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Formulation and Evaluation of Enteric Coated tablets of Pantoprazole.

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ABSTRACT:

Pantoprazole reduces the amount of acid your stomach makes. It's used for heartburn, acid reflux and gastro-oesophageal reflux disease (GORD) – GORD is when you keep getting acid reflux. It's also taken to prevent and treat stomach ulcers. Sometimes, pantoprazole is taken for a rare condition caused by a tumour in the pancreas or gut called Zollinger-Ellison syndrome. It 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 compared to wet granulation since it requires fewer unit operations. 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 180min. 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 months.

Key words: Super disintegrates, HPMC, PVP, Direct compression, Proton pump inhibitor, Cellulose acetatephthalate.

1.0 INTRODUCTION:

More than 50% of pharmaceutical products are orally administered for several reasons. This route of administration is considered as the most widely used route as it offers advantages like ease of administration, versatility, patient compliance and accurate dosing. Undesirable taste is one of the important formulation problems that are encountered withsuch oral product.

Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They are the most widely preferred form of medication both by pharmaceutical manufacturer as well as physicians and patients. They offer safe and convenient ways of active pharmaceutical ingredients (API) administration with excellent physicochemical stability in comparison to some other dosage forms, and also provide means of accurate dosing. They can be mass produced with robust quality controls and offer different branding possibilities by means of colored film coating, different shapes, sizes or logos.

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 most important reasons for enteric coating can be summarized as follows: - to protect acid-labile drugs from gastric fluid (e.g. enzymes and certain antibiotics), - to prevent gastric distress or nausea due to irritation from a drug (e.g. sodium salicylate), - to deliver drugs intended for local action in the intestines (e.g. intestinal antiseptics could be delivered to their site of action in a concentrated form and bypass systemic absorption in the stomach), - to deliver drugs that are optimally absorbed in the small intestine to their primary absorption site in their most concentrated form, - to provide a delayed-release component for repeat action .

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). 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. 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.

2.0 MATERIAL AND METHODS:

2.1 LIST OF CHEMICALS USED:

Table No. 01 List of chemicals

Sr. No.	Materials	Manufacturer / Supplier
1	Acetone	SD Pharma, Mumbai, India
2	Calcium phosphate	Fine Chem Industries, India
3	Disodium hydrogen phosphate	Fine Chem Industries, India
4	Potassium dihydrogen phosphate	Cipla Pharma, Mumbai, India
5	Cellulose acetate phthalate	SD Pharma, Mumbai, India
6	Micro crystalline cellulose	Cipla Pharma, Mumbai, India

7	Mannitol	Signet Chemical Corporation
8	Croscarmellose sodium	SD Chemical Corporation
9	Pantoprazole sodium sesquihydrate	Signet Chemical Corporation
10	Talc	Spectrochem Pvt. Ltd. Mumbai.
11	Magnesium stearate	Spectrochem Pvt. Ltd. Mumbai.
12	Eudragit L-100	Sd fine Chem. Ltd., Mumbai, India.
13	Potassium dihydrogen Phosphate	Spectrum reagent and chemicals Pvt. Ltd., India.
14	Hydrochloric acid	Swastik Pharmaceuticals, Mumbai,India.

2.2 PRE-FORMULATION STUDIES:

2.2.1 Preparation of standard graph for pantoprazole sodium using acidic buffer (pH 1.2):

2.2.1.1 Determination of absorption maxima (λmax)-

100 mg of pantoprazole sodium sesquihydrate was weighed accurately and dissolved in 100 mL of pH 1.2 acidic buffer in 100 mL volumetric flask (stock solution). 2 mL was taken from the stock solution and transferred into 100 mL volumetric flask and diluted up to 100 mL with pH 1.2 acidic buffer. The resulting solution was labeled as standard working Solution. 2 mL of the working solution was withdrawn and diluted up to 10 mL with pH 1.2 acidic buffer in 10 mL volumetric flask. The spectrum of this solution was run in 200 to 400 nm range in UV-visible spectrophotometer. The λ max of the pantoprazole sodium sesquihydrate was found to be 283 nm.

2.2.1.2 Preparation of standard graph-

From above standard working solution, 1, 2, 3, 4, 5 and 6 mL was withdrawn and diluted up to 10 mL with pH 1.2 acidic buffer in 10 mL volumetric flask to get concentration of 2 µg, 4 µg, 6 µg, 8 µg, 10 µg and 12 µg respectively. The absorbance of each solution was measured by UV-visible spectrophotometer at 283 nm using the pH 1.2 acidic buffer as blank.

2.2.2 Preparation of standard graph for pantoprazole sodium using phosphate buffer (pH 6.8):

2.2.2.1 Determination of absorption maxima (λmax)-

100 mg of pantoprazole sodium sesquihydrate was weighed accurately and dissolved in 100 mL of pH 6.8 phosphate buffer in 100 mL volumetric flask (stock solution). 2 mL was taken from the stock solution and transferred into 100 mL volumetric flask and diluted up to 100 mL with pH 6.8 phosphate buffer. The resulting solution was labeled as standard working Solution. 2 mL of the working solution was withdrawn and diluted up to 10 mL with pH 6.8 phosphate buffer in 10 mL volumetric flask. The

spectrum of this solution was run in 200 to 400 nm range in UV-visible spectrophotometer. The λ max of the pantoprazole sodium sesquihydrate was found to be 288 nm.

2.2.1.2 Preparation of standard graph-

From standard working solution, 1, 2, 3, 4, 5 and 6 mL has withdrawn and diluted up to 10 mL with pH 6.8 phosphate buffer in 10 mL volumetric flask to get concentration of 2 µg, 4 µg, 6 µg, 8 µg, 10 µg and 12 µg respectively. The absorbance of each solution was measured by UV-visible spectrophotometer at 288 nm using the phosphate buffer (pH 6.8) as blank.

2.2.3 FTIR spectra study:

This was carried out to find out the compatibility between the drug pantoprazole sodium sesquihydrate and the croscarmellos sodium, MCC, manito and other exicipients. 10 mg of the sample and 400 mg of KBr were taken in a mortar and triturated. A small amount of the triturated sample was taken into a pellet maker and was compressed at 10 Kg/cm^2 using a hydraulic press. The pellet was kept on to the sample holder and scanned in Bruker FT-IR spectrophotometer. The spectra obtained were compared and interpreted for the functional group peaks.

2.3 FORMULATION STUDIES:

2.3.1 Preparation of powder blend:

Pantoprazole sodium sesquihydrate powder blend for tabletting were prepared by direct compression method. Specified quantity of pantoprazole, croscarmellos sodium, manitol, calcium phosphate, and MCC were weighed according to the formula and transferred in a mortar and pestle and mixed thoroughly. The powder was passed through sieve no 80 to obtain the granules. The specified quantity of magnesium stearate and talc were finally added and mixed for the compression of tablets.

2.3.2 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.

Table No. 02. 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

2.4 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.

2.5 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 1cm2 area the prepared polymeric film was studied for film thickness, and film solubility. 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 1×1 cm2 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.

2.6 IN-VITRO DRUG RELEASE STUDIES:

USP dissolution apparatus type II 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.

2.7 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.

3.0 RESULTS AND DISCUSSION:

The study was performed on enteric coating tablets with different formulation F1 to F9. Pantoprazole sodium sesquihydrate were prepared by direct compression method using different concentration of, microcrystalline cellulose, mannitol, dicalcium phosphate, croscarmellose sodium, magnesium stearate and talc, CAP and Eudragit L100 were used as enteric coating polymer, which prevent drug form gastric pH and release in intestinal pH.

3.1. Pre-formulation studies:

3.1.1 Preparation of standard graphs

Standard graph for the drug pantoprazole sodium was done separately in pH 1.2 acidic buffer and pH 6.8 phosphate buffer. Refer Table 3 and 4 for concentrations of pantoprazole sodium in pH 1.2 acidic and pH 6.8 phosphate buffers and the respective absorbance. The Figure 1 and 2 show the calibration curves of pantoprazole sodium in pH 1.2 acidic buffer and pH 6.8 phosphate buffer respectively.

Table No. 03. Calibration data of pantoprazole sodium in 0.1N HCl (pH 1.2)

Sr. No.	Concentration (mg /mL)	Absorbance* (nm)
1	0	0
2	2	0.082+0.0005
3	4	0.145+0.0015
4	6	0.231+0.0101
5	8	0.289+0.0023
6	10	0.361+0.0025
7	12	0.459+0.0047

Figure 1. Standard graph of pantoprazole sodium in 0.1N HCl (pH 1.2)

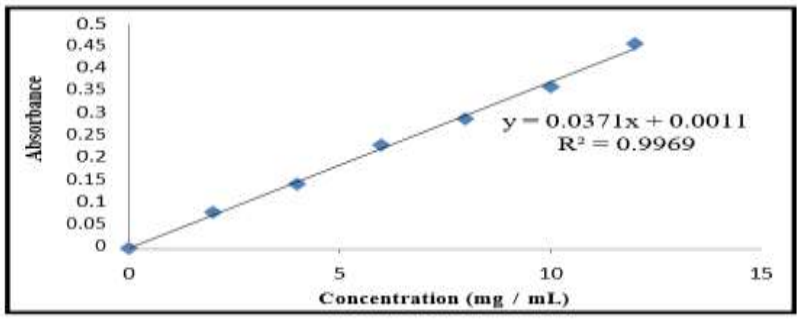
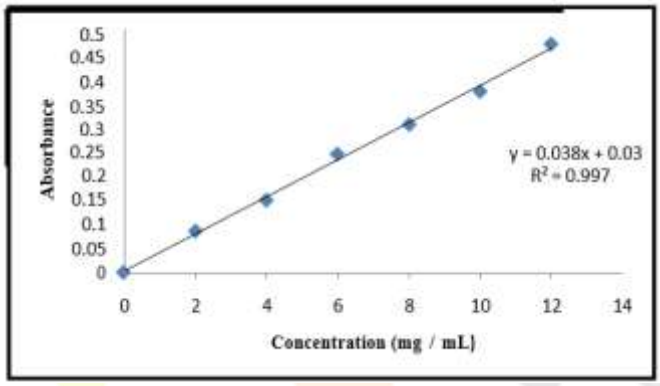


Table No. 04. Calibration data of pantoprazole sodium in phosphate buffer (pH 6.8)

Sr. No.	Concentration (mg /mL)	Absorbance*(nm)
1	0	0
2	2	0.085±0.0040
3	4	0.149±0.0036
4	6	0.243±0.0015
5	8	0.305±0.0075
6	10	0.373±0.0051
7	12	0.468±0.0020

*Mean±SD, $n = 3$

Figure 2. Standard graph of pantoprazole sodium in phosphate buffer (pH 6.8)



3.1.2 FTIR spectral study:

FT-IR spectroscopy study was carried out separately to find out the compatibility between the drug pantoprazole and Microcrystalline cellulose, mannitol, dicalcium phosphate, croscarmellose sodium. The FT-IR was performed for drug, polymer and the physical mixture of drug-polymer. The spectral obtained from FT-IR spectroscopy studies shows in **Table 05.**

The peaks obtained in the spectra of drug and polymers mixtures correlates with each other. This indicates that the drug was compatible with the formulation components. IR studies indicated no interaction between drug and polymers.

Table No. 05 Standard band frequency of Pantoprazole Sodium

Wave number in cm^{-1}	Characteristic
1900	C=H
1650 - 1580	N-H bending
1600 - 1400	Aromatic C=C stretching
1400 - 1000	C-N bending
1373	C-F
1049	S=O

3.2 Evaluation:

3.2.1 Precompression parameters

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 5. 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 30 º (25.79 ± 0.24 to 29.52 ± 0.14) also indicate the good flowability of the prepared granules.

Table No. 05 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 (Θ)*
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

3.2.2 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 06).**

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 favourable result.

Table 06. Post compression parameters of pantoprazole sodium core tablets

Formulation Code	Parameter				
	Hardness (Kg/cm²)*	**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

3.2.3 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 07).**

Table 07 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

3.2.4 Physicochemical evaluation of pantoprazole sodium enteric coated tablets:

The tablets which shows 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 08. 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 / cm^2.

Table 08. 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, $n = 3$

3.2.5 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 andreached 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 Table 09-16 and Figure 03-04.

Table No. 09. *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 No. 10. In vitro drug release of pantoprazole sodium (C2F3)

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	0.019	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

***** Mean+SD, n = 3

Table No. 11. 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 No. 12. 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 No. 13. 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 No. 14. 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 No. 15. 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 No. 16. 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 03. *In vitro* drug release of pantoprazole sodium (C1F3 to E2F3)

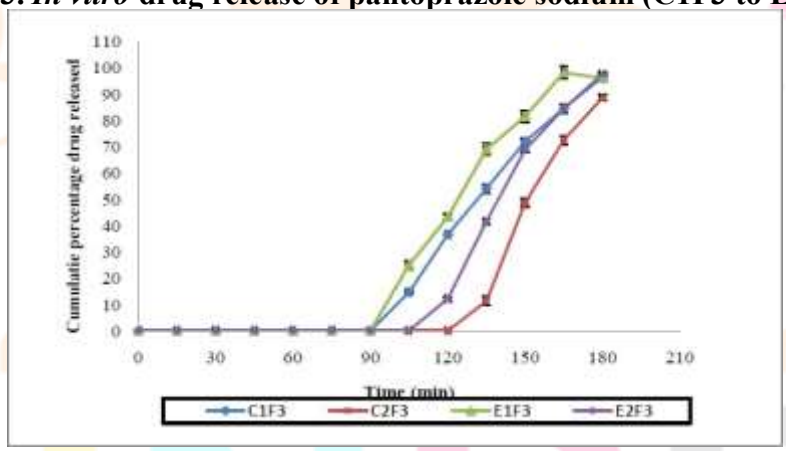
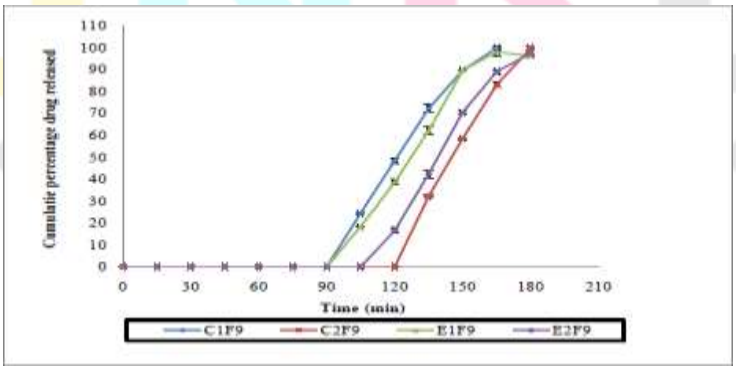


Figure 04. *In vitro* drug release of pantoprazole sodium (C1F9 to E2F9)



3.2.6 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, odour, 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 17. 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 analysed 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 17. 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 / cm²) *	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

*Mean ± SD, n=3

4.0 CONCLUSION:

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 have 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.

Hence the study concluded that the pantoprazole enteric coated tablets can be used for ulcer and GERD disease. 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.

5.0 REFERENCES:

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