 $\pm$ 4.7         |
| P3         | 8.9 $\pm$ 0.61         |
| P4         | 7.3 $\pm$ 0.58         |
| P5         | 10.5 $\pm$ 0.75        |

### Friability test

The test showed that no brands were exposed to abrasion or dust formation, and there was no change in weight.

### Disintegration test

All the tested products showed no evidence of disintegration cracks or swelling in 0.1M HCl, except the generic product (P4), which showed complete disintegration of all the tablets after 15 min. However, the disintegration of other products in phosphate buffer 0.05M (pH 6.8) met USP requirements, indicating that they will completely disintegrate in the intestine within minutes, but no disintegration takes place in the stomach. The disintegration times for all five brands were determined, with results shown in (Table 4). Brands P1, P2, P3, and P5 disintegrated in 15 minutes, 20 minutes, 4 minutes, and 16 minutes, respectively.

**Table 4: Disintegration of pantoprazole enteric coated tablets in 0.1 M HCl and 0.05 M phosphate buffer (pH 6.8)**

| Brand Code | Disintegration time at 0.1M HCl (min)    | Disintegration time at 0.05M phosphate buffer (min) |
|------------|------------------------------------------|-----------------------------------------------------|
| P1         | No disintegration after 60 mins          | 15                                                  |
| P2         | No disintegration after 60 mins          | 20                                                  |
| P3         | No disintegration after 60 mins          | 4                                                   |
| P4         | Complete disintegration after 15 minutes | 2                                                   |
| P5         | No disintegration after 60 mins          | 16                                                  |

## Discussion

This study aims to assess the pharmaceutical quality of five different brands of Pantoprazole tablets commonly available in the local market in Sebha pharmacies, Southern Libya.

Our results, obtained through physical examination of the drugs, indicated that the packaging and labelling of all brands comply with the WHO minimum requirements for pharmaceuticals. This suggests that the tested samples do not exhibit any signs of false labelling, improper packaging, or falsification [6].

The results of the weight variation test serve as an essential indicator of compliance with good manufacturing practices (GMP) and the quality of pharmaceutical formulations. The observed average weights of the products ranged from 103 mg to 204 mg, suggesting that different excipients were employed in their manufacturing. The variability in weights is not uncommon, as the choice of excipients can significantly influence the final product's mass and characteristics [7].

According to the United States Pharmacopeia (USP) guidelines, the permissible deviation from the mean weight is contingent upon the average weight of the tablets. In this study, brands P1, P2, and P5, which have average weights below 130 mg, were subject to a deviation of  $\pm 10\%$ . Meanwhile, brands P3 and P4, with average weights between 130 mg and 324 mg, adhered to a stricter deviation limit of  $\pm 7.5\%$ . Remarkably, all brands tested demonstrated compliance with these specified limits, reinforcing their adherence to established manufacturing standards [8].

Hardness test is essential for a tablet because the structural integrity of the tablet should be maintained throughout the whole process, starting from manufacturing till the use of medication by the patient. The hardness of the tablet should overcome factors like storage conditions after manufacturing, packaging, and shipping [9]. Tablet hardness may affect tablet friability, disintegration time, and drug dissolution. The crushing strength of 4 kg is usually considered to be the minimum for satisfactory tablets [6]. Our findings are consistent with USP specifications, indicating that the Pantoprazole tablets examined meet the required hardness standards. (Table 3) presents the hardness variation among the different brands of Pantoprazole.

The friability test evaluates the susceptibility of tablets to crumbling or breaking. In our tests, there was no dust formation or change in the weight of the tablets, which reflects the strength of the coating used in the product. All brands in this study complied with the USP friability specification, with results showing less than one percent friability. This demonstrates that the tablets are durable, maintaining their appearance and ensuring accurate dosing. The disintegration test is used to determine the time elapsed for tablets to disintegrate into smaller particles that will pass through a 10-mesh screen. The disintegration time affects the drug absorption rate as well as its therapeutic efficacy. The type and number of excipients used in tablet formulation and the manufacturing process, such as coating, are possible reasons that affect the disintegration time of tablets [9].

Pantoprazole is sensitive to degradation in the acidic medium of the stomach, so the drug is formulated in enteric-coated formulations [3]. The present study indicated that all of the pantoprazole sodium tablet brands did not show any signs of disintegration when immersed in an acidic medium of 0.1M HCl for 1 hr, except product (P4), which showed complete disintegration of all the tablets after 15 minutes, indicating an inappropriate enteric coating of the tablets. After transferring the samples to phosphate buffer (pH 6.8) for 30 minutes to simulate intestinal fluid, all brands disintegrated within this timeframe, passing the disintegration test. Notably, product P4 disintegrated the fastest, taking only 2 minutes, while product P2 exhibited a relatively longer disintegration time of 20 minutes compared to the other brands. (Table 4) shows the disintegration time in both media.

Although all brands align well with USP specifications, there is notable variation in the results. This variation can be attributed to differences in drug formulation, specifically the type and quantity of disintegrant used. Ingredients such as sodium starch glycolate, binders, microcrystalline cellulose, and lubricants contribute to faster disintegration, thereby enhancing drug stability.

## Conclusion

In conclusion, the evaluated tablet batches demonstrated overall quality and consistency, exhibiting

uniform appearance, acceptable hardness, and resistance to friability. While all products maintained integrity during testing in a simulated acidic medium, the generic product (P4) raised concerns due to its complete disintegration within 15 minutes, suggesting issues with its enteric coating, which indicates an ineffective product. Thus, local regulatory authorities must implement stricter control of the marketed product. The other products successfully met USP disintegration requirements, ensuring effective performance in their intended applications.

### Conflicts of Interest

The authors declare no conflicts of interest.

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