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# Formulation and evaluation of enteric coated tablets of Pantoprazole

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## ABSTRACT

Pantoprazole is a proton pump inhibitor, belongs to group of benzimidazole, Pantoprazole sodium were prepared by direct compression method using different concentration of, microcrystalline cellulose as filler, mannitol and dicalcium phosphate as diluents, crosscarmellose sodium as disintegrating agents, magnesium stearate and talc was used as a glidant and lubricant respectively. Direct compression is economic compare to wet granulation since it requires fewer unit operations. This means less equipment, lower power consumption, less space, less time and less labour leading to reduced production cost of tablets. The prepared tablets were evaluated for hardness, weight variation, friability and drug content uniformity and it was found that the results comply with official standards. The prepared tablets were coated using enteric coating polymer such as cellulose acetate phthalate, Eudragit L100 and by dip coating method. The *in vitro* release was studied using acidic buffer pH 1.2 and phosphate buffer pH 6.8. Prepared all batch's C2F9 was found best, with hardness 5.60 ± 0.24 (Kg/cm2**)**, drug content 99.08 ± 0.35(%), disintegration time 7.02± 0.21(min), and percentage cumulative drug released which started after 120 min and reached 99.72 after 180 min. Stability studies indicated that the developed tablets were stable and retained their pharmaceutical properties at room temperature and 40 °C / 75% RH for a period of 3 month.

**Key words:** Pantoprazole, Direct compression, Proton pump inhibitor, Cellulose acetate phthalate, Eudragit L100

## INTRODUCTION

The tablet enteric coating is perhaps one of the oldest pharmaceutical processes still in existence. Enteric refers to the small intestine; therefore enteric coatings prevent release of medication before it reaches the small intestine. Enteric-coated dosage forms do not release the active ingredient until they have been transported down to the neutral reacting part of the small intestine; hence they offer the best possibilities for the protection of unstable drugs at low pH values. The modified enteric-coated Pantoprazole sodium formulation that provide immediate release in the small intestine and simultaneously provide sustained input of drugs that have an absorption window and at the same time may improve or maintain bioavailability of the formulation.The most potent suppressors of gastric acid secretion are inhibitors of the gastric H+, K+-ATPase (proton pump) (Nicole, 2010). In typical doses, these drugs diminish the daily production of acid (basal and stimulated) by 80% to 95%. Available PPI's for clinical use: Omeprazole, esomeprazole, lansoprazole, pantoprazole, rabeprazole.

The primary treatment goal patients with peptic ulcer and GERD are relief of symptoms, prevention of complications related to the disease and healing of ulceration. Pantoprazole is a substituted benzimidazole derivative that targets gastric acid proton pumps, the final common pathway for gastric acid secretion. The drug covalently binding to the proton pumps, causing prolonged inhibition of gastric acidsecretion (Richard, 2009). But the drug causes irritation to gastric mucosa which may lead to nausea and vomiting. The stability of pantoprazole is rapidly degrades in acid medium of the stomach, but has acceptable stability in alkaline conditions. Therefore, pantoprazole should be delivered into the intestine. Hence, formulation of pantoprazole as an enteric coated tablet may solve the stability problem of drug in the stomach and release the drug in the intestine.

The main objectives of the present study was To formulate and evaluate enteric coated tablets Pantoprazole sodium by direct compression method, Selection of suitable coating material to develop the dosage form,To overcome the drug degradation by the gastric enzymes as well as the acidic environment of the stomach.

## MATERIALS AND METHODS MATERIALS

Pantoprazole sodium (Signet Chemical Corporation), Mannitol (Signet Chemical Corporation) Croscarmellose sodium (SD Chemical Corporation), Micro crystalline cellulose (Cipla Pharma, Mumbai, India), Dicalcium phosphate (Fine Chem Industries, India), Magnesium stearate (Spectrochem Pvt Ltd. Mumbai), Talc (Spectrochem Pvt. Ltd. Mumbai) Eudragit L-100 (Sd fine Chem. Ltd., Mumbai, India), Cellulose acetate phthalate (SD Pharma, Mumbai, India).

**Preparation of pantoprazole sodium tablets:** An ideal mixture of granules were directly punched into tablets weighing about 200 mg containing 40 mg of pantoprazole sodium sesquihydrate, using rotary tablet compression machine (Riddhi 10 stn mini tablet press RDB4-10, Rimek, Ahmedabad, India), using 8 mm diameter concave punches. The different batches of pantoprazole tablets were collected and stored in air tight containers (Sumit, 2009; Anroop, 2010).

**Table.1.Composition of pantoprazole sodium enteric coated sodium tablets**

| Composition | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Pantoprazole sodium (mg) | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Croscarmellose sodium (mg) | 2 | 4 | 6 | 2 | 4 | 6 | 2 | 4 | 6 |
| Microcrystalline cellulose(mg) | 27 | 25 | 23 | 27 | 25 | 43 | 80 | 50 | 23 |
| Mannitol (mg) | 50 | 75 | 100 | 40 | 85 | 80 | 43 | 50 | 75 |
| Dicalcium phosphate (mg) | 75 | 50 | 25 | 85 | 40 | 25 | 75 | 50 | 50 |
| Talc (mg) | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Magnesium stearate (mg) | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Total weight (mg) | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |

**Coating of compressed pantoprazole sodium tablets:**

**Preparation of enteric coating solution:** The enteric coating solution was prepared by simple solution method. It was prepared by 6% w/w and 8% W/W of Eudragit L100 (E1 and E2) or cellulose acetate phthalate (C1 and C2) as an enteric polymer, PEG 1.5% w/w as plasticizer and acetone and isopropyl acetone was used as solvent. Diethyl phthalate was added and made up the volume with rest of the solvent mixture; this mixture was constantly stirred for 1h with paddle mechanical stirrer at the rate of 1000 rpm and the stirred coating solution was again filtered through muslin cloth, a coating solution was obtained (Neelam, 2011).

**Table.2.Composition of coating solution**

| Ingredients | Quantity (%) |
|---|---|
| Cellulose acetate phthalate/ Eudragit L100 | 6.0 / 8.0 |
| PEG | 1.5 |
| Acetone | 59.4 |

**Enteric coating of pantoprazole sodium compressed tablets by dipping method:** The compressed tablets were coated with enteric coating polymer (Eudragit L100 or cellulose acetate phthalate) solution by dipping method. Desired tablet coating continued the dipping and weight gain was achieved. The coated tablets were studied for its weight variation, thickness, uniformity of drug content and *in vitro* dissolution study (Senthil, 2010; Rupesh, 2010).

**Physicochemical evaluation of coating films:** The same polymer solution was used to prepare the polymeric films and was subjected for film thickness, film solubility.

The polymeric films were prepared by casting the acetone with PEG the polymer solution was poured on the glass plate. The film was dried for 24 h at room temperature under a special cover with reduced solvent evaporation to obtained smooth homogenous films. The dried films were cut in to $1cm^2$ area the prepared polymeric film was studied for film thickness, and film solubility (Martin, 2001; Liberman, 1991; Saffar, 2007). The thickness of dried films was determined by thickness Digital micrometer. The film solubility was studied with pH 1.2 and pH 6.8. The $1\times1$ $cm^2$ coating film was selected, weighed and transferred in a beaker containing 20 mL of specified pH medium, which was mixed in a magnetic stirrer for 1 h at 37 ± 1°C and finally film solubility was examined.

***In vitro* drug release studies:** USP dissolution apparatus type II (Electrolab TDT-08L, Mumbai,I ndia) was employed to study the *in vitro* drug release from various formulations prepared. The dissolution medium used was 900 mL of acidic buffer of pH 1.2 for 2 h and phosphate buffer of pH 6.8 for 1 hrs. The tablet was kept in to the basket. The temperature was maintained at 37 ± 0.5°C and the stirring rate was 100 rpm. Samples were withdrawn at regular time intervals and the same volume was replaced with fresh dissolution medium. The samples were measured by UV spectrophotometer at 283 nm (pH 1.2) and at 288 nm (pH 6.8) against a blank. The release studies were conducted in triplicate and the mean values were plotted versus time (Bozdag, 1999).

**Stability studies:** Stability studies were performed as per the ICH guidelines. Selected formulations of Pantoprazole sodium tablet were sealed in aluminum foil cover and stored at (40 ± 2 °C / 75 ± 5 % R.H) for a

period of 3 months. Samples from each formulation which are kept for examination were withdrawn at definite time intervals. The withdrawn samples were evaluated for physical appearance, hardness, drug content (Singh, 2009).

## RESULTS AND DISCUSSION

The prepared pantoprazole powder blend for tabletting was prepared by direct compression method. The prepared pantoprazole powder blend were evaluated angle of repose, bulk density, tapped density, Hausner's ratio and compressibility index as given on Table 3.

The bulk densities of the granules were found to be in the range of 0.306 ± 0.03 to 0.384. ± 0.04 gm/mL, while the tapped densities were ranged between 0.313 ± 0.04 to 0.429 ± 0.05 gm/mL. The flow characteristics of the granules were assessed by determining their angle of repose and Carr's Index. The values of compressibility (5.74 ± 0.13 to 10.48 ± 0.20%) signify good flowability. The angle of repose of all formulation was less than 30º (25.79 ± 0.24 to 29.52 ± 0.14) also indicate the good flowability of the prepared granules.

**Table.3.Pre compression parameters of pantoprazole sodium**

| Formulation Code | Parameter | | | | |
|---|---|---|---|---|---|
| | Bulk density (gm/mL) * | Tapped Density (gm/mL) * | Carr's Index (%)* | Hausner's ratio* | Angle of repose (Ɵ)* |
| F1 | 0.357±0.03 | 0.384±0.05 | 7.03±0.09 | 1.075±0.04 | 28.31±0.26 |
| F2 | 0.312±0.04 | 0.335±0.02 | 6.86±0.15 | 1.073±0.05 | 27.20±0.14 |
| F3 | 0.306±0.03 | 0.326±0.03 | 6.13±0.12 | 1.065±0.02 | 29.13±0.34 |
| F4 | 0.312±0.03 | 0.334±0.06 | 6.58±0.14 | 1.070±0.06 | 26.13±0.26 |
| F5 | 0.306±0.03 | 0.334±0.05 | 8.38±0.17 | 1.091±0.08 | 26.78±0.18 |
| F6 | 0.384±0.04 | 0.429±0.05 | 10.48±0.20 | 1.117±0.07 | 25.79±0.24 |
| F7 | 0.358±0.05 | 0.385±0.04 | 7.01±0.13 | 1.075±0.03 | 29.52±0.14 |
| F8 | 0.286±0.05 | 0.313±0.04 | 8.62±0.07 | 1.094±0.03 | 26.95 ±0.15 |
| F9 | 0.348±0.08 | 0.328±0.05 | 5.74±0.13 | 1.06±0.08 | 26.13±0.26 |

***Mean ± SD; n=3**

**Post compression parameters of pantoprazole sodium core tablet:** The pantoprazole tablets were prepared by direct compression method and were evaluated for their hardness, weight variation, content uniformity, friability and *in vitro* drug release (Table 4).

Hardness has to be controlled to ensure that the product is firm enough to withand handling without breaking or crumbling and not so hard that the disintegration time is unduly prolonged. The average hardness of the tablets to be in range was found within 4.93 ± 0.15 to 6.20 ± 0.35 Kg / cm2. Friability value which also affected by the hardness value of tablets should be in the range 1% limits, which is the usual friability range of tablets. The friability of the prepared tablets was found less than 1% w/w. The drug content uniformity of pantoprazole sodium present in tablets formulation ranged from 96.28 ± 0.15to 100.34 ± 0.13%. The average weight found 198 ± 0.15 to 206 ± 0.24 mg. Disintegration time varied between 11.48 ± 0.15 to 5.38 ± 0.23, hence all shows favorable result.

**Table.4.Post compression parameters of pantoprazole sodium core tablets**

| Formulation Code | Parameter | | | | |
|---|---|---|---|---|---|
| | Hardness ($Kg/cm^2$)* | Friability (%)* | Weight Variation (mg) * | Drug content (%)* | Disintegration Time (min) * |
| F1 | 5.80 ± 0.12 | 0.69 ± 0.015 | 199 ± 0.12 | 96.28 ± 0.15 | 10.6± 0.62 |
| F2 | 5.56 ± 0.24 | 0.51 ± 0.017 | 206 ± 0.24 | 97.62 ± 0.27 | 8.26± 0.56 |
| F3 | 5.83 ± 0.08 | 0.48 ± 0.014 | 201 ± 0.17 | 99.51 ± 0.36 | 5.38± 0.23 |
| F4 | 4.93 ± 0.15 | 0.64 ± 0.015 | 208 ± 0.20 | 98.17 ± 0.16 | 11.48± 0.15 |
| F5 | 5.73 ± 0.25 | 0.71 ± 0.016 | 203 ± 0.16 | 98.92 ± 0.42 | 9.32± 0.18 |
| F6 | 5.12 ± 0.34 | 0.68 ± 0.026 | 206 ± 0.14 | 100.34 ± 0.13 | 6.13± 0.25 |
| F7 | 5.66 ± 0.17 | 0.54 ± 0.026 | 199 ± 0.22 | 98.50 ± 0.48 | 10.54± 0.43 |
| F8 | 6.20 ± 0.35 | 0.49 ± 0.025 | 204 ± 0.18 | 98.41 ± 0.34 | 9.12± 0.71 |
| F9 | 5.60 ± 0.24 | 0.42 ± 0.018 | 198 ± 0.15 | 99.08 ± 0.35 | 6.02± 0.21 |

*** Mean ± SD, n=3**

**Physicochemical evaluation of coating films:** Physicochemical evaluation of cellulose acetate phthalate, Eudragit L100 and were studied for different parameters such as film thickness, film weight and film solubility. The enteric polymer cellulose acetate phthalate, Eudragit L100 were found to be completely soluble in pH6.8 and insoluble in pH1.2 (Table.5).

**Physicochemical evaluation of pantoprazole sodium enteric coated tablets:** The tablets which show most satisfactory result in disintegration, and drug content parameters (F3 and F9) coated by dip coating method. The results of physicochemical evaluation of prepared coated tablets are shown in **Table 6**. The weight variation was found to be between 0.211 ± 0.024 % to 214 ± 0.021 mg. The drug content was found to be between 93.47 ± 0.23% to 98.45 ± 0.12%. The hardness was found to be from 5.2 ± 0.11 to 6.5 ± 0.15 Kg / cm2.

**Table.5.Physicochemical evaluation of different polymer coating films**

| Polymer | Parameter | | |
|---|---|---|---|
| | Film solubility | | Film thickness (mm) * |
| | pH 1.2 | pH 6.8 | |
| **CAP** | Insoluble | Soluble | 0.21 ± 0.07 |
| **Eudragit L 100** | Insoluble | Soluble | 0.24 ± 0.08 |

***Mean±SD, *n* = 3**

**Table.6.Physicochemical evaluation parameters of enteric coated tablets**

| Polymer | Batch Code | Parameter | | |
|---|---|---|---|---|
| | | Weight Variation (mg) * | Hardness ($Kg/cm^2$*) | Drug content (%)* |
| **CAP** | **C1F3** | 211 ± 0.035 | 6.5 ± 0.15 | 96.75 ± 0.14 |
| | **C2F3** | 214 ± 0.016 | 5.9 ± 0.24 | 93.65 ± 0.35 |
| | **C1F9** | 212 ± 0.006 | 5.4 ± 0.09 | 94.45 ± 0.26 |
| | **C2F9** | 210 ± 0.024 | 6.3 ± 0.14 | 98.54 ± 0.12 |
| **Eudragit L 100** | **E1F3** | 214 ± 0.021 | 5.5 ± 0.16 | 93.47 ± 0.23 |
| | **E2F3** | 213 ± 0.012 | 6.0 ± 0.06 | 94.56 ± 0.14 |
| | **E1F9** | 215 ± 0.015 | 6.5 ± 0.31 | 98.27 ± 0.45 |
| | **E2F9** | 211 ± 0.024 | 5.7 ± 0.20 | 96.35 ± 0.12 |

***Mean±SD, *n* = 3**

***In vitro* drug release studies of enteric coated tablets:** The *in vitro* release of pantoprazole sodium from the prepared tablets was studied in ph 1.2 for 2 h and in phosphate buffer pH 6.8 for 1 h. *In vitro* dissolution studies were performed using USP Type II rotating paddle dissolution apparatus (Electrolab TDT-08L, India) by using 1.2 N HCl and phosphate buffer (pH 6.8) as a dissolution medium. Formulation which shows most satisfactory result is C2F9, where drug release started after 2 hrs, and released maximum 99.72 by 3 hrs. Remaining were respectively, released started and reached maximum, CIF3-90 min and 96.42 in 3 hrs, C2F3-2 hrs and 94.59 in 195 min, E1F3-90 min and 98.15 in 165 min, E2F3-105 min and 97.54 in 3 hrs, C1F9-90 min and 99.79 in 165 min, EIF9-90 min and 97.97 in 165 min, E2F9-2 hrs and 97.39 in 3 hrs. The cumulative percentage releases of pantoprazole sodium from the tablets were shown in Table7-14 and Figure 1-2.

**Table.7. *In vitro* drug release of pantoprazole sodium (C1F3)**

| Time (min) | Absorbance | Conc. (µg/mL) | Conc. in 900 mL (mg /mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released * |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0.024 | 0.6469 | 5.822 | 0 | 0 | 5.822 | 14.62±0.52 |
| 120 | 0.06 | 1.6172 | 14.555 | 0.0064 | 0.0064 | 14.561 | 36.58±0.40 |
| 135 | 0.091 | 2.3884 | 21.496 | 0.0161 | 0.0226 | 21.518 | 54.05±0.90 |
| 150 | 0.121 | 3.1758 | 28.582 | 0.0238 | 0.0465 | 28.629 | 71.91±0.39 |
| 165 | 0.142 | 3.7270 | 33.543 | 0.0317 | 0.0782 | 33.621 | 84.46±0.17 |
| 180 | 0.162 | 4.2519 | 38.267 | 0.0372 | 0.1155 | 38.383 | 96.42±0.40 |

*** Mean±SD, *n* = 3**

**Table.8. *In vitro* drug release of pantoprazole sodium (C2F3)**

| Time | Absorbance | Conc. (µg/mL) | Conc in 900 | Loss | mulative loss | Cumulative | Cumulative |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 120 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 135 | 0.019 | 0.4986 | 4.488 | 0 | 0 | 4.488 | 11.27 ±0.90 |
| 150 | 0.082 | 2.1522 | 19.370 | 0.0049 | 0.0049 | 19.375 | 48.67±0.27 |
| 165 | 0.122 | 3.2021 | 28.818 | 0.0215 | 0.0265 | 28.845 | 72.46±0.18 |
| 180 | 0.149 | 3.9107 | 35.196 | 0.0320 | 0.0585 | 35.255 | 88.56±0.42 |
| 195 | 0.159 | 4.1732 | 37.559 | 0.0391 | 0.0976 | 37.656 | 94.59±0.70 |

**Table.9. *In vitro* drug release of pantoprazole sodium (E1F3)**

| Time (min) | Absorbance | Conc. (µg/mL) | Conc. in 900 mL(mg/mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released * |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0.041 | 1.1051 | 9.946 | 0 | 0 | 9.946 | 24.98±0.34 |
| 120 | 0.071 | 1.9137 | 17.223 | 0.0110 | 0.0110 | 17.234 | 43.29±0.62 |
| 135 | 0.116 | 3.0446 | 27.401 | 0.0191 | 0.0301 | 27.431 | 68.91±0.72 |
| 150 | 0.137 | 3.5958 | 32.362 | 0.0304 | 0.0606 | 32.422 | 81.44±0.58 |
| 165 | 0.165 | 4.3307 | 38.976 | 0.0359 | 0.0965 | 39.072 | 98.15±0.40 |

*** Mean±SD, *n* = 3**

**Table.10. *In vitro* drug release of pantoprazole sodium (E2F3)**

| Time (min) | Absorbance | Conc. (µg/mL) | Conc. in 900 mL (mg/mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 120 | 0.02 | 0.5390 | 4.851 | 0 | 0 | 4.851 | 12.18±0.82 |
| 135 | 0.07 | 1.8372 | 16.535 | 0.0053 | 0.0053 | 16.540 | 41.55±0.66 |
| 150 | 0.116 | 3.0446 | 27.401 | 0.0183 | 0.0237 | 27.425 | 68.89±0.72 |
| 165 | 0.142 | 3.7270 | 33.543 | 0.0304 | 0.0542 | 33.597 | 84.39±0.48 |
| 180 | 0.164 | 4.3044 | 38.740 | 0.0372 | 0.0914 | 38.831 | 97.54±0.70 |

*** Mean±SD, *n* = 3**

**Table.11. *In vitro* drug release of pantoprazole sodium (C1F9)**

| Time (min) | Absorbance | Conc. (µg/mL) | Conc. in 900 mL(mg/mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released* |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0.04 | 1.0781 | 9.703 | 0 | 0 | 9.703 | 24.48±0.18 |
| 120 | 0.079 | 2.1293 | 19.164 | 0.0107 | 0.0107 | 19.175 | 48.38±0.67 |
| 135 | 0.121 | 3.1758 | 28.582 | 0.0212 | 0.0320 | 28.614 | 72.20±0.58 |
| 150 | 0.15 | 3.9370 | 35.433 | 0.0317 | 0.0638 | 35.496 | 89.56±0.42 |
| 165 | 0.167 | 4.3832 | 39.448 | 0.0393 | 0.1032 | 39.552 | 99.79±0.70 |

*** Mean±SD, *n* = 3**

**Table.12. *In vitro* drug release of pantoprazole sodium (C2F9)**

| Time (min) | Absorbance | Conc. (µg/mL) | Conc. in 900 mL (mg / mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released* |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 120 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 135 | 0.054 | 1.417 | 12.755 | 0 | 0 | 12.755 | 32.18±0.34 |
| 150 | 0.098 | 2.572 | 23.149 | 0.0141 | 0.0141 | 23.163 | 58.44±0.58 |
| 165 | 0.139 | 3.648 | 32.834 | 0.0257 | 0.0398 | 32.874 | 82.94±0.18 |
| 180 | 0.167 | 0.038 | 0.043 | 39.448 | 0.0364 | 0.076 | 99.72±0.46 |

*** Mean±SD, *n* = 3**

Table.13. *In vitro* drug release of pantoprazole sodium (E1F9)

| Time (min) | Absorbance | Conc. (µg/mL) | Conc.in 900 mL (mg/ mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released* |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0.03 | 0.8086 | 7.277 | 0 | 0 | 7.277 | 18.36±0.42 |
| 120 | 0.063 | 1.6981 | 15.283 | 0.0080 | 0.0080 | 15.291 | 38.58±0.22 |
| 135 | 0.104 | 2.7296 | 24.566 | 0.0169 | 0.0250 | 24.592 | 62.05±0.58 |
| 150 | 0.15 | 3.9370 | 35.433 | 0.0272 | 0.0523 | 35.485 | 89.53±0.39 |
| 165 | 0.164 | 4.3044 | 38.740 | 0.0393 | 0.0917 | 38.831 | 97.97±0.48 |

*** Mean±SD, *n* = 3**

Table.14. *In vitro* drug release of pantoprazole sodium (E2F9)

| Time (min) | Absorbance | Conc. (µg/mL) | Conc. in 900 mL (mg / mL) | Loss | Cumulative loss | Cumulative drug released | Cumulative percentage drug released |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 105 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 120 | 0.027 | 0.7277 | 6.549 | 0 | 0 | 6.549 | 16.52±0.16 |
| 135 | 0.071 | 1.8635 | 16.771 | 0.0072 | 0.0072 | 16.778 | 42.33±0.35 |
| 150 | 0.118 | 3.0971 | 27.874 | 0.0186 | 0.0259 | 27.899 | 70.39±0.63 |
| 165 | 0.149 | 3.9107 | 35.196 | 0.0309 | 0.0568 | 35.253 | 88.95±0.44 |
| 180 | 0.163 | 0.0381 | 0.042 | 38.503 | 0.0391 | 0.095 | 97.39±0.61 |

*** Mean±SD, *n* = 3**

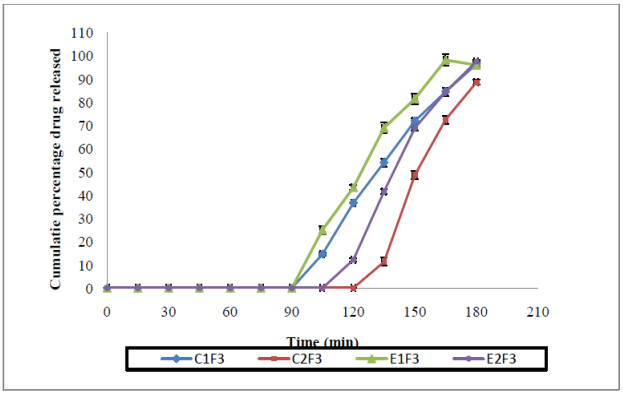


**Figure.1.*In vitro* drug release of pantoprazole sodium (C1F3 to E2F3)**

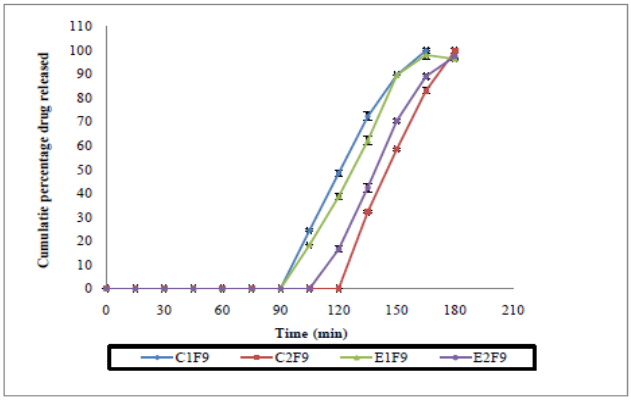


**Figure.2.*In vitro* drug release of pantoprazole sodium (C1F9 to E2F9)**

**Stability studies:** Stability of a drug in a dosage form at different environmental conditions is important as it determines the expiry date of that particular formulation. Changes in the physical appearance, color, odor, taste or texture of the formulation indicate the drug instability. Among the three enteric coated Formulation, Formulation C2F9 was selected for stability studies based on the physicochemical characterization of coating films and release characteristics.

The stability studies were carried out at 40 ± 2 °C with 75 ± 5%% RH which shown in Table 20. There were no significant changes in their physical appearance, average weight of tablets and hardness. It was observed that the initial drug content and the drug contents of the samples analyzed after 1,2,3 month of storage were similar. The release profile also not showed any significant changes indicating that there were no significant changes in the physical as well as chemical characteristics of the formulation. Hence, it can be concluded from the results that the developed tablets were stable and retain their pharmaceutical properties over a period of 3 month.

**Table.15.Stability studies of cellulose acetate phthalate coated tablet formulation C2F9**

| Evaluation parameters | Observation in month | | | |
|---|---|---|---|---|
| | Initial | 1st month | 2nd month | 3rd month |
| Physical appearance | white color tablets | No change | No change | No change |
| Hardness ($Kg / cm^2$) * | 6.3 ± 0.14 | 6.2 ± 0.56 | 6.2 ± 0.64 | 6.2 ± 0.26 |
| Drug Content (%)* | 98.54 ± 0.12 | 98.36 ± 0.52 | 98.16 ± 0.36 | 98.07 ± 0.28 |

## CONCLUSION

An attempt was made in this research work to formulate an oral enteric coating pantoprazole sodium tablet and evaluate it. An ulcer is the disease caused by an imbalance between aggressive and defensive factors. Ulcer sarecrater-like sores which form in the lining of the stomach, just below the stomach at the beginning of the small intestine in the duodenum. Pantoprazole is a substituted benzimidazole derivative that targets gastric acid proton pumps, the final common pathway for gastric acid secretion. The drug covalently binding to the proton pumps, causing prolonged inhibition of gastric acid secretion. The stability of pantoprazole is depending on pH and it rapidly degrades in acid medium of the stomach, but stable in alkaline conditions. Therefore, pantoprazole should be delivered into the intestine. Hence, an attempt was made to formulate an enteric coated drug delivery system for pantoprazole by using various enteric coating polymers.

From the reproducible results obtained from the executed experiments it can be concluded that CAP and Eudragit L 100 can be used as enteric coated polymer. Both the polymer can protect the drug from the acid environment that is in gastric pH and release the drug when it's reached in intestinal pH.

In this present research work, both the polymer has been used as an enteric coating polymer, with the best formulation. CAP and EudragitL100 have been used 6% and 8% with the best formulation. From the dissolution studies it was observed that, the enteric coated both polymer was intact for 2 hours in pH 1.2 buffer. The formulation which is said to the best formulation is C2F9, which is formulation no. 9 and coated with 8% CAP.

Therefore thestudyprovedthat the pantoprazole enteric coated tablets can be used for ulcer and GERD disease. Hence, formulation of pantoprazole as an enteric coated tablet may solve the stability problem of drug in the stomach and release the drug in the intestine. After satisfied pre-compression and post compression result the of core tablets, tablets were coated with suitable coating material to develop the dosage form which is to overcome the drug degradation by the gastric enzymes as well as the acidic environment of the stomach.

## REFERENCES

Anroop N, Rachna G, Rachna K, Shery J, Mahesh A, Formulation and Evaluation of Enteric Coated Tablets of Proton Pump Inhibitor, Journal of Basic and Clinical Pharmacy, 1(4), 2010, 45-49

Bozdag S, Çalis S, Sumnu M, Formulation and stability evaluation of enteric-coated omeprazole formulations. S.T.P. Pharma Sciences, 9 (4), 1999, 321-327.

Chanchal M, Anil G, Mukesh S, Asha R, Pantoprazole and its enteric coating polymer concentration for stable coating in acid media in stomach, International Journal of Pharmaceutical and Clinical Research, 3(2), 2011, 45-47.

Liberman H, Lachman L, The Theory and Practice of Industrial Pharmacy. 3rd Ed. Bombay: Verghese Publication House, 1991, 171-193.

Martin A, Micromeretics. In: Martin A, ed. Physical Pharmacy, Baltimores, MD: Lippincott Williams and Wilkins, 2001, 423-454.

Mohamed N, and Hazem H, Pharmacokinetics and bioequivalence evaluation of two omeprazole enteric-coated formulations in healthy egyptian male volunteers, Journal of Applied Sciences Research, 5(9), 2009, 1190-1194.

Neelam DK, Prafulla SC, Rajesh J, Innovations In Tablet Coating Technology: A Review, IJABPT, 2(1), 2011, 214-217.

Nicole GM, Clinical effects of proton pump inhibitors, Erasmus University, 2010, 1-2.

Putta K, Hiremath D, S. Rajendra, Enteric coated tablets of novel proton pump inhibitor with super disintegrants design, in-vitro evaluation and stability studies, Journal of Applied Pharmaceutical Science, 01 (06), 2011, 106-111.

Rakesh T, Prashant P, Rabiprazole sodium delayed release multiparticulates: Effect of enteric coating layer on product performance. Journal of Advance Pharmaceutical Technology & Research, 2(3), 2011, 184-191.

Richard F, Michelle A, Luigi X. Lippincott's Illustrated Reviews: Pharmacology, 4th Ed. Lippincott Williams & Wilkins, 2009; 331.

Rupesh K, Archana D, Kajale, Keshao P, Giradkar V, Formulation and development of enteric coated dosage form using ketorolac tromethamine, International Journal of Pharmaceutical Research and Development, 2(8), 2010, 126-135.

Saffar M, Rajeev S, Sophia D, Comparative in vitro evaluation of commercially available pantoprazole tablets. Kathmandu University Journal of Science, Engineering and Technology, 1(3), 2007, 1-7

Senthil K, Ashokkumar S, Ezhilmuthu RP, Formulation and evaluation of didanosine enteric coated sustained release tablet, J Biomed Sci and Res, 2(3), 2010, 126-131.

Singh C, Kumar R, Agarwal K, Nema K, Development and evaluation of enteric coated tablet containing diclofenac sodium. International Journal of Pharmaceutical Sciences and Nanotechnology, 2(1), 2009, 443-449.

Sumit C, Sibaji S, Sujit D, Formulation Development and Evaluation of Pantoprazole Enteric Coated Tablets, Int. J. Chem Tech Res,1(3), 2009, 663-666.

Vivek U, Haranadh S, Sreerama T, Seetha D, P Teja, KPR Chowdary, Formulation and invitro evaluation of enteric coated tablets of didanosine, Pharmanest - An International Journal of Advances In Pharmaceutical Sciences, 2 (1), 2011, 40-45.