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Formulation & Evalution of Entric Coated Tablets of Anti- Ulcer Drugs of Pantaprazole.

Mr. Bhushan Sambhaji Paikrao, Dr. Abhijeet Raosaheb Shete, Dr. Megha T. Salve

Shivajirao Pawar College of Pharmacy, Pachegaon

ABSTRACT

Pantoprazole 5-(difluoromethoxy)- 2-((3,4- dimethoxypyridin-2-yl) methylsulfinyl)- 3H benzoimidazole is a proton pump asset belongs to group of benzimidazole. This emulsion inhabits gastric acid conformation and thereby it's veritably effective for the treatment of gastric and duodenum ulcers. In waterless media more acidic than pH 4 it suffers a virtually complete corruption within a period shorter than 10 twinkles. Indeed, in solid state it's sensitive to heat, moisture, light and especially to substances containing an acidic group. Pantoprazole which has an irritant effect on the stomach, can be carpeted with a substance that will only dissolve in the small intestine. For similar types of medicines, enteric coating added to the expression tends to avoid the stomach's acidic exposure, delivering them rather to a introductory pH terrain (bowel pH 5.5 and over) where they do n't degrade, and give their asked action. This stumulate us to formulate and estimate pantoprazole as a enteric carpeted tablet.

Keywords: Pantoprazole, Enteric Coated, Development and Evaluation.

INTRODUCTION

A solid lozenge form is a delivery system that includes tablets, capsules, sachets and bulk or unit lozenge maquillages and granules1. The most generally used pharmaceutical solid lozenge forms moment include grains, bullets, tablets and capsules. A simplified inflow- map of the relationship of pharmaceutical lozenge forms is shown in Figure 1. These lozenge forms are designed either for perfecting the physical and mechanical parcels of accoutrements during manufacture and/ or for furnishing a asked medicine delivery system. The tablets and capsules can be made directly from maquillages or from grains and bullets, or from film- carpeted multiple units.

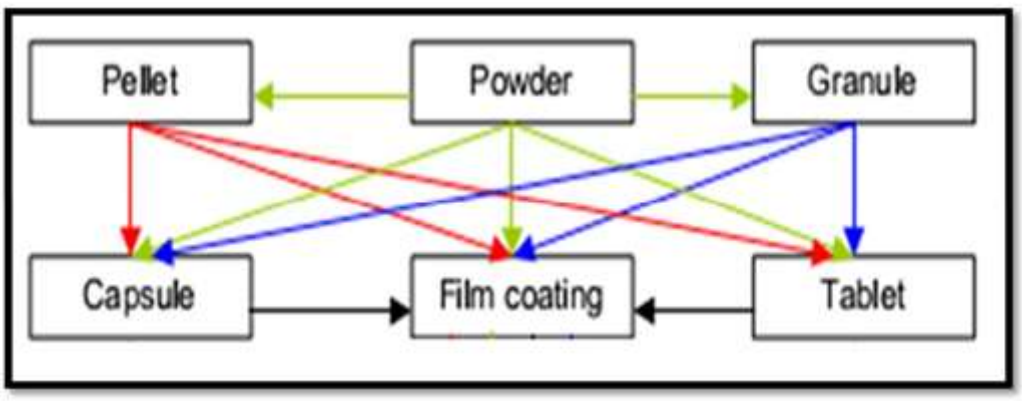


Fig. 1 Relationship of pharmaceutical solid dosage forms.

Advantages of solid dosage forms:

- More stable than liquids, with longer expiration dates.
- Easy shipping and running.
- lower demanded shelf space.
- No preservation conditions.

- Accurate lozenge(single cure).
- Suitable for sustained release medication.

Disadvantages of solid lozenge forms

- Their medication needs complicated and precious machines.

PHARMACEUTICAL TABLETS:

Oral Lozenge form is the most popular route for medicine remedy and over 80 of the medicines formulated to produce systemic goods are produced as oral lozenge forms1, 2. The tablet lozenge form accounts for roughly 50 of all lozenge forms on the request. Tablets and capsules are presently reckoned for the loftiest proportion of all medicine lozenge forms. Tablets are defined by the European Pharmacopeia 2001, as "solid medications each containing a single cure of one or further active substances and generally attained by compressing invariant volumes of patches. Tablets are intended for oral administration. Some are swallowed whole, some after being masticated, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is delivered". When a new medicine is discovered the pharmaceutical company makes all possible sweats to insure that the medicine can be so formulated that it's competent of being administered orally.However, and should a more complex parenteral route be the only choice, also the medicine is basically disrated for administration in a sanitarium setting or croaker's office, If it cannot be administered by oral route.However, the deals of the medicine may comprise only a small portion of what the request would be otherwise3, If tone- administration of medicines cannot be attained. Despite the long and continuing history of the development of new technologies for administration of medicines, the tablet form remains the most generally used lozenge form because of the following advantages,

Advantages of tablets as a dosage form:

- They offer the greatest capabilities of all oral dosage forms for the greatest dose precision and the least content variability.
- Good physical, chemical stability and microbiological stability.
- Competitive unit production costs
- High level of patient acceptability
- High convenience
- Product identification of potentially the simplest and the cheapest

Disadvantages of tablets as a dosage form

- Inconvenience goods on the GI mucosa by some solids (e.g., aspirin).
- Possibility of bioavailability problems performing from slow decomposition and dissolution.
- Difficulty in swallowing in some cases; pediatrics and elders.
- Some medicines repel contraction into tablet.
- In exigency cases, intravenous or intramuscular injections are more effective.
- A tablet lozenge form scores over all other orally administered lozenge form due to the following aspects.

Materials And Methods

Pantoprazole, Microcrystalline Cellulose, Lactose Anhydrous, Croscarmellose Sodium, Sodium Starch Glycolate, Cross povidone, Povidone K-30, Povidone K-90, Aerosil, Magnesium Stearate

- **Preparation of core tablets by Direct Compression technique**

The core tablets of Pantoprazole phrasings were prepared by direct contraction system. The tablets were prepared after through webbing of colorful tableting excipients similar as Diluents, Binders, and Disintegrants using suitable experimental designs. The attention of Diluents, Binders, and Disintegrants were optimized using ANOVA. The optimization of colorful excipient attention was carried out using pre & Post contraction response variables similar as Angle.

Table : Composition of Pantoprazole Tablets

Ingredients (mg/tablet)	**FR5**	**FR6**	**FR7**	**FR8**	**FR9**	**FR10**	**FR11**	**FR12**	**FR13**
Pantoprazole	40	40	40	40	40	40	40	40	40
MCC	14	14	14	14	14	14	14	14	14
Lactose anhydrous	28	28	28	28	28	28	28	28	28
Croscarmellose sodium	5.0	10.0	15.0	-	-	-	-	-	-
SSG	-	-	-	5	10	15	-	-	-
Cross Povidone	-	-	-	-	-	-	5	10	15
Aerosil	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0

CONSTRUCTION OF CALIBRATION CURVE FOR PANTOPRAZOLE IN 0.1 M HYDROCHLORIC ACID

Preparation of pantoprazole primary stock solution (1000 µg/ml):

Hundred milligrams of pantoprazole was directly counted and transferred to a 100 ml volumetric beaker. A small volume of 0.1 M Hydrochloric acid buffer results was added and the result was shaken completely to dissolve pantoprazole. Eventually, the volume was made up to 100 ml of 0.1 M Hydrochloric acid results.

Determination of absorption maxima (λ max) in 0.1 M Hydrochloric acid

The immersion maxes(λ maximum) was determined by running diapason checkup of the secondary stock result in 200- 400 nm range in UV-visible spectrophotometer.

Preparation of working standard solution

A series of dilute results from the secondary stock result were prepared similar as 2, 4, 6, 8, 10, 12, 14, 16, 18 and 20 µg/ ml in 10 ml volumetric beaker. The absorbance of the results was measured at 283 nm using 0.1 M Hydrochloric acid result as a blank. A graph was colluded by taking attention(µg/ ml) on X axis and absorbance on Y axis. The measure(R2) value, pitch(m) and the intercept(c) were determined.

PREFORMULATION STUDIES:

Solubility of Pantoprazole:

Solubility trials were performed with a large excess of the substance. redundant of the substance was tested for solubility in water and pH 6.8 phosphate buffer using agitation system, in 100 ml steins at temperature of 25 °C ± 0.1 °C in a water shaking bath for 48 h, with shaking breadth of 50. Samples were taken after regular time intervals and quantified by UV/ VIS spectrometry.

Organoleptic properties:

The colour of pantoprazole medicine greasepaint was taken in adulation paper and viewed in well illuminated place. The odour and taste was characterized by taking a small volume and assessed with the help of an annotator.

pH of the solution

About 0.650 gm. of pantoprazole was dissolved with distilled water and eventually volume is made up to 10 ml with distilled water. The pH of that result was read with the help of pH cadence.

Loss on drying:

About 1gm of pantoprazole was placed in the plate of the digital humidity balance instrument. The temperature was set to 105oC and the instrument was run till a constant weight was attained. Eventually, the chance loss on drying was read out automatically on the panel.

Melting point

A small volume of greasepaint was placed into a emulsion tube. That tube is placed in the melting point determining outfit containing castor oil painting. The temperature of the castor oil painting was gradational increased automatically and read the temperature at which greasepaint started to melt and the temperature when all the greasepaint gets melted.

Tapped Density

Tapped viscosity is achieved by mechanically tapping a measuring cylinder containing a greasepaint sample. After observing the original volume, the mechanical tapping is achieved by irrigating the cylinder and allowing it to drop under its own weight a specific distance(by either of two styles). Device that rotates the cylinder during tapping may be preferred to minimize any possible separation of the mass during tapping down. Cylinder dropping distance 14 ± 2 mm at a normal rate of 300 drops/ nanosecond. Unless else tap the cylinder 500 times originally and measure the tapped volume, Va, to the nearest graduated unit, repeat the tapping an fresh 250 times and measured the tapped volume, Vb, to the nearest graduated unit.However, Vb is the final tapped volume, Vf, If the difference between the two volumes is lower than 2. reprise in lower than 2.

EVALUATON PARAMETERS

The formulation blend and compressed tablets were tested for the following properties.

Precompression Parameters

The scrap parcels play a vital part in the final performance of a tablet; for illustration, scrap size can affect the flowability and, hence, the average tablet weight and weight variation, and drying rate kinetics of wet granulations. The effect of scrap size and size distribution on final mix parcels and tablet characteristics is dependent on expression constituents and their attention

Angle of repose

The greasepaint mix was flown from the channel onto a distance of paper to form a mound and the compass of the mound and height of the pile were noted. The angle of repose was calculated by formula $\theta = \tan^{-1} (h / r)$

Bulk density

Bulk Viscosity is the viscosity held by total mass of the greasepaint. The counted greasepaint mix was taken ina graduated cylinder and the volume of the greasepaint covered was noted. The bulk viscosity was determined by the formula.

$$\mathbf{Db} = \frac{M}{Vo}$$

Where, **M** is the mass of powder, **V0** is the bulk volume of the powder

Tapped density

Tapped viscosity was determined by subjugating the cylinder containing bulk mass of greasepaint to 100 tapings placing it on bulk viscosity outfit. The tapping was done from a height of 10 cm every 2 seconds interval. also the volume of the greasepaint was noted and tapped viscosity was calculated from the formula.

$$\mathbf{DT} = M/Vt$$

Where, **M** is the mass of powder, **Vt**is the tapped volume of the powder

POST COMPRESSION PARAMETERS FOR EVALUATION

Weight variation test

Weight variation of tablets was determined by taking 20 tablets from each expression and importing them collectively on importing balance. The average weight of tablets and the total weight were calculated, and also weight variation was determined.

$$\%\text{weight variation} = \frac{\text{Average weight}}{\text{total weight}} \times 100$$

Thickness :

Aimlessly 10 tablets were taken from each expression and their consistence was measured using a digital micrometer(Mitutoyo Corp, Kawasaki, Japan). Average consistence and standard divagation values were calculated. The tablet consistence should be controlled within a ± 5 variation of standard value.

Tablet hardness

The contraction force of the punch with which the tablet is compressed imparts hardness to the tablet. It was tested by Monsanto or Pfizer hardness tester and expressed in kg/ cm2. Hardness influences the decomposition time of tablet. Generally, a minimal hardness of 2.5 kg/ cm2 is considered respectable for uncoated tablets. The hardness for FDTs should be rather 2.5 to 3 kg/ cm2.

Tablet Frability:

Tablet with unit mass equal to or lower than 650 mg requires a sample of tablets original to 6.5 g to conduct the test. Tablets are precisely dedusted previous to testing and directly counted before placing in the barrel. This weight was taken as W1. The barrel was rotated 100times and the tablets were removed. Any loose dust from the tablets was removed and was counted again directly. This was taken as final weight W2. The frangibility of the tablets can be caluculated from the formula

$$\%\text{Friability} = \frac{W1 - W2}{W1} \times 100$$

Where, W1= Weight of tablet before test, W2 = Weight of tablet after test. The weight loss of the tablets after friability test should not be more than 1%.

Drug content uniformity:

From each batch of the expression, 10 tablets were collected aimlessly and powered using a mortar and pestle. A volume of the greasepaint fellow to the weight of one tablet(300 mg medicine) was transferred to a 100 ml volumetric beaker. To this, about 50 ml of distilled water was added and subordinated to sonication for 15 twinkles. The volume was also made up to 100 ml with the same result. This result was suitably adulterated using distilled water to get a attention between 5µg/ ml to 25µg/ ml. These results are also anatomized by UV spectrometer as per the estimation graph system by recording the absorbance at 222.6 nm.

In- vitro Disintegration studies

In vitro medicine release of the samples was carried out using USP – type II dissolution outfit(paddle type). The dissolution medium, 900 ml 0.1 N HCl result, was placed into the dissolution beaker maintaining the temperature of 37 0.5 oC and rpm of 50. One pantoprazole tablet was placed in each paddle of dissolution outfit. The outfit was allowed to run for 12hours. Samples measuring 1 ml were withdrawn at regular intervals up to 12 hours using 1 ml hype**.** The fresh dissolution medium(37oC) was replaced every time with the same volume(1 ml) of dissolution medium. Collected samples were suitably adulterated with 0.1 N HCl and anatomized at 222.6 nm using 0.1 N HCl as blank. The accretive chance medicine release was calculated.

Result and Discussion

Preparation of Standard graph for Pantoprazole using 0.1 M Hydrochloric acid ***Determination of absorption maxima (λ max) in 0.1 M Hydrochloric acid***

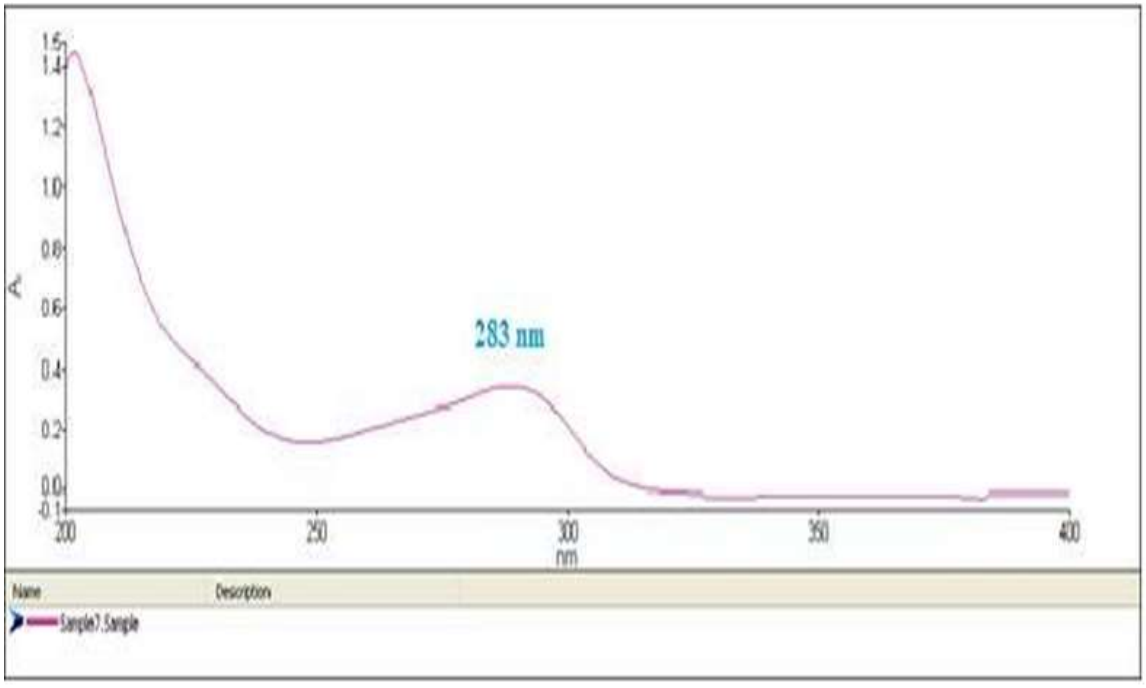


Fig : Absorption maxima of pantoprazole in 0.1 M Hydrochloric Acid

Table : Calibration Curve of Pantoprazole in 0.1 M Hydrochloric acid:

Concentration (µg/ml)	Absorbance (nm)
2	0.057
4	0.089
6	0.112
8	0.139
10	0.174
12	0.197
14	0.231
16	0.261
18	0.306
20	0.327

Fig : Calibration curve of Pantoprazole in pH 1.2 Hydrochloric Acid Buffer

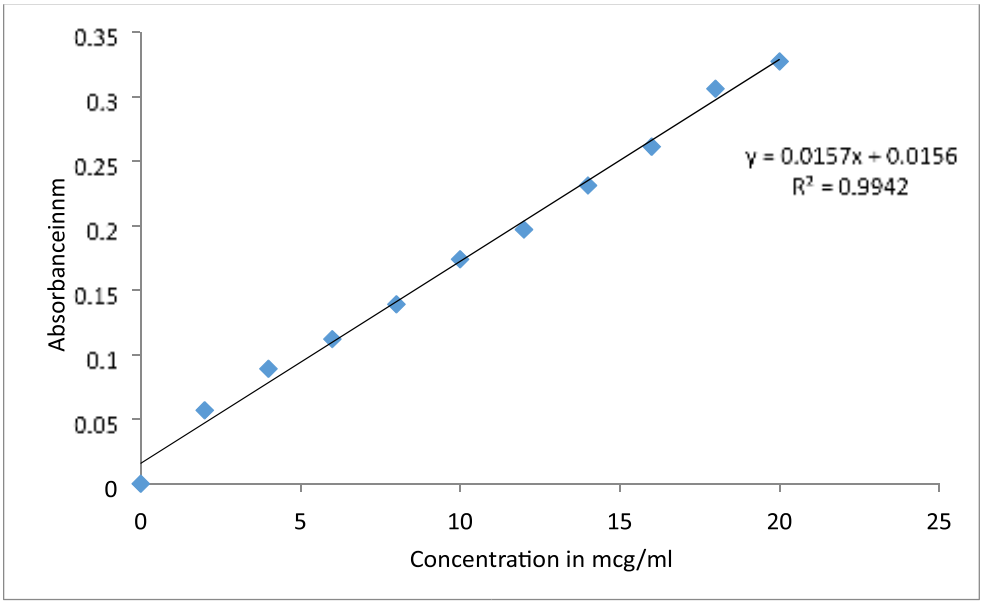
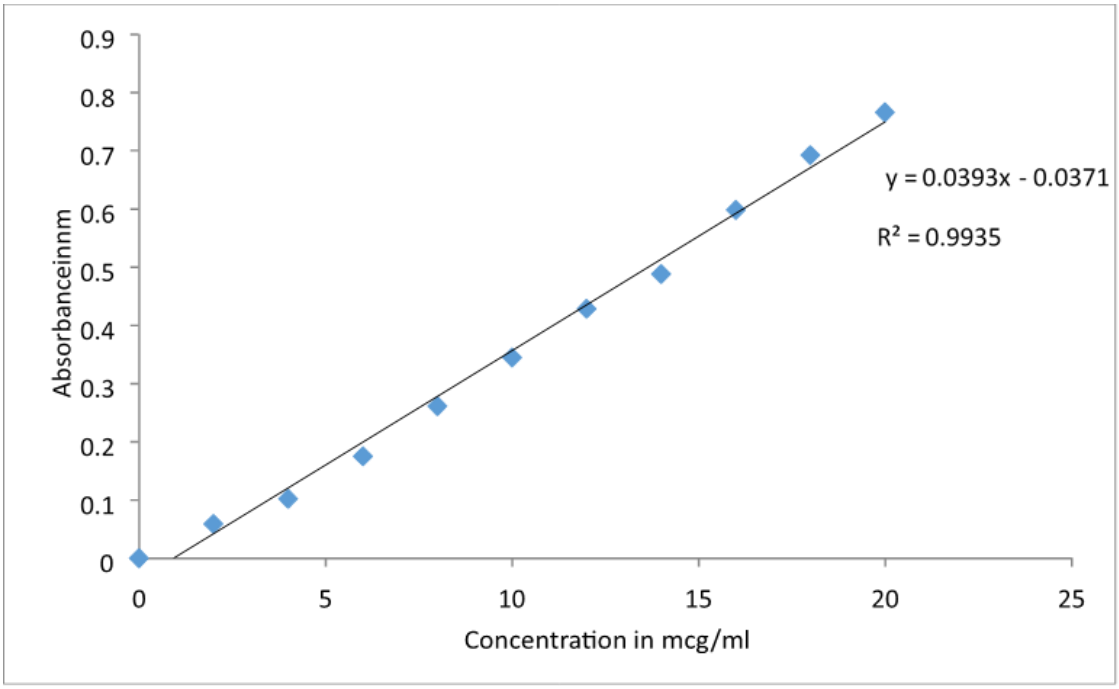


Table : Calibration Curve of Pantoprazole in pH 6.8 phosphate buffer

Concentration (µg/ml)	**Absorbance (nm)**
2	**0.059**
4	**0.1019**
6	**0.1752**
8	**0.2615**
10	**0.3447**
12	**0.4281**
14	**0.4886**

16	**0.5985**
18	**0.6925**
20	**0.766**

Fig : Calibration Curve of Pantoprazole in pH 6.8 phosphate buffer



PREFORMULATION STUDIES:

- **Solubility of Pantoprazole:**

Table : The solubility of Pantoprazole in water and phosphate buffer pH 6.8 25 ºC and 37 ºC at the end of 24 hrs

Media	**Solubility (µg/ml)**	
	25 ºC	**37 ºC**
Water	38.47 ± 0.413	39. 29 ± 0.026
Phosphate buffer pH 6.8	49.16 ± 8.259	52.69 ± 1.26s

- **Organoleptic properties:**

Table: Organoleptic properties of Pantoprazole

Organoleptic Test	**specification/limits**	**Observations**
Colour	white to off white powder	Off white crystalline powder
Taste	Bitter	Bitter
Odour	Almost odourless	odourless blend

- **Physical characters:**

Table : Physical characteristics of Pantoprazole

Test	**specification/limits**	**Observations**
Loss on drying	4% - 6%	5.2%
Melting point	139 -140 ºC	148 ºC
pH	9.0 and 11.5.	9.82

CONCLUSION

Series oftrials were performed during pre-expression studies to elect suitable excipient. Combination of different excipient were used to formulate pantoprazole enteric carpeted tablet. Colorful chance of the excipient was also used to get stylish phrasings with high bioavailability. Evaluation trials similar as frangibility, hardness, content uniformity, consistence, weight variation, decomposition time were carried out and set up that the results were satisfactory. Dissolution system was developed and validated. Dissolution of three batches of pantaparazole enteric carpeted tablet were carried out and set up that RSD (Relative standard divagation) is below 2 including good reproducibility from batch to batch. Results of evaluation trials were compared with retailed expression.

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