Research Article

Comparative comparison of five different marketed pantoprazole (antacid) tablet formulations

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ABSTRACT

Aim and Objective: The proposed methodology was aimed at comparing the five different brands of pantoprazole (40 mg) to ensure safety, efficacy, accepted quality, and rationality of use to protect public health. The comparison was based on some physicochemical properties of drug and other parameters such as weight variation test, thickness test, hardness test, disintegration test, dissolution test, pure drug analysis, ultraviolet (UV) spectrophotometry, assay of brands, and infrared spectroscopy. **Methods Used:** Different paracetamol brands were evaluated on the basis of preparation of standard sample, assay of drug, limit of detection, limit of quantification, weight variation test, thickness test, hardness test, disintegration test, dissolution test, pure drug analysis, UV spectrophotometry, assay of brands, and infrared spectroscopy. **Results:** All brands were evaluated using established procedures to assess the pharmaceutical quality characteristics. The measured thickness of studied brand tablets ranged from 2.79 mm to 3.49 mm. The disintegration time test indicated that any of the pantoprazole sodium tablet brands did not disintegrate in 0.1 N HCl acidic medium for 2 h but all disintegrated in the time range of 12.43–24.42 min in phosphate buffer. **Conclusion:** This study aimed with comparative *in vitro* evaluation of different brands of pantoprazole sodium tablets available in different retail outlets in Addis, Ababa, Ethiopia. All brands were evaluated using established procedures to assess the pharmaceutical quality characteristics. The study results revealed that all of the tested brands of the pantoprazole sodium enteric coated tablet fulfilled the criteria set in the official monograph for *in vitro* quality control tests.

Keywords: Pantoprazole, GERD, 0.1 N HCl, *In-vitro* evaluation, ATPase enzyme.

Introduction

Antacids are alkali preparations that neutralize hydrochloric acid in the stomach. Antacids can contain aluminum, magnesium, calcium, or combined substances. Antacids are indicated for dyspepsia, gastroesophageal reflux disease (GERD), reflux esophagitis, and gastritis.[1] Their onset of action is fast but they require frequent administration (4–6 times a day) because of their short duration of section. Antacids are the substances which neutralize stomach acidity and are used to relieve heartburn, indigestion, or an upset stomach. Antacids are available over the counter and are taken by mouth to quickly relieve occasional heartburn, the major symptom of gastroesophageal reflux disease and indigestion.[2] Treatment with antacids alone is symptomatic and only justified for minor symptoms.

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Antacids are distinct from acid-reducing drugs such as H_2-receptor antagonists or proton-pump inhibitors and they do not kill the bacteria *Helicobacter pylori*, which causes most ulcers.[3,4] Non-particulate antacids increase gastric pH with little or no effect on gastric volume. When excessive amount of acids is produced in the stomach, the natural mucous barrier that protects the lining of the stomach can damage the esophagus in people with acid reflux. Antacids contain alkaline ions that chemically neutralize stomach gastric acid, reducing damage, and relieving pain.[5]

Pantoprazole is the first generation proton-pump inhibitor used for the management of GERD, for gastric protection to prevent recurrence of stomach ulcers or gastric damage from chronic use of nonsteroidal anti-inflammatory drugs, and for the treatment of pathological hypersecretory conditions including Zollinger-Ellison syndrome. Pantoprazole exerts its stomach acid-suppressing effects by preventing the final step in gastric acid production by covalently binding to sulfhydryl groups of cysteines found on the (H+,K+)-ATPase enzyme at the secretory surface of gastric parietal cell.

This includes headaches, diarrhea, vomiting, abdominal pain, and joint pain.[6,7] It is taken by mouth and intravenous. Pantoprazole is 6-(difluoromethoxy)-2-([3, 4-dimethoxypyridin-2-yl]methylsulfinyl)-1H-benzo(d)imidazole [Figure 1]. It is a white to off-white crystalline substance with molecular weight 383.4 g/mol [Table 1].

Table 1: Physical properties of pantoprazole

Trade Name	Protonix, pan, and Pantosec
IUPAC name	6-Difluoromethoxy-2-([3,4-dimethoxypyridin2-yl] methylsulfinyl)-1H-benzodimidazole
Molecular formula	$C_{16}H_{15}F_2N_3O_4S$
Molecular weight	383.371 g/mol
Physical state	A white to off-white crystalline powder
Category	Antacids
Solubility	Freely soluble in water, very slightly soluble in phosphate buffer, practically insoluble in hexane
Melting point	149–150°C
Half-life	About 1 h

Drug profile

Pantoprazole is 6-(difluoromethoxy)-2-[(3, 4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzo[d]imidazole. It is a white to off-white crystalline substance with molecular weight 383.4 g/mol.

Materials and Methods

Collection of samples

Five brands of marketed pantoprazole tablets were obtained from various drug stores. The samples were properly checked for their, manufacturer name, physical appearance, batch number, date of manufacturing, and expiry date before purchasing. They were coded as brand A, B, C, D, and E. The labeled active ingredients of pantoprazole 40 mg were obtained from packaged strip or blister.[8]

Chemicals required

0.1 N NaOH, buffer, pantoprazole powder.

Methods

Preparation of standard solution of pantoprazole

The standard stock of solution pantoprazole was prepared by accurately weighing and transferring. The standard pantoprazole (40 mg) was weighed accurately and transferred to volumetric flask (100 ml) and further dilutions were prepared range from 5 to 50 microgram per ml also solution prepared in water dissolved properly and diluted with 0.1 N NaOH to obtained the final concentration of 100 ppm/100 ml and the resulting solution was used as working standard solution. From the stock solution, the different dilutions were prepared in the range of 50-5 microgram per ml.[9,10]

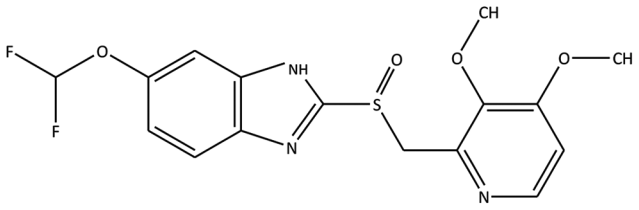

Figure 1: Structure of pantoprazole

Assay of tablet

For the preparation and analysis of sample solution, each tablet containing 40 mg of pantoprazole. Twenty tablets were accurately weighed and calculate average weight then drug equivalent to 10 mg was taken and treated in similar manner as that of standard. The absorbance was measured at 294 nm against reagent blank.[11-13] The calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range 50–5 μg/ml.[14,15]

Limit of detection (LOD) and limit of quantification (LOQ)

LOD is the smallest concentration of the analyte that gives the measurable response. LOD was calculated.[16]

$$LOD = 3(SD/SLOPE)$$

The LOQ is the smallest concentration of the analyte, which gives response that can be accurately quantified. LOQ was calculated using the following formula[17]

$$LOQ = 10(SD/SLOPE)$$

Six sets of known concentrations were prepared and scanned. Using these spectra, regression equations were obtained. By taking average of slopes and standard deviation of y intercept, LOD and LOQ were calculated.[18-20] The values of LOQ and LOD were calculated.

Weight variation test

Twenty tablets from each batch were collected randomly and weight of individual tablet was determined using an electric balance. The average weight of the 20 tablets and percentage deviation in weight of each tablet from the average weight were calculated and tabulated [Table 2]. The test was carried according to British pharmacopeia.[18-20] The weight variation of the tablets was calculated using the following formula:

Weight variation= (Initial weight –Average weight)/Average weight × 100

Thickness test

Tablets thickness is an important characteristic in reproducing appearance variation in the tablet thickness may cause problems in

Table 2: List of limits of weight variation (BP)

Average weight (mg)	Percentage deviation (%)
50 mg or less than	±10
More than 50 mg or <250 mg	±7.5
More than 250 mg	±5

counting and packaging in addition to weight variation beyond the permissible limits. The six tablets of each brand were analyzed with thickness tester. Thickness should be controlled within ±5% variation of standard value.[21]

Hardness test

The resistance of tablets to capping, abrasion, or breakage under conditions of storage, transportation, and handling before usage depends on its hardness. Tablet hardness is defined as the load required crushing or fracture a tablet placed on its edge. Sometimes, it is also termed as tablet crushing strength. Ten tablets from each brand were taken, a tablet was placed between the spindle of the hardness tester instrument and pressure was applied. The pressure was then increased as uniformly as possible until the tablet breaks and the pressure required to break the tablet was then read off the instrument and recorded.[21]

Disintegration time test

Preparation of 0.1 N Hydrochloric Acid:

To prepare 0.1 N HCl, 8.33 mL of hydrochloric acid pellets dissolved in 1000 ml of water. Disintegration is the first physical change observed for a drug when it enters into the body, disintegration test helps in knowing the API solubility in the gastric fluids of the digestive system. The breaking of tablet into smaller fragments is called disintegration of tablet. At random, six tablets were selected from each brand and each tablet was placed in each of the tubes of the basket rack system of disintegration apparatus. The assembly was inserted in 0.1 N HCl at 37°C ± 2°C and stirred at 50 rpm. The disintegration time was taken to be time no granule of any tablet was left on the mesh.[22]

In vitro dissolution test

The dissolution test was carried out using USP apparatus II (paddle method) five in six replicates for each brand. The dissolution medium was 900 ml 0.1 N HCl which was maintained at 37°C ± 0.5°C. In all the experiments, 5 ml of dissolution sample was withdrawn at 0, 10, 20, 30, 40, 50, and 60 min and replaced with equal volume of dissolution medium to maintain sink condition. Samples were filtered and assayed by ultraviolet spectrophotometry at 276 nm. The amount of drug present in samples was calculated.[22-25]

Results and Discussion

Physical appearance of pantoprazole was examined by the various organoleptic properties as

1. Color: A white to off-white
2. State: Crystalline powder.

The melting point was recorded by capillary fusion method and compared to monograph (IP) and reported in Table 3.

The solubility was carried out in different solvent such as distilled water, methanol, ethanol, and sodium hydroxide. A pinch of pantoprazole was added into separate test tubes containing 5 ml of each solvent. The entire test tubes were shaken for 5–10 min. Then, the solubility was visually determined and following results were obtained as given on Table 4.

In terms of weight variation, all the brands showed that the deviations from the average weight are within limits in all branded tablets and showed different mean weight indicates the use of different excipients in the different brands [Table 5].

The hardness of the tablet varied between 4 and 7 kg/cm for all the tablet brands [Table 6].

The disintegration time of all brands is within limits. The disintegration times of all brands lie between 15 and 30 min [Table 7].

Table 3: Melting point comparison with IP Values

Method used	Experimental value	Literature value
Capillary fusion method	149°C	149–150°C

Table 4: Qualitative solubility data of pantoprazole in different solvents

Solvents	Solubility
Distilled water	+++
Methanol	++
Ethanol	+++
Sodium hydroxide	++

++ Slightly soluble, +++ freely soluble

Table 5: Average weight of different brands of pantoprazole

Brands	Total weight (g)	Average	Mean±SD
A	20.85	1.042	1.042±0.00187
B	19.63	0.981	0.981±0.01792
C	14.32	0.716	0.716±0.0067
D	21.23	1.061	1.0616±0.00326
E	15.03	0.751	0.751±0.0035

Table 6: Hardness variation of different brands of pantoprazole

Brands	Total hardness (kg/cm2)	Average	Mean±SD
A	48.29	8.04	8.04±0.01870
B	53.27	8.87	8.87±0.0187
C	57.30	9.55	9.55±0.0216
D	52.32	8.72	8.72±0.0294
E	54.21	9.03	9.03±0.0018

Table 7: Disintegration time test for all the brands of pantoprazole

Brands	Total disintegration time (s)	Average	Mean±SD
A	5193	865.5	865.5±0.2581
B	5859	976.5	976.5±0.1870
C	5217	869.5	869.5±0.2428
D	5511	918.5	918.5±0.2438
E	5247	874.5	874.5±0.2160

Conclusion

All brands of pantoprazole were evaluated using established procedures to assess the pharmaceutical quality characteristics. The disintegration time test indicated that any of the pantoprazole sodium tablet brands did not disintegrate in 0.1 N HCl acidic medium for 2 h but all disintegrated in the time range of 12.43–24.42 min in phosphate buffer. Therefore, this study results revealed that all of the tested brands of the pantoprazole sodium enteric coated tablet fulfilled the criteria set in the official monograph for *in vitro* quality control tests.

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