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# Aqueous Enteric Coating of Hpmc-Ason Pantprazole Sodium Tablets

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**ABSTRACT**
Pantoprazole sodium is an antiulcer drug of proton pump inhibitor category. Pantoprazole is acid-labile in nature, so enteric coating is necessary to protect the active drug from the acidic atmosphere of stomach. The purpose of the research work presented in this thesis was to optimize the enteric coating of HPMC-AS on pantoprazole sodium tablet by aqueous process.
Uncoated tablets of pantoprazole sodium were formulated by wet granulation process. Various in process quality control test for granulation and uncoated tablets were determined. The tablet was seal coated with the help of HPMC E5 for 2% w/w weight gain. Subsequently seal coated tablets were further enteric coated by aqueous process using polymer HPMC-AS for weight gain of 10, 12, 14, 16 and 18 %) and designated as formulations F1, F2, F3, F4 and F5 respectively.
All the formulations (F1, F2, F3, F4, and F5) was evaluated for content of medicine (assay), disintegration & in-vitro dissolution test in 0.1 N hcl for 2 hr and phosphate buffer for 45 minutes. Formulation F4 released less than 5% w/w drug release in acid media and more than 80% in buffer media and was considered best that fulfill the acceptance standards for drug release.
**Keywords-** Pentaprazole sodium, Proton Pump Inhibitor, UV spectroscopy, Dissolution, Disintegration, Friability.

## I. INTRODUCTION

The parietal cell of stomach secreted hydrochloric acid (HCL). The excess release of HCL in the stomach can cause gastrointestinal reflux disease (GERD). The primary symptom of GERD include – damage of esophageal mucosa, heartburn, acid regurgitation etc. (Gobinath T, et al., 2014).

Proton pump inhibitors (PPI) are most use full drugs for the treatment of gastric ulcers and gastro- esophageal disease. This category of drugs includes pantoprazole, omeprazole, lansoprazole, rabeprazole, and esomeprazole. Proton pump inhibitor act by suppression of acid secretion of parietal cell. In the average dose of PPI products, normal acid (basal and stimulated) production is inhibited by 80 to 90 percent.

Pantoprazole is sulfonyl}-1H-1,3-benzodiazole 6-(difluoromethoxy)-2-{[(3,4-dimethoxypyridin-2yl) methane (Fig 1.1). Pantoprazole's bioavailability is significantly higher than omeprazole, remains constant after repeated administration, and is not impaired by food. Pantoprazole does not significantly influence hepatic cytochrome (Richter and Bochenek, 2000) and unlike other PPIs does not include multiple metabolic pathways (Garner and Fadlallah 1997). Pantoprazole is used to treat inflammation and ulceration of the esophagus due to esophageal reflux disease in the short term (Kumar et al., 2011). It accumulates in the acidic portion of the parietal cell and is changed to the active form, a sulfanilamide that binds the secretory surface of gastric parietal cells to hydrogen potassium ATPase. Hydrogen-potassium inhibition ATPase blocks final step in the synthesis of gastric acid, resulting inhibition of both basal and induced acid secretion (Devi et al., 2010 and Patel et al., 2012).

The length of the acid excretion inhibition does not correspond with the much smaller removal of PTZ Thiophilic sulfonamide cations half-life.
The gastric proton pump inhibitors have structural resemblance to H2 antagonist. They are the pro-drugs and after absorption get converted to reactive Thiophilic sulfonamide cations. The Sulfonamide reacts with the H+/K+ ATP-ase, forming a covalent, disulfide bond, thereby inactivating the

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enzyme irreversibly (Kalaichelvi et al., 2010 and Pimpodkar et al, 2009).

**Fig.1.1** Chemical structure of pantoprazole sodium

PPIs are unstable gastric fluid and therefore are formulated as enteric coated tablet. The enteric coating is a membrane that governs the oral placement of oral drugs in the gastrointestinal system where they are absorbed. The enteric means small intestine; thus enteric coating stops medicine from being released before it enters the small intestine. The enteric coated polymer remains unionized at short pH, and thus remains unsolvable, but the pH in GIT increases, the acidic feature that can ionize and polymer swells or becomes soluble in intestinal fluid. Enteric coatings polymers include HPMC-AS, CAP, HPMCP, CAT, and PVAP (Singh Deep Hussan et al., 2012).

**Drug Profile**

**Name of drug:** Pantoprazole sodium

**Chemical formula**:

$C_{16}H_{14}F_2N_3NaO_4S$

**Molecular weight**: 405.33g/mol

**Melting point:** 151-155ºc

**Colour:** Yellowish color

**Solubility**: Pantoprazole sodium easily soluble in phosphate buffer (pH 7.4) and water.

**Pharmacokinetic of pantoprazole sodium**

**Absorption:** An absolute bioavailability of pantoprazole sodium is approximately is 77 percent. The absorption of pantoprazole is not affected by antacids.

**Distribution:** Distribution of pantoprazole sodium is near about 11.0 - 23.6 L, mainly in extracellular fluid.

**Metabolism:** It metabolized into the liver by CYTOCHROME P450 (CYP) system.

**Excretion:** It is approximately 81% of dose excreted in the urine and 18% excreted in feces through biliary excretion.

**Protein binding:** Protein binding of pantoprazole is found 98%

**Half-life:** The half-life of pantoprazole sodium is 7.5-14.02/h.

**Mechanism of action**

Pantoprazole sodium is a PPI that inhibits excretion of gastric acid from parietal cell of stomach. It covalently binds to ($H^+/K^+$) ATPase enzyme system. The binding of pantoprazole with $H^+/K^+$-ATPase results in anti-secretory effect of gastric acid. Pantoprazole sodium finally suppresses or stops the emission of HCl from parietal cell of stomach.

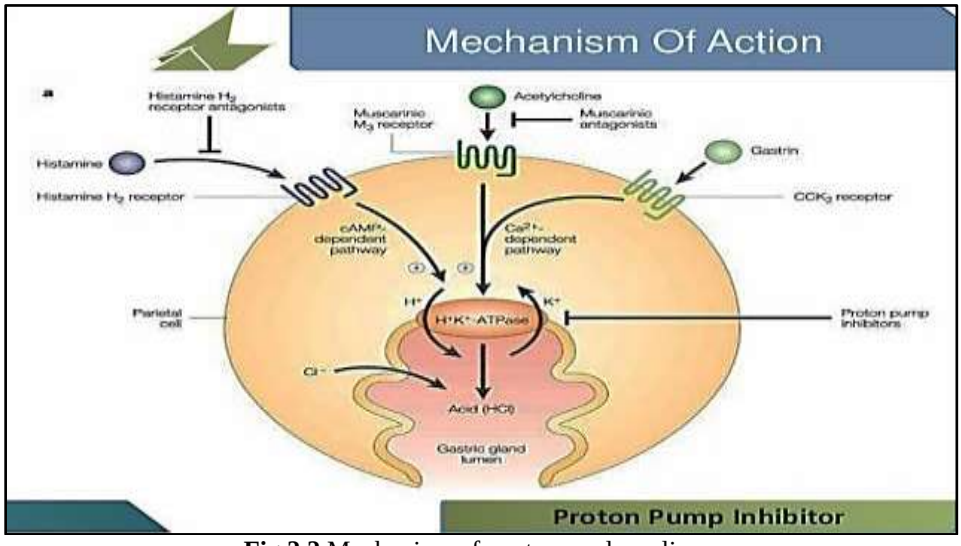


**Fig 2.2** Mechanism of pantoprazole sodium

**Side effects of pantoprazole sodium**

Headache, Diarrhea, Flatulence, Rash, Stomach Pain, Eructation, Insomnia, Hyperglycemia, Sickness, and Vomiting etc.

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**Various Marketed Formulation of Pantoprazole Sodium**

Various formulations of pantoprazole sodium are available in the market (Table 2.1).

**Table 2.1** Different types of formulation given in table with brand name.

| Brand name | Manufacturer | Dose | Routes |
|---|---|---|---|
| Aciban | Cadila Pharmaceutical | 20 mg | Oral |
| Asoprazole | As Pharmaceutical ltd | 40 mg | Oral |
| Lupipan | Lupin Laboratories | 20 mg | Oral |
| Nexpan | Zuventus Healthcare | 40 mg | Oral |
| Nupenta | Macleods pharmaceutical | 40 mg | Oral |
| Nixopan | Phoenix Pharmaceutical | 40 mg | Oral |
| Pamtrazole | Modi Mundipharma | 20 mg | Oral |
| Pan 20 | Alkem laboratories | 20 mg | Oral |
| Pantakind | Mankind pharma | 40 mg | Oral |
| Penta | Intra labs | 20 mg | Oral |
| Zovanta | Dr. Reddy's laboratories | 40 mg | Oral |

**Enteric coating**

Enteric coating is a membrane that controls the release of drug into the stomach, enteric coating protects the acid labile drug from gastric juice (HCL). Enteric coating tablet are swell in stomach pH but release of drug not found in stomach, but when enteric coated tablet reached into the upper part of small intestine tablet dissolved and release the drug in basic pH. There is different type of enteric coating polymer, which is used in enteric coating.

There are following causes of enteric coating,

Enteric coating protected drug release into the stomach and prevents disintegration into the gastric juice.

- Enteric coating prevents the nausea or vomiting caused by drug incompatibility.
- Enteric coating also protected the HCL labile drugs

**Polymer used as enteric coating**

There are following types of polymers used in enteric coating

- Cellulose acetate phthalate (CAP)
- HPMC-AS (Hydroxy propyl methyl cellulose acetate succinate)
- HPMCP (Hydroxy propyl methyl cellulose phthalate)
- Methyl acrylate-methacrylic acid polymers
- Polyvinyl acetate phthalate (PVAP)

**HPMC-AS (Hydroxypropyl methyl cellulose acetate succinate)**

**Trade name:** Shin-Etsu AQOAT

**Chemical Name:** Cellulose 2-hydroxypropyl methyl ether acetate hydrogen butane diate.

**Molecular Weight:** 5500-9300Da

The first approval of HPMC-AS polymer as an enteric coating polymer was given by the japan in 1987. After that in 2001 all European countries found the approval of HPMC-AS as an enteric coating polymer.

HPMC-AS is a combination of acetic acid & mono-succinic acid it is white colour powder or granules. HPMC-AS is insoluble in gastric juice but swell in this pH. When HPMC-AS reached in upper part of small intestine, its dissolved very fast. The enteric coating of HPMC-AS remains stable to the drug in gastric pH and protected the degradation of drug in the stomach. If acid labile drug released in the stomach it cannot produce the therapeutic effect.

**Grade of HPMC-AS polymer**

HPMC-AS obtained in the following types of grade which are pH dependent.

**L-grade HPMC-AS**

L-grade of HPMC-AS is combination of high ratio of succinyl substitution to acetyl substitution(S/A).

L-grade HPMC-AS is dissolve at pH≥ 5.5

**M-grade HPMC-AS**

M-grade of HPMC-AS is combination of medium ratio of the S/A.

M-grade is dissolve at the pH ≥ 6.0

**H-grade HPMC-AS**

H-grade 0f HPMC-AS is combination of low ratio of S/A.

This is also dissolve at pH ≥6.8.

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**Table 2.3** Composition of HPMC-AS polymer

| Substituents/groups | Composition of HPMC-AS polymer | | |
|---|---|---|---|
| | L- grades | M-grades | H-grades |
| **Hydroxypropyl** | 5.0 - 9.0 | 5.0 - 9.0 | 6.0 - 10.0 |
| **Methoxyl** | 20.0 - 40.0 | 21.0 - 25.0 | 22.0 - 26.0 |
| **Acetyl** | 5.0 - 9.0 | 7.0 - 11.0 | 10.0 - 14.0 |
| **Succinoyl** | 14.0 - 18.0 | 10.0 - 14.0 | 4.0 - 8.0 |

## II. OBJECTIVES

1. Formulation and development of enteric coated pantoprazole sodium tablet.
2. Optimization of enteric of HPMC-AS on pantoprazole sodium.
3. Evaluation and characterization of enteric coated tablets pantoprazole sodium.

**RATIONALE**

Proton pump inhibitors are used from the many years for treatment of GERD. Pantoprazole is a pump inhibitor that is used since a long time for treatment of GERD patient suffering from ulcer and hyper acidosis. In this study the enteric coating of HPMC-AS on pantoprazole provide stability in the acidic medium. This polymer swells properly in stomach but not released drug in acidic pH.

The approach of the study will be to enhance the stability of pantoprazole after administration into stomach. When drug comes in contact of acid then it degraded in stomach. So prevention of degradation will be stops by use of enteric coating polymer.

## III. MATERIAL AND METHODOLOGY

**Drug and Chemicals**

Pantoprazole sodium, Sodium carbonate, Talc, Cross-povidone,,Polyvinylpyrrolidone K90 (PVP K-90), Magnesium stearate, Lactose, Hydroxypropylmethyl cellulose E5 (HPMC-E5), Isopropyl alcohol (IPA), Dichloromethane (DCM), Hydroxypropylmethyl cellulose acetate succinate (HPMC-AS, Grade HF), Monoethanol amine, Triethyl citrate, Ammonia solution, Sodium lauryl sulfate, Potassium-dihydrogen phosphate, Sodium hydroxide pallets, Hydrochloric acid (HCl)

**Instruments**

UV visible spectrophotometer, Pharma R & D coater, Moisture analyzer balance, Tap density tester, Magnetic s3tirrer, pH meter, Micropipette, Punching machine, Hardness tester, Tray dryer, Friability tester, Dissolution apparatus, Electromagnetic sieve, Homogenizer, Vernier calipers, Electronic balance.

**Drug Identification**

**UV spectrophotometry**

Pantoprazole sodium was identified by UV visible spectrophotometry; a working standard solution of pantoprazole sodium was prepared in buffer solution and scanned for UV absorption within range of 200–400 nm. The wave-length of maximum absorbance ($\lambda_{max}$) of drug was determined and compared with reported $\lambda_{max}$ given in literature.

**Analytical Method Development**

**Determination of $\lambda_{max}$ of pantoprazole sodium**

1mg/ml concentration of pantoprazole sodium was prepared in buffer solution and was further diluted to obtain sample of 10µg/ml concentration. The sample was then scanned in UV spectrophotometry within wavelength 200–400 nm against buffer as reference blank and wavelength of maximum absorbance ($\lambda_{max}$) of drug was determined.

**Calibration curve**

**Preparation of standard stock solution**

Pantoprazole sodium (100mg) was weighed into 100 ml volumetric flask. 25ml buffer solution was added and vortex mixed. When drug was dissolved, volume was made to 100ml to obtain 1mg/ml concentration of pantoprazole sodium.

**Preparation of working stock solution**

10 ml standard stock solution was

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withdrawn and transmitted into 100 ml volumetric flask. Volume was makeup 100 ml with buffer solution.

**Preparation of calibration samples and validation samples**

The working stock solution was again diluted with buffer solution to obtain 5, 10, 15, 20, and 25 µg/ml solutions (calibration samples).

From the same working solution triplicate samples of 3 different concentrations at upper (24 µg/ml), middle (16 µg/ml) and, lower (6 µg/ml) concentration level of the calibration range were made by appropriately diluting the working stock solution with buffer solution.

**Preparation of calibration curve**

The absorbance values of calibration and validation samples were measured against buffer solution as a blank in UV visible spectrophotometer at the $\lambda_{max}$ (292 nm) of pantoprazole sodium. After that obtained absorbance value was plotted against their respective concentration and least square linear regression was used to obtain the calibration equation.

**Validation of analytical method**

**Linearity**

The obtained value of calibration samples was plotted against their respective concentration to obtain the calibration curve and linear regression coefficient and correlation coefficients were calculated.

**Accuracy**

Concentration values for three sets of validation samples at lower, middle and upper concentration was computed by putting the respective absorbance value in calibration curve equation. Then mean concentration value of three set of validation sample was calculated. Accuracy of the concentration value was computed using the following formula.

$$\% \text{ BIAS} = \frac{\left(\text{calculated mean concentration} - \text{actual concentration}\right)}{\text{actual concentration}} \times 100$$

**Precision**

For each set of validation sample, standard deviation of calculated concentration value was calculated. The precision of each concentration of validation sample was further computed in terms of percentage relative standard deviation (%RSD) using following formula.

$$\% \text{ RSD} = \frac{\text{standard deviation}}{\text{calculated mean concentration}} \times 100$$

**Formulation of Enteric Coated Pantoprazole Sodium Tablets**

**Preparation of Granules**

Pantoprazole sodium (40 mg), sodium carbonate (8.86 mg), lactose (37.87 mg), cross-povidone (44.35 mg), PVP K-90 (3.54mg), magnesium stearate (2.83 mg) were passed through # 40 sieve and all the ingredients except PVP K-90 and magnesium stearate were mixed. Binder solution PVP-90 was prepared in IPA, then prepared solution of PVP-90 was added in above mixed powder and wet mass was prepared. The wet mass was passed through #20 sieve to make the granules. The prepared wet granules were dried at 50 °C in hot air oven for approximately 50 minute, until the LOD as determined by moisture balance was not less than 2% w/w. Magnesium stearate was mixed with the dry granules.

**Evaluation of granules**

**Angle of repose**

It is a qualitative technique for determination of flow property of powder. The angle of repose was determined by use of funnel. The granules were kept in funnel and allowed to freely pass through the orifice of funnel and make the pile of granules. The height (h) and diameter (2r) of granule cone was measured. Angle of repose was calculated using following method.

$$\theta = \tan^{-1}(h/r)$$

'h' is height and 'r' is radius of powder cone.

**Bulk density (BD)**

It was measured by pouring a blend of granules into a measuring cylinder. The volume covered by granules was measured by fallowing method.

$$\text{Bulk density} = \frac{\text{weight of granules}}{\text{untapped volume of granules}}$$

**Tapped density (TD)**

The pre-weighed mass of blend granules was poured in a graduated measuring cylinder and the cylinder was tapped on a tapped density apparatus, the lowest volume occupied in measuring cylinder was measured. The tapped density was considered by fallowing formula.

$$\text{Tapped density} = \frac{\text{weight of granules}}{\text{tapped volume of granules}}$$

**Compressibility index**

The compressibility index of granules was determined by use of following formula

$$\text{Carr's index (\%)} = \frac{\{(\text{TD} - \text{BD}) \times 100\}}{\text{TD}}$$

**Hausner's ratio**

Percentage of tapped density and bulk density of the powder is identified as Hausner's ratio. It is calculated by fallowing method

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$$\text{Hausner's ratio} = \frac{\text{tapped density}}{\text{bulk density}}$$

**Compression of uncoated tablets**

The granules were compacted into core tablets using 6 mm biconvex circular punch using tablet punching machine. The weight of single tablet was equivalent to 40 mg of pantoprazole (134 -145 mg).

**Tablet coating**

**Sub coating of prepared core tablets**

The optimized process parameters maintained during sub-coating, and formulation of sub-coating solution for 100 g are given in table 4.3 and 4.4.

**Table 4.3** Optimized parameter of sub-coating

| Coating parameter | Values | Coating parameter | Values |
|---|---|---|---|
| Inlet temperature | 50 °C | Pan RPM | 37 |
| Bed temperature | 47 °C | Gun to bed distance | 5 cm |
| Spray feed RPM | 2 | Atomizing air | 1.5 PSI |

**Table 4.4** Amount of ingredients for sub-coating solution

| Ingredient | Amount (in g) |
|---|---|
| HPMC-E5 | 5 |
| IPA | 57 |
| Dichloromethane | 38 |

In the sub-coating HPMC-E5 was used as sub-coating polymer. IPA and dichloromethane were mixed into a beaker and kept on a magnetic stirrer with continuous stirring. The accurately weighed amount of HPMC-E5 was added to mixed solvents with continuous stirring until a homogenous solution of polymer was formed. The sub-coating was done by spraying above solution on the tablet core of pantoprazole sodium tablet in a pan type coating machine.

**Enteric coating of the sub-coated pantoprazole sodium tablets**

The optimized process parameters maintained at time of enteric coating of sub-coated tablets and formulation of enteric coating solution (100 g) are shown in table 4.5 and 4.6.

**Table 4.5** Optimized required parameter of enteric coating.

| Coating parameter | Values | Coating parameter |
|---|---|---|
| Inlet temperature | 65 °C | Pan RPM |
| Bed temperature | 55-65 °C | Gun to bed distance |
| Spray feed RPM | 1 | Atomizing air |

All the required materials used in preparation of enteric coating solution, for the 80 g batch of tablet of pantoprazole sodium are shown in table.

**Table 4.6** Formula of enteric coating solution required for 80 g batch.

| Ingredient | Amount (in g) |
|---|---|
| HPMS-AS | 26 |
| Monoehanolamine | 1.53 |
| NH4OH | 0.945 |

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| | |
|---|---|
| Triethyl citrate | 6.66 |
| SLS | 0.73 |
| Talc | 9.0 |
| Water | 255 |

Water was continuous stirred on a magnetic stirrer and HPMC-AS was dispersed until dissolved completely. Subsequently all other materials were added, dispersion was passed through #50 sieve. The enteric coating was done by spraying the above prepared solution on the sub-coated tablet of pantoprazole sodium in a pan type coating machine. Coating was done till the desired percentage weight gain was achieved. Twenty tablets were periodically withdrawn from the pan and weighed. And Percentage weight gain was computed by use of following formula.

$$\% \text{ wt. gain } = \frac{\text{wt. of 20 enteric coated tablets} - \text{wt. of 20 subcoated tablet}}{\text{wt. of 20 subcoated tablets}} \times 100$$

When the target weight gain was achieved, coating was stopped.

**Evaluation of Enteric Coated Tablets of Pantoprazole Sodium**

**Assay**

20 enteric coated tablets of a batch was weighed and crushed in mortar pestle. Powder equivalent to 40 mg of pantoprazole sodium was taken in a 100 ml of volumetric flask & approximately 40 ml of phosphate buffer was added, vortex mixed for 10 minute and volume was prepared to mark. Solution was filtered, suitably diluted with buffer and UV absorbance of diluted sample was determined at 292 nm. The concentration of diluted sample was calculated from calibration curve use of the absorbance value. The amount of pantoprazole sodium was determined by use of the following formula.

$$\text{Amount of Drug} = \text{Conc. of sample} \times \text{dilution factor}$$

**Thickness**

Twenty tablets was selected randomly from the prepared batch. And the thickness of tablets was determined by use of Vernier calipers and average thickness was calculated.

**Weight variation**

Twenty tablets were selected randomly from the prepared batch and usual weight of individual tablets was measured by electronic weighing balance. Average weight of 20 tablets was calculated.

**Hardness**

The hardness of enteric coated tablet was determined by Monsanto hardness tester. Ten tablets were selected from a batch and hardness of all ten tablets was measured.

**Friability test**

In the friability test twenty tablets were selected randomly and weighed. These selected tablets placed into friabilator and rotated for 4 minute at 25 rpm. Subsequently tablets were removed and clean with brush for any adherent powder and again weighed. Percentage weight loss (friability) was calculated.

$$\% \text{ friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

**Disintegration test**

The disintegration test of enteric coated tablets was carried out using disintegration test apparatus at 37 °C initially in 0.1 N HCl for 2 h solution and later in phosphate buffer for 45 minutes. Six enteric coated tablets from batch were kept in each tube of disintegration vessel and time for tablet disintegration was noted.

**In-vitro dissolution study**

The dissolution study of enteric coated tablet was performed for two hours in 0.1N HCl solution and subsequently for 45 minute in phosphate buffer pH 6.8. The dissolution test conditions are given in table 4.7.

**Table 4.7** Dissolution test conditions

| | |
|---|---|
| **Type of Apparatus** | Paddle Type |
| **Dissolution Media** | Acid Stage: 0.1 N HCl, 900 ml<br>Buffer Stage: Phosphate Buffer 6.8, 900 ml |
| **Temperature** | 37 ± 0.5 °C |
| **RPM** | Acid Stage: 50 rpm<br>Buffer Stage: 75 rpm |
| **Test Duration** | Acid Stage: 2 h |

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Buffer Stage: 45 minutes

## IV. RESULTS AND DISCUSSION

**Drug Identification**

**UV Spectrophotometry**

$\lambda_{max}$ of pantoprazole sodium was found to be 292nm and was similar to literature reported value.

**Analytical Method Development**

**Calibration of UV-visible spectroscopy method**

The calibration data record of pantoprazole sodium in buffer solution as obtained by the UV-visible spectroscopy at the 292nm are shown in table

**Table 5.1** Absorption data of calibration samples

| Concentration (µg/ml) | Absorbance |
|---|---|
| 5 | 0.249 |
| 10 | 0.353 |
| 15 | 0.468 |
| 20 | 0.587 |
| 25 | 0.702 |

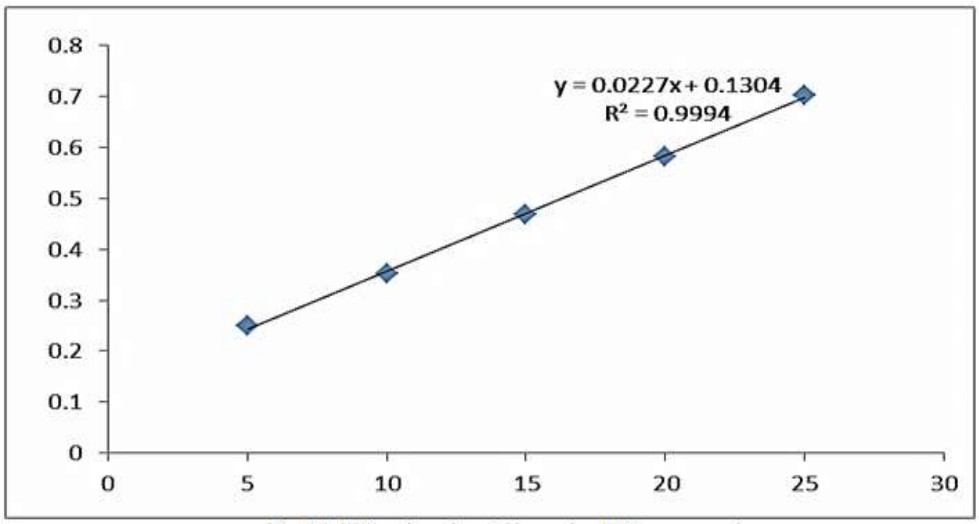


**Fig 5.1** Calibration plot of absorption V/S concentration

**Validation of UV analytical method**

**Linearity range**

The value of correlation (r) was found to be 0.9994 at the concentration range 5, 10, 15, 20, and 25µg/ml that shows linear relationship between absorbance and concentration. The sample range for this method was 5-25 µg/ml.

**Accuracy and precision**

The accuracy (% bias) and precision (% RSD) of validation samples for the intraday and interday was studied and is described in the table 5.3 and 5.2. Both the % error and % RSD were within the acceptable range of 2%.

**Table 5.2 Intraday accuracy (% error) and precision (% RSD) data of validation sample (λmax 292nm)**

| | Concentration (µg/ml) | | |
|---|---|---|---|
| | **6** | **16** | **24** |
| **Day-1 calculated conc. mean(µg/ml)** | 6.022 | 15.708 | 24.541 |
| **% BIAS** | 0.382 | 1.822 | 2.256 |
| **% RSD** | 0.732 | 0.429 | 0.180 |

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| | | | | |
|---|---|---|---|---|
| **Day-2 calculated conc. mean(µg/ml)** | 5.949 | 15.650 | 24.453 |
| **% BIAS** | 0.843 | 2.247 | 1.889 |
| **% RSD** | 1.543 | 0.430 | 0.361 |
| **Day-3 calculated conc. mean(µg/ml)** | 5.979 | 15.650 | 24.350 |
| **% BIAS** | 0.353 | 2.190 | 1.456 |
| **% RSD** | 1.475 | 0.586 | 0.276 |

**Table 5.3 Interday accuracy (% error) and precision (% RSD) data of validation sample (λmax 292nm)**

| Conc. (µg/ml) | Calculated Mean Conc. (µg/ml) | | | Mean Conc. (µg/ml) | % BIAS | % RSD |
|---|---|---|---|---|---|---|
| | **Day-1** | **Day-2** | **Day-3** | | | |
| **6** | 5.979 | 5.949 | 6.023 | 5.983 | 0.271 | 1.533 |
| **16** | 15.650 | 15.650 | 15.708 | 15.669 | 2.064 | 0.430 |
| **24** | 24.350 | 24.453 | 24.541 | 24.448 | 1.833 | 0.361 |

**Evaluation Studies of Granules of pantoprazole sodium.**

In process quality control parameters namely angle of repose, bulk density, tapped density, Hausner's ratio, and compressibility index for granules is listed in table 5.4.

**Table 5.4** Evaluation parameter of granules of pantoprazole sodium.

| Parameter | Value |
|---|---|
| Angle of repose | 27.98 (good flow) |
| Bulk density | 0.65 gm/ml |
| Tapped density | 0.76 gm/ml |
| Hausner's ratio | 1.26 (passable flow) |
| Compressibility index | 23.92 (passable flow) |

**Evaluation of Uncoated and Seal Coated Tablets**

Thickness, hardness, diameter, weight of uncoated and seal coated pantoprazole sodium tablet was determined which are given in the table 5.5.

**Table 5.5** Evaluation parameter of uncoated and seal coated tablets

| Tablet | Mean thickness (mm) | Mean hardness (Kg/cm2) | Mean diameter (mm) | Weight (mg) | Friability |
|---|---|---|---|---|---|
| Uncoated | 4.63 | 4±0.4 | 5.4±4.3 | 138±2.1 | 0.052% |
| Seal coated | 4.66 | 5±0.1 | 5.7±2.7 | 141±3.14 | 0.010% |

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**Evaluation of Enteric Coated Tablets**

Thickness, hardness, diameter, weight of 5 batches (F1, F2, F3, F4, F5) of enteric coated pantoprazole sodium tablet was determined which are shown in the table 5.6

**Table 5.6** Physical parameter of enteric coated pantoprazole sodium tablets

| Formulation | Mean thickness (mm) | Mean hardness (Kg/cm2) | Mean diameter (mm) | Weight (mg) |
|---|---|---|---|---|
| F1 | 4.78 | 4±0.2 | 5.5±2.1 | 155 ±2.9 |
| F2 | 5.08 | 4±0.4 | 5±3.8 | 158± 3.5 |
| F3 | 5.11 | 4±0.5 | 5±2.8 | 160.9 ± 3.1 |
| F4 | 5.20 | 5±0.1 | 5±4.9 | 164±2.6 |
| F5 | 5.28 | 4±0.5 | 5±6.1 | 166.8 ±3.4 |

**Disintegration time of tablets**

The disintegration time of six tablets of each batch was determined by disintegration test apparatus at the 37 °C in 0.1 N HCl and phosphate buffer. The disintegration time of uncoated, seal coated and enteric coated (F1, F2, F3, F4 and F5) are given in table 5.7.

**Table 5.7** Disintegration time of uncoated, seal coated and enteric coated tablets

| Formulation | Time (min) in acidic medium | Time (min) in buffer Medium | Result |
|---|---|---|---|
| Uncoated | 4 | - | Fail |
| Seal coated | 7 | - | Fail |
| F1 (Enteric coated) | - | 6 | Pass |
| F2 (Enteric coated) | - | 6 | Pass |
| F3 (Enteric coated) | - | 7 | Pass |
| F4 (Enteric coated) | - | 7 | Pass |
| F5 (Enteric coated) | - | 7 | Pass |

**Dissolution test**

The dissolution test of enteric coated tablet of pantoprazole sodium was performed by use of USP dissolution apparatus type 2 (paddle) in acid and buffer. The percentage of drug release in both media is given into the table 5.8.

**Table 5.8** Percent (%) drug release of different batches

| Dissolution Media and Test Duration | % of Drug Release | | | |
|---|---|---|---|---|
| | F1 | F2 | F3 | F4 F5 |

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| | | | | |
|---|---|---|---|---|
| **In 0.1N HCl, 2h** | 17.32±0.45 | 8.99±0.12 | 3.22±0.24 | 2.04±0.19 |
| | 2.83±0.14 | | | |
| **Phosphate buffer pH 7.4, 45 minutes** | 36.47±1.14 | 53.68±1.22 | 59.26±1.2 | 87.26±1.54 |
| | 68.23±1.16 | | | |

## V. CONCLUSION

Pantoprazole sodium tablets were seal coated (2 % w/w weight gain) with HPMC E5 and subsequently enteric coated with polymer HPMC-AS for weight gain of 10%, 12%, 14%, 16% and 18% by aqueous process. Tablet formulations were evaluated for in vitro disintegration & dissolution tests. Tablet formulation with 16% w/w weight gain gave best drug release among all with less than 5% drug release within two hours in acidic medium and more than 80% drug release within 45 minute in basic medium.

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