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COMPARISION AND EVALUATION OF DIFFERENT BRANDS OF COMMERCIALLY AVAILABLE PANTOPRAZOLE TABLETS

B.Brahmaiah[*1],
CH.Dileep[1], K.Manasa[1], Prasanna Kumar Desu[1]

[1]Priyadarshini Institute of Pharmaceutical Education & Research, Guntur,India

ABSTRACT

Now a days, many pharmaceutical companies are manufacturing the drugs for their commercial purpose with insufficient active ingredient in the dosage form as they claimed on the strip. So, this study was undertaken with the objective of evaluating different brands of commercially available Pantoprazole tablets, which are used in the treatment of ulcer, to get awareness that which pharmaceutical company gives appropriate active ingredient present in dosage forms released into the market. The delayed-action tablet dosage form is intended to release a drug after sometime, or after the tablet has passed through one part of the GI tract into another. The enteric coated tablet is the most common example of a delayed-action tablet product.

KEYWORDS : *Pantoprazole,* Comparision of Brands, Evaluation of Brands etc.

Correspondence Author

B.Brahmaiah

Priyadarshini Institute of Pharmaceutical Education & Research, Guntur,India.

Email: brahmaiahmph@gmail.com

INTRODUCTION

The delayed-action tablet[1,2,3,4] dosage form is intended to release a drug after sometime or after the tablet has passed through one part of the GI tract into another. The enteric coated tablet is the most common example of a delayed-action tablet product. Not all delayed-action tablets are enteric or are intended to produce the enteric effect. An **enteric coating** is a barrier applied to oral medication that controls the location in the digestive system where it is absorbed. *Enteric* refers to the small intestine; therefore enteric coatings prevent release of medication before it reaches the small intestine. Drugs that have an irritant effect on the stomach, such as aspirin, can be coated with a substance that will only dissolve in the small intestine. Similarly, certain group of azoles (esomeprazole, omeprazole, pantoprazole a nd all grouped azoles) are acid-unstable. For such types of drugs, enteric coating added to the formulation tends to avoid the stomach's acidic exposure, delivering them instead to a basic pH environment (intestine's pH 5.5 and above) where they do not degrade, and give their desired action. The enteric coating of the tablets utilizes the pH differences of gastric pH 1-3 and intestinal pH 6-7. The GIT pH range in healthy human is from 0.5-8.Most enteric coatings won't dissolve in solutions

with a pH lower than 5.5. And the commonly used enteric coating are made using Methacrylic acid copolymers, Cellulose acetate, Polymethacrylic acid/acrylic acid copolymer, Hydroxy propyl methyl cellulose phthalate, Polyvinyl acetate phthalate, Hydroxy methyl ethyl cellulose phthalate, Acrylic resin, Shellac.

Pantoprazole[5,6,7] is a proton pump inhibitor used to treat peptic ulcer, duodenal ulcer, gastro oesophageal reflux disease by inhibiting the enzyme H^+/K^+ATPase , the acidic pump. It is also used to treat Zollinger-Ellison syndrome, erosive esophagitis. The active ingredient is a substituted benzimidazole, sodium 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfinyl]1H-benzimidazole sesquihydrate, a compound that inhibits gastric acid secretion

OBJECTIVE:

Now a days, many pharmaceutical companies are manufacturing the drugs for their commercial purpose with insufficient active ingredient in the dosage form as they claimed on the strip. So, this study was undertaken with the objective of evaluating different brands of commercially available Pantoprazole tablets, which are used in the treatment of ulcer, to get awareness that which pharmaceutical company gives appropriate active ingredient present in dosage forms released into the market.

MATERIALS:

Different Brands of Pantoprazole Enteric Coated tablets used: These tablets were kindly provided by Siva sankar Medical stores located at Brahmanapalli, Piduguralla, Guntur. The 40 mg tablets have expiry date till JAN-2013, JUNE-2012, JULY-2013 and JULY-2012 respectively. The 20 mg tablets have expiry date till FEB-2013, JUNE-2013, JULY-2012 and JUNE-2012respectively

Table No 1: List of different brands and their doses of pantaprazole

S.No:	BRAND NAME	MANUFACTURED BY	DOSE(B)	DOSE(b)
1.	Pentab	CRESCENT Therapeutics Ltd.	40 mg	20 mg
2.	Nupenta	MACLEODS Pharmaceutical Ltd.	40 mg	20 mg
3.	Pantocid	SUN PHARMA SIKKIM	40 mg	20 mg
4.	Pantosec	CIPLA Pharmaceuticals Ltd.	40 mg	20 mg

EQUIPMET USED: High Precision Balance for Weight variation, Vernier Calipers for measuring Thickness, Monsanto Hardness Tester for testing Hardness, Roche Friabilator for Friability, USP Type II Dissolution apparatus for Dissolution, USP Disintegration Apparatus for Disintegration, EI Double beam UV-Visible Spectrophotometer model no: 1372 for Assay.

EVALUATION OF PANTOPRAZOLE TABLETS:[4,8]

i. Weight Variation Test:

With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug.Individual weights of 20 tablets were taken and the average weight was calculated and weight variation was calculated by using the following formula.

$$\text{Weight variation} = \frac{(\text{Weight of tablet} - \text{Average weight})}{\text{Average weight of tablets}} \times 100$$

Weight variation should not be more than 7.5%.The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

ii. Hardness:

Tablet hardness is defined as the force required to break a tablet diametrically. A tablet is placed between two anvils, force is applied to the anvils, and the crushing strength that just causes the tablet to break is recorded. Hardness is also termed as the Tablet Crushing Strength.Devices used to measure the hardness were Monsanto tester, Strong-Cobb tester, Pfizer tester, Erweka

tester, Schleuniger tester. Hardness of the tablets was observed by the use of Monsanto hardness tester. Monsanto tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet, and a zero reading is taken. The upper plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture is recorded, and the zero force reading is deduced from it. Desired hardness was 2-4 Kg/square cm.

iii. Thickness:

Tablet thickness should be controlled within a ± 5% variation of a standard value. Any variation in tablet thickness within a particular lot of tablets or between manufacturer's lot should not be apparent to the unaided eye for consumer acceptance of the product.Thickness of the tablets was calculated by the use of vernier calipers. Desired thickness was calculated to be 3.5 to 4 mm.

iv. Friability:

The laboratory friability tester subjects a number of tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping the tablets a distance of 6 inches with each revolution. Normally, a preweighed tablet is placed in the friabilator, which is then operated for 100 revolutions. The tablets are then dusted and reweighed. Tablets that lose less than 0.5 to 1% of their weight are generally considered acceptable. When capping is observed on friability testing, the tablet should not be considered for commercial use, regardless of the percentage of loss seen. Friability of the tablets was calculated by the use of Roche friabilator. Friability should be less than 1%.

% Friability = $(1- w_0/w) \times 100$

W_0 = weight of the tablet before test.

W = weight of the tablet after test.

v. Disintegration Time:

Disintegration is the breakdown of tablet into smaller particles or granules.Disintegration time of the tablet was observed with the help of USP disintegration test apparatus. The USP device to test disintegration uses 6 glass tubes that are 3 inches long, open at the top, and held against a 10-mesh screen at the bottom end of the basket rack assembly. To test for disintegration time, one tablet is placed in each tube, and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid, or simulated intestinal fluid, at $37^oC \pm 2^oC$, such that the tablet remains 2.5 cm below the surface of the liquid on their upward movement and descend not closer than 2.5 cm from the bottom of the beaker. A standard motor drive device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute.

To be in compliance with the USP standards, the tablets must disintegrate, and all particles must pass through the 10-mesh screen in the time specified. If any residue remains, it must have a soft mass with no palpably firm core. Enteric coated tablets are to show no evidence of disintegration after 1 hour in simulated gastric fluid. The same tablets are then tested in simulated intestinal fluid and are to disintegrate in 2 hours plus the time specified in the monograph.

vi. Dissolution Study:

The equipment consists of a cylindrical flask with a hemispherical bottom. The flask is maintained at 37ºC± 0.5 ºC by a constant temperature bath. The motor is adjusted to turn at the specified speed, and samples of the fluid are withdrawn at intervals to determine the amount of drug in solution. A paddle, formed from a blade and a shaft, is used as the stirring element. The dosage form is allowed to sink to the bottom of the flask before stirring. First two hours dissolution was done acidic medium of pH 1.2 and next is carried out in phosphate buffer og pH 6.8. Absorbance was found for the samples withdrawn using phosphate buffer as blank and λ-max at 289 nm. Dilutions were made as required.

Dissolution testing and interpretation can be continued through three stages if necessary. In stage 1(S1), six tablets are tested and are

acceptable if all the tablets are not less than the monograph tolerance limit (Q) plus 5%. If the tablets fail S1, an additional 6 tablets are tested (S2). The tablets are acceptable if the average weight of the twelve tablets is greater than or equal to Q and no unit is less than Q minus 15%. If the tablets still fail the test, an additional 12 tablets are tested. The tablets are acceptable if the average of all 24 tablets is greater than or equal to Q and if not more than 2 tablets are less than Q minus 15%.

$$\text{Amount of the drug dissolved} = \frac{\text{Test Absorbance} \times \text{Standard concentration} \times \text{dilution factor} \times \text{Dissolution fluid vol.}}{\text{Standard absorbance} \times 1000}$$

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RESULTS AND DISCUSSION:

Evaluation of Characteristics:

Physicochemical Characteristics of tablet:

Tablets are evaluated for Weight variation, Thickness, Hardness, Friability, Disintegration time and the values were listed below table.

Table No 2: Physical evaluation of differnet 'B' brands of Pantoprazole tablets:

S.No:	PHYSICAL PARAMETER	B1	B2	B3	B4
1.	Weight variation	2.4%	4.6%	3.7%	1.9%
2.	Thickness	3.6mm	3.7mm	3.7mm	3.8mm
3.	Hardness	3 Kg/sq.cm	2.5kg/sq.cm	2.5 kg/sq.cm	2.5 kg/sq.cm
4.	Friability	0.62%	0.49%	0.18%	0.33%
5.	Disintigration time a) In 0.1 N HCl (gastric fluid)	No evidence of disintigration for 1 hr	No evidence of disintigration for 1 hr	No evidence of disintigration for 1 hr	No evidence of disintigration for 1 hr
	b) In 6.8 pH phosphate buffer (intestinal fluid)	Complete disintigration in 2 hrs	Complete disintigration in 2 hrs	Complete disintigration in 2 hrs	Complete disintigration in 2 hrs

Table No 3: Physical evaluation of different 'b' brands of Pantoprazole tablets:

S.No:	PHYSICAL PARAMETER	b1	b2	b3	b4
1.	Weight variation	2%	3.8%	1.96%	2.2%
2.	Thickness	3.6mm	3.7mm	3.7mm	3.8mm
3.	Hardness	3 kg/sq.cm	2.5 kg/sq.cm	2.5 kg/sq.cm	2.5 kg/sq.cm

4.	Friability	0.26%	0.33%	0.48%	0.54%
5.	Disintigration time a) In 0.1 N HCl (gastric fluid)	No evidence of disintigration for 1 hr	No evidence of disintigration for 1 hr	No evidence of disintigration for 1 hr	No evidence of disintigration for 1 hr
	b) In 6.8 pH jk 0 phosphate buffer (intestinal fluid)	Complete disintigration in 2 hrs	Complete disintigration in 2 hrs	Complete disintigration in 2 hrs	Complete disintigration in 2 hrs

Dissolution Studies:

Table No 4: Dissolution profile for brand B1 in 0.1 N HCL:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.12± 0.06

Table No 5: Dissolution profile for brand B1 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	20± 0.12
3.	10	34± 0.14
4.	15	46.3± 0.18
5.	30	65.25± 0.13
6.	45	82.95± 0.16
7.	60	95± 0.15

Table No 6: Dissolution profile for brand B2 in 0.1 HCL:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.43 ± 0.04

Table No 7: Dissolution profile for brand B2 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	14± 0.17
3.	10	36± 0.16
4.	15	52± 0.14
5.	30	71± 0.12
6.	45	82± 0.19
7.	60	91± 0.15

Table No 8: Dissolution profile for brand B3 in 0.1 N HCL:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.36 ± 0.08

Table No 9: Dissolution profile for brands B3 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	16± 0.19
3.	10	31± 0.17
4.	15	52± 0.13
5.	30	63.62± 0.14

6.	45	78.34± 0.17
7.	60	92± 0.16

Table No 10: Dissolution profile for brand B4 in 0.1 N HCL:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.22 ± 0.07

Table No 11: Dissolution profile for brand B4 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	18± 0.11
3.	10	34± 0.18
4.	15	48± 0.16
5.	30	68± 0.14
6.	45	84± 0.12
7.	60	93± 0.15

Table No 12: Dissolution Profile for brand b1 in 0.1 N HCl:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.12 ± 0.04

Table No 13: Dissolution profile for brand b1 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	18± 0.11
3.	10	33± 0.12
4.	15	41.5± 0.19
5.	30	66.5± 0.16
6.	45	82.5± 0.13
7.	60	96.5± 0.18

Table No 14: Dissolution Profile for brand b2 in 0.1 N HCl:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.46 ± 0.08

Table No 15: Dissolution profile for brand b2 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	15± 0.14
3.	10	32± 0.18
4.	15	53± 0.16
5.	30	76± 0.15
6.	45	81± 0.19
7.	60	90± 0.13

Table No 16: Dissolution Profile for brand b3 in 0.1 N HCl:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.32 ± 0.03

Table No 17: Dissolution profile for brand b3 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	16.55± 0.16
3.	10	41.8± 0.15
4.	15	53.9± 0.18
5.	30	59.5± 0.13
6.	45	70.3± 0.17
7.	60	91± 0.12

Table No 18: Dissolution Profile for brand b4 in 0.1 N HCl:

S.No:	Time	% of drug dissolved
1.	2 hrs	0.21 ± 0.05

Table No 19: Dissolution profile for brand b4 in pH 6.8 phosphate buffer:

S.No:	Time (min)	% drug dissolved
1.	0	0
2.	5	16.25± 0.11
3.	10	33.6± 0.16
4.	15	55± 0.17
5.	30	78.5± 0.14
6.	45	82± 0.12
7.	60	93± 0.15

Figure No.1: Drug Release profile for brand B1 in pH 6.8 Phosphate buffer:

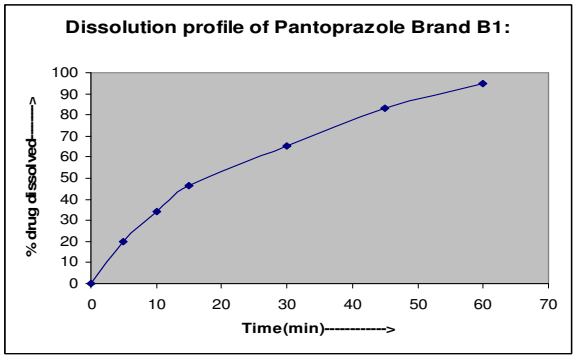


Figure No.2: Drug Release profile for brand B2 in pH 6.8 Phosphate buffer:

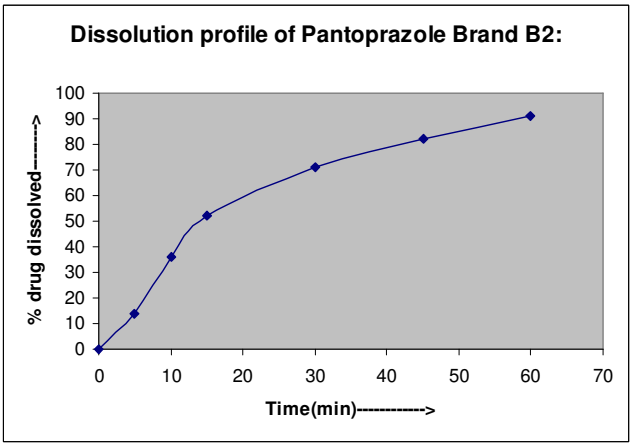


Figure No.3: Drug Release profile for brand B3 in pH 6.8 Phosphate buffer:

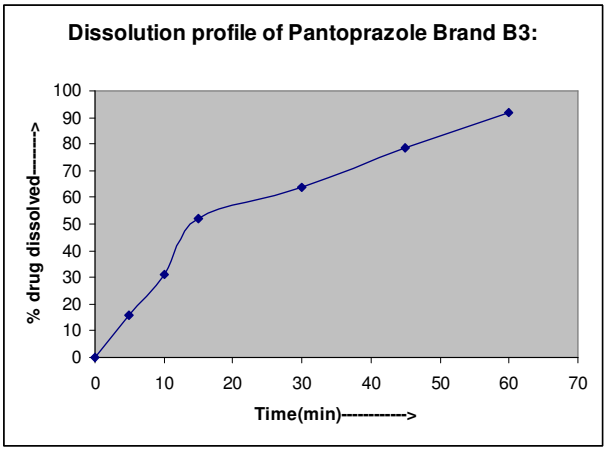


Figure No.4: Drug Release profile for brand B4 in pH 6.8 Phosphate buffer:

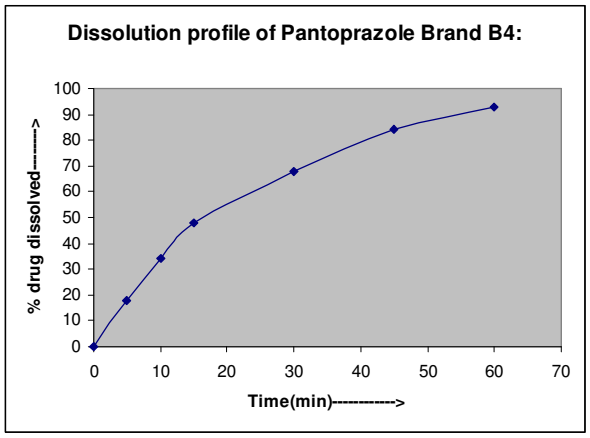


Figure No.5: Drug Release profile for brand b1 in pH 6.8 Phosphate buffer

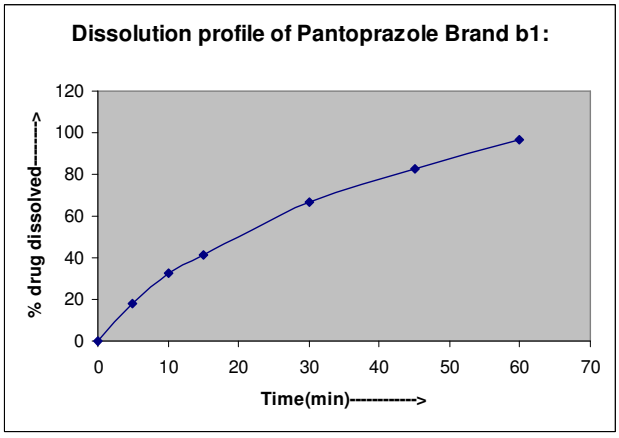


Figure No.6: Drug Release profile for brand b2 in pH 6.8 Phosphate buffer

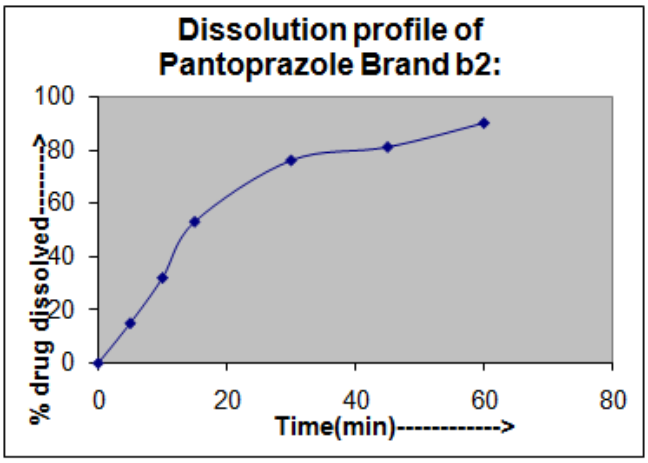


Figure No.7: Drug Release profile for brand b3 in pH 6.8 Phosphate buffer

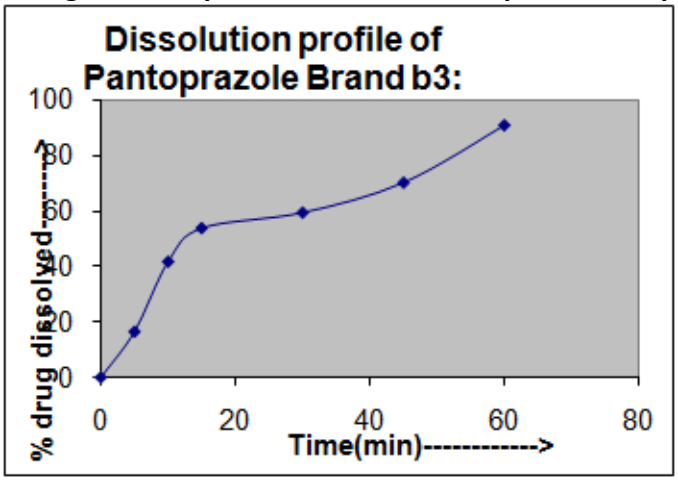
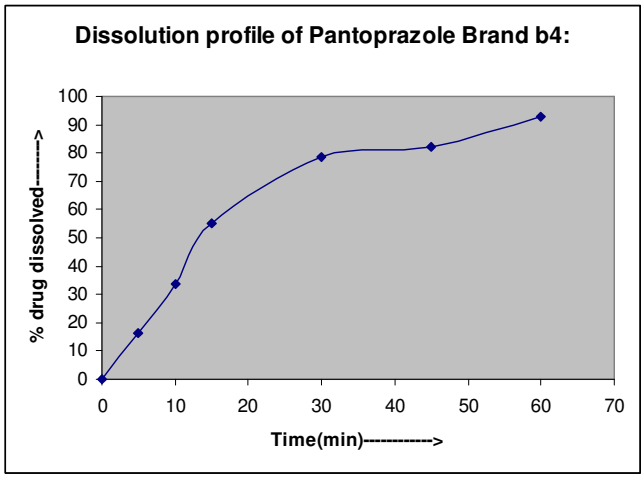


Figure No.8: Drug Release profile for brand b4 in pH 6.8 Phosphate buffer



ASSAY:

Table No 20: Assay of different brands and doses of Pantaprazole

S.No:	Brand	Labelled Amount(mg)	Amount found(mg)	% purity
1.	B1	40	38.4	96
2.	B2	40	36	90
3.	B3	40	36.8	92
4.	B4	40	37.2	93
5.	b1	20	19.3	96.5
6.	b2	20	18.2	91
7.	b3	20	18.2	91
8.	b4	20	18.6	93

DISCUSSION:

All the brands exhibited good hardness strength, which is required for safe handling and transportation. Brand 1 exhibited maximum hardness while all the other brands exhibited similar hardness. All the brands had a friability of less than 1%. Tablets having fewer tendencies to generate powder on handling and transportation will have low friability values. The content of Pantoprazole in each tablet brand was within the limits prescribed by U.S.P. All the brands of tablets passed the weight variation test. According to I.P., if the tablets are uniform in weight, it is likely that the tablets will be uniform in drug content also. Hence, I.P. prescribes only weight variation test on tablets when the drug forms the major bulk of the tablet. As all the brands passed the weight variation test, it is concluded that all the tablets are uniform in drug content also. All the brands of tablets passed the U.S.P disintegration test indicating that they will completely disintegrate in the intestine within 2 hours but no disintegration in the stomach. All the brands of Pantoprazole tablets passed the dissolution test as prescribed by U.S.P. Even though all brands passed the dissolution test as prescribed by U.S.P., there was variation in Pantoprazole dissolution rate from brand to brand.

SUMMARY AND CONCLUSION:

All the brands passed all the official tests as prescribed by the Pharmacopoeia.All the brands were within the limit when tested for thickness, weight variation, Hardness, Friability and Disintegration. The amount of drug obtained and percentage purity is less when compared to that of labeled claim. Among the four brands, both 40 mg and 20 mg, brand 1 i.e. B1 and b1 was found to have more amount of the drug and brand 2 i.e. B2 and b2 was found to have less amount of the drug.Formulation additives in the tablet, physical form of the drug used in the tablet and manufacturing processes vary from manufacturer to manufacturer which is responsible for the variation in the observed dissolution profiles. We strongly recommend the manufacturers to change their manufacturing process to meet the requirements regarding the amount of the drug present in the dosage form as per label claim so that there will be better in-vitro performance and thereby better in-vivo performance of the Pantoprazole enteric coated tablets.

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