



FORMULATION AND EVALUATION OF ENTERIC COATED TABLETS OF PANTOPRAZOLE

Mr. Veerbhadra Tripathi^{1†}, Dr Yogendra Singh², Dr Ashok Baghel³, Mr. Pradeep Yadav⁴,
Vishnu Kant Rai⁵

¹⁻⁴Shri Ramnath Singh Mahavidyalaya (Pharmacy), Gormi, Bhind (M.P.)- 477660, India

⁵Azad College of Education (Pharmacy), Sakha Janwara, Ghatampur, Kanpur Nagar, U.P., India

ARTICLE INFO

Review Article History

Received: 25th September, 2025

Accepted: 06th October, 2025

Corresponding Author:

† Mr. Veerbhadra Tripathi,

† Shri Ramnath Singh
Mahavidyalaya (Pharmacy),
Gormi, Bhind (M.P.) - 477660,
India

E-mail ID-

dryogendrasingh1707@gmail.com

ABSTRACT

Pantoprazole is a proton pump inhibitor, belongs to group of benzimidazole, Pantoprazole sodium tablets were prepared by direct compression method using different concentration of microcrystalline cellulose as filler, mannitol and dicalcium phosphate as diluents, croscarmellose 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 0.1 N HCl (pH 1.2) and phosphate buffer (pH 6.8). Among all the prepared batches 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 was started after 120 min and reached upto 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 months. Tablets were prepared and developed successfully.

Keywords: Pantoprazole, Direct compression, Proton pump inhibitor, Cellulose acetate phthalate, Eudragit L100.

© www.albertscience.com, All Right Reserved.

How to cite the article?

Veerbhadra Tripathi, Yogendra Singh, Ashok Baghel, Pradeep Yadav, Vishnu Kant Rai, Formulation and evaluation of enteric coated tablets of pantoprazole, ASIO Journal of Drug Delivery (ASIO-JDD), 2025, 7(1): 10-22.

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

with such oral product. Drugs are employed with the following therapeutic aims: (1) to relieve pain; (2) to accelerate healing; and (3) to prevent ulcer recurrence. Therapeutic approaches are three fold: (a) to reduce aggressive forces by lowering H⁺ output; (b) to increase protective forces by means of muco-protectants; and (c) to eradicate *Helicobacter pylori*[1-4].

Ulcers are crater-like sores (generally 1/4 inch to 3/4 inch in diameter, but sometimes 1 to 2 inches in diameter) which form in the lining of the stomach (called gastric ulcers), just below the stomach at the beginning of the small intestine in the duodenum (called duodenal ulcers) or less commonly in the esophagus (called esophageal ulcers). In general, ulcers in the stomach and duodenum are referred to as peptic ulcers. An ulcer is the result of an imbalance between aggressive and defensive factors. On one hand, too much acid and pepsin can damage the stomach lining and cause ulcers. On the other hand, the damage comes first from some other causes, making the stomach lining susceptible to even an ordinary level of gastric acid [5].

A peptic ulcer, also known as *ulcus pepticum*, peptic ulcer disease (PUD), [6,7] is an ulcer (defined as muco-salerosions equal to or greater than 0.5cm) of an area of the gastrointestinal tract that is usually acidic and thus extremely painful. 80% of ulcers are associated with *Helicobacter pylori*, a spiral-shaped bacterium that lives in the acidic environment of the stomach. Ulcers can also be caused or worsened by drugs such as aspirin and other non-steroid anti-inflammatory drugs (NSAIDs) [8]. The lifetime risk for developing a peptic ulcer is approximately 10%. In Western countries the prevalence of *Helicobacter pylori* infections roughly matches age. Prevalence is higher in third world countries. Transmission is by food, contaminated groundwater and through human saliva. Classical causes of ulcers (tobacco smoking, blood groups, spices and a large array of strange things) are of relatively minor importance in the development of peptic ulcers. A major causative factor (90% of gastric and 75% of duodenal ulcers) is chronic inflammation due to *Helicobacter pylori*, a spirochete that inhabits the antral mucosa and increases gastric production. Gastric, in turn, stimulates the production of gastric acid by parietal cells. A family history is often present in duodenal ulcers, especially when blood group O is also present. Inheritance appears to be unimportant in gastric ulcers [9].

Gastro-esophageal reflux disease occurs in both adults and children. Although mortality associated with GERD is rare (1 death per 100,000 patients), GERD symptoms have a greater impact on quality of life than do duodenal ulcers, untreated hypertension, mild congestive heart failure, angina, or menopause. Parietal cells in the stomach express receptors for acetylcholine, gastric and histamine. Stimulation of these receptors results in gastric acid production. H₂-receptor antagonists (H₂RAs) inhibit acid production by reversibly competing with histamine for binding to H₂-receptors on the parietal cells. Four different H₂RAs are available: cimetidine, famotidine, nizatidine and ranitidine. Although H₂RAs have reasonable efficacy, patients develop tolerance in

particular with continuous therapy. Proton pump inhibitors (PPIs) suppress gastric acid secretion by specific inhibition of the H⁺/K⁺-ATPase in the gastric parietal cell. This process starts with absorption of the PPI in the parietal cell. PPIs are weak bases, so protonation takes place in the acidic region of the secretory canaliculus of the parietal cell. PPIs are indicated for the treatment of GERD, reflux oesophagitis, peptic ulcers and Zollinger-Ellison syndrome. In addition, PPIs are used for gastro-protection in patients using NSAIDs. In combination with two suitable antibiotics, PPIs are also used for the eradication of *H. pylori* infection. In the Netherlands five PPIs are available: esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole [10-12]. 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. 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 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 [13-18].

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. 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 [19-25].

The main objectives of the present study was to formulate and evaluate enteric coated tablets of pantoprazole sodium by direct compression

method, selection of suitable coating material to develop the dosage form and to overcome the drug degradation by the gastric enzymes as well as the acidic environment of the stomach.

MATERIALS AND METHODS

Pantoprazole sodium was obtained as a gift sample from Cipla Pharma, Mumbai, India. Magnesium Stearate, and Talc were purchased from LobaChemie, Mumbai, India. EudragitL-100, Croscarmellose Sodium and all others excipients were obtained from Merck Ltd, Ahmedabad, India. All other ingredients and reagents were of analytical grade.

Preformulation studies

Preparation of standard graph for pantoprazole sodium using acidic buffer (pH1.2)

Determination of absorption maxima (λ_{max})

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.

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 μ g, 4 μ g, 6 μ g, 8 μ g, 10 μ g and 12 μ g respectively. The absorbance of each solution was measured by UV-visible spectrophotometer at 283 nm using the pH 1.2 acidic buffers as blank.

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

Determination of absorption maxima (λ_{max})

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.

Preparation of standard graph

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

FTIR spectra study

This was carried out to find out the compatibility between the drug pantoprazole sodium sesquihydrate and the croscarmellos sodium, MCC, mannitol and other excipients. 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/cm² 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.

Evaluation [26-47]

Pre-compression parameters

Bulk density (Db)

Accurately weighed granules were carefully transferred into graduated measuring cylinder. The granules bed was then made uniform and the volume occupied by the granules was noted as per the graduation marks on the cylinder as mL. It is expressed in gm/mL.

Tapped density (Dt)

It is the ratio of total mass of granule to the tapped volume of granule. The graduated measuring cylinder containing accurately weighed granule was manually tapped for 50 times. Volume occupied by the granule was noted. It is expressed in gram/mL.

Compressibility index (I) and Hausner's ratio

Carr's index and Hausner's ratio measure the propensity of granule to be compressed and the flow ability of granule. Carr's index and Hausner's ratio were calculated using following formula.

$$I = [(Dt - Db) / Dt] \times 100$$

Hausner's ratio = Dt/Db

Where, Dt–Tapped density of the powder; Db–Bulk density of the powder

Angle of repose (θ)

The frictional forces in a loose powder can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder and the horizontal plane. Sufficient quantities of pantoprazole granules were passed

through a funnel from a particular height (2 cm) onto a flat surface until it formed a heap, which touched the tip of the funnel. The height and radius of the heap were measured. The angle of repose was calculated using the formula.

Angle of repose (θ) = $\tan^{-1} (h/r)$ Where, h–Height of the pile in cm ; r –Radius of the pile

Preparation of pantoprazole sodium tablets

Preparation of powder blend

Pantoprazole sodium sesquihydrate powder blend for tableting were prepared by direct compression method. Specified quantity of pantoprazole, croscarmellos sodium, mannitol, calcium phosphate, and MCC were weighed according to the formula (Table 1) 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.

Preparation of pantoprazole sodium tablets

An ideal mixture of granules were directly punched into tablets weighing about 200mg containing 40 mg of pantoprazole sodium sesquihydrate, using rotary tablet compression machine (Riddhi 10 station 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 1: Composition of pantoprazole sodium enteric coated sodium tablets

Compositions	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

Post compression parameters

Hardness test

The prepared tablets were subjected to hardness test. It was carried out by using hardness tester and expressed in kg/cm².

Friability test

The friability was determined using friabilator and expressed in percentage (%). 20 tablets from each batch were weighed separately (W initial) and placed in the friabilator, which was then operated for 100 revolutions at 25 rpm. The tablets were reweighed (W final) and the percentage friability (F) was calculated for each batch by using the following formula.

$$F = \frac{(W \text{ initial}) - (W \text{ final})}{(W \text{ initial})} \times 100$$

Weight variation test

Twenty tablets were selected at random from the lot, weighed individually and the average weight was determined. The percent deviation of each tablets weight against the average weight was calculated. The test requirements are met, if not more than two of the individual weights deviate from the average weight by more than 5% and none deviates more than 10%.

IP limit for weight variation in case of (ts weighing more than 80 mg but less than 250 mg is ± 7.5 %.

Drug content uniformity

The prepared pantoprazole sodium sesquihydrate tablets were tested for their drug content. Three tablets of each formulation were weighed and finely powdered. About 40 mg equivalent of pantoprazole sodium sesquihydrate was accurately weighed and completely dissolved in pH 6.8 phosphate buffer and the solution was filtered. 1 mL of the filtrate was further diluted to 100 mL with pH 6.8 phosphate buffer. Absorbance of the resulting solution was measured by UV spectrophotometer at 288nm.

Disintegration time of Pantoprazole sodium core tablets

Disintegration test was carried out using the tablet disintegration test apparatus (Servewell Instruments pvt. Ltd., Electrolab ED-2L, India) pH 6.8 phosphate buffer at $37 \pm 0.5^\circ\text{C}$ was used as the disintegration media and the time in second taken for complete disintegration of the tablet.

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 (table 2). 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.

Table 2: Composition of coating solution

Ingredients	Quantity (%)
Cellulose acetate	6.0 / 8.0
Eudragit L100	
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.

Physico chemical 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 24h at room temperature under a special cover with reduced solvent evaporation to obtained smooth homogenous films. The dried films were cut into 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 at 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.

In vitro drug release studies

USP dissolution apparatus type II (Electrolab TDT-08L, Mumbai, India) 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.

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 was kept for examination and all were withdrawn at definite time intervals. The withdrawn samples were evaluated for physical appearance, hardness, drug content.

RESULTS AND DISCUSSIONS

Present study was done 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.

Preformulation studies

Preparation of standard graphs

Standard graph for the drug pantoprazole sodium was done separately in pH 1.2 acidic buffers and pH 6.8 phosphate buffers. **Table 3 and 4** show the concentrations of pantoprazole sodium in pH 1.2 acidic and pH 6.8 phosphate buffers and the respective absorbance.

Table 3: Calibration data of pantoprazole sodium in 0.1N HCl (pH1.2) *Mean±SD, n=3

SL. NO.	Concentration (mcg/mL)	Absorbance*
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

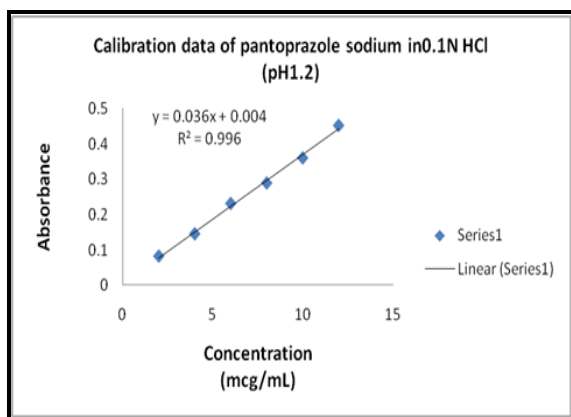


Figure 1: Calibration curve of pantoprazole sodium in 0.1N HCl (pH 1.2)

Table 4: Calibration data of pantoprazole sodium in phosphate buffer (pH 6.8)

SL. NO.	Concentration (mcg /mL)	Absorbance*
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

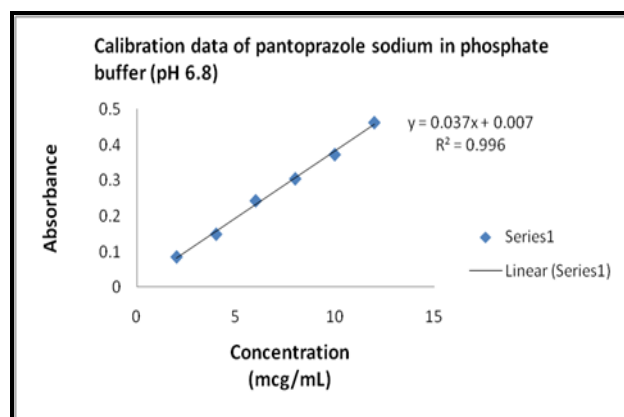


Figure 2: Calibration curve of pantoprazole sodium in phosphate buffer (pH 6.8)

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 5 and Figures 3-6

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.

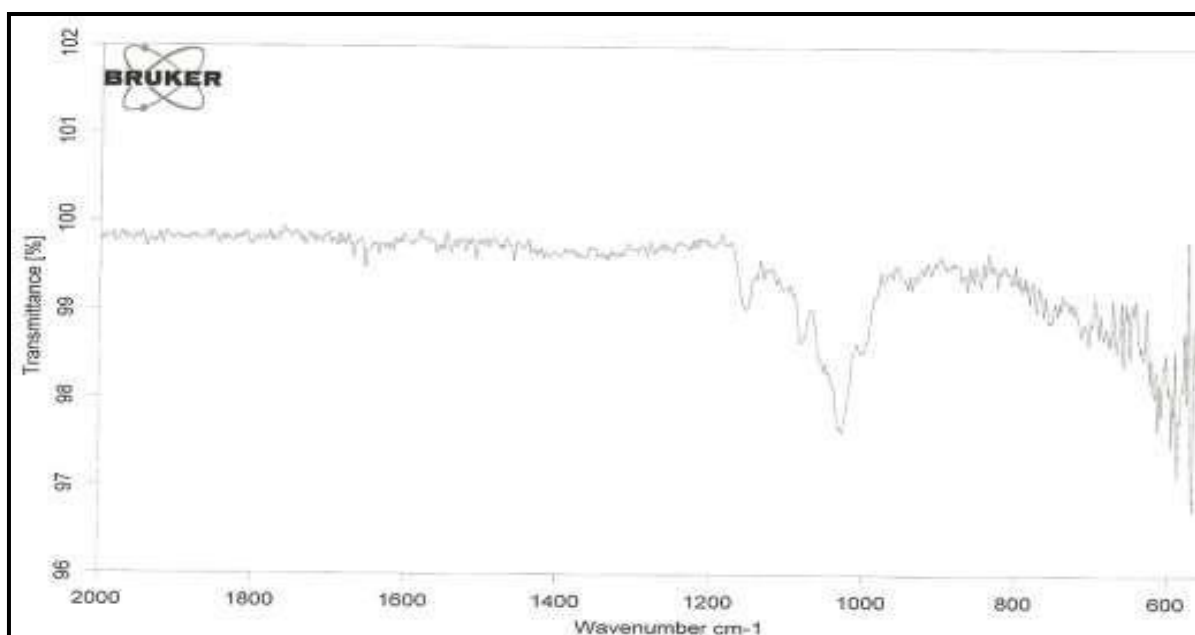


Figure 3: FTIR Spectrum of pantoprazole sodium

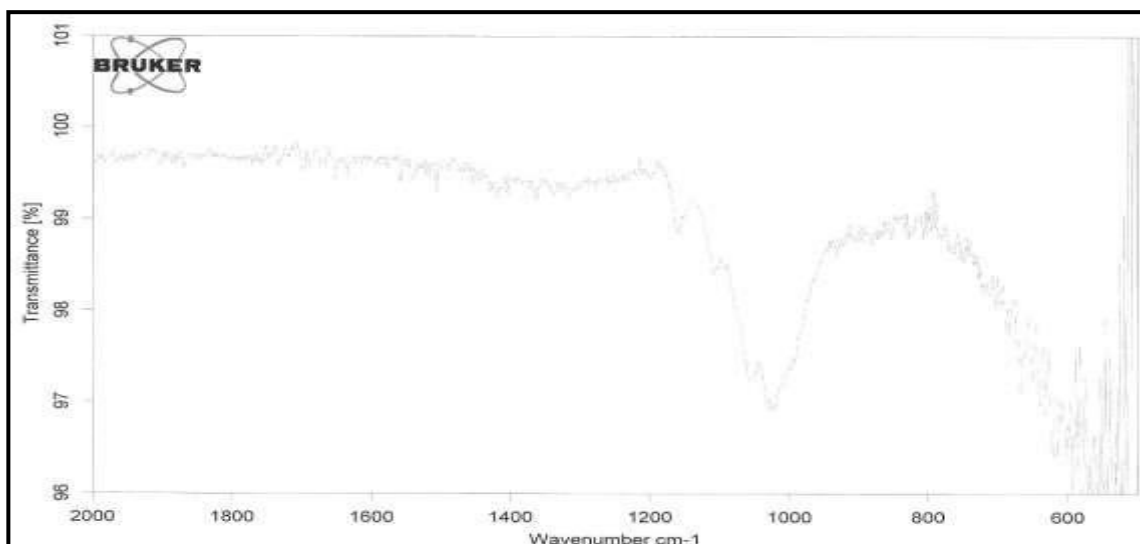


Figure 4: FTIR Spectrum of physical mixture of pantoprazole sodium with mannitol

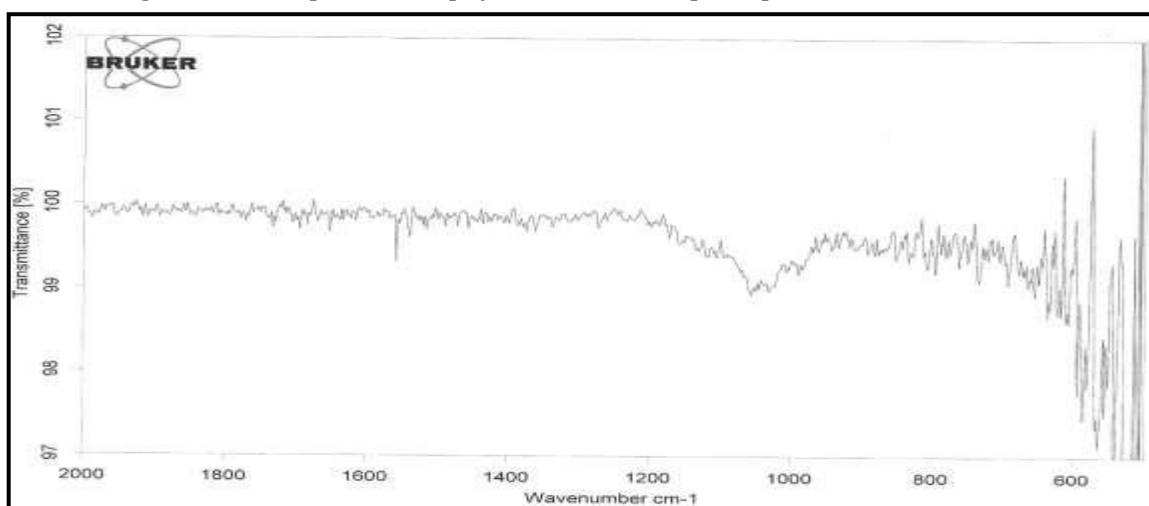


Figure 5: FTIR Spectrum of physical mixture of pantoprazole sodium with dicalcium phosphate

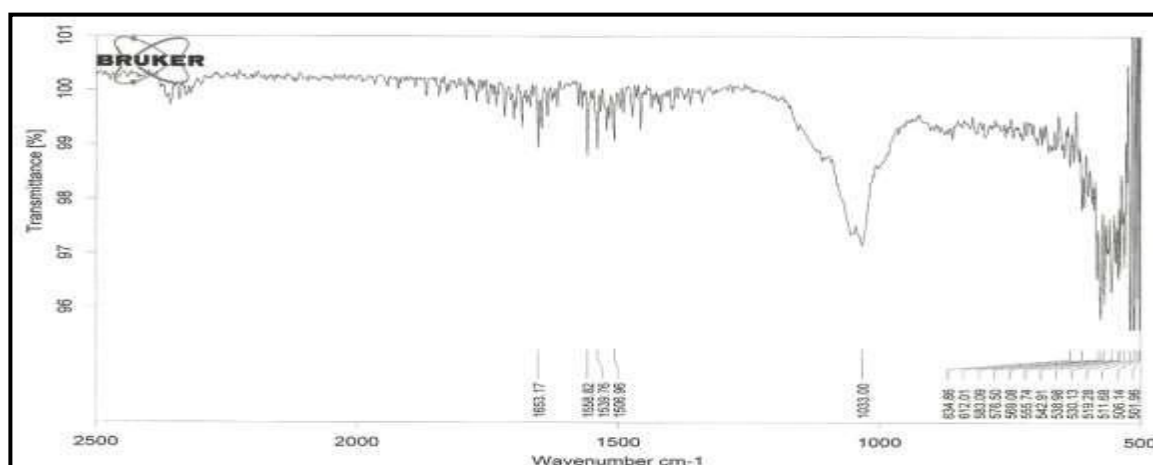


Figure 6: FTIR Spectrum of physical mixture of pantoprazole sodium with Dicalcium phosphate and mannitol.

The standard band frequency of the pantoprazole sodium is shown in the Table 5.

Table 5: 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

The spectra obtained from the physical mixture show that all the principle peaks are at or around the requisite wave number of pure drug. Thus it may be inferred that there was no chemical interaction between drug and polymer and the purity and integrity of drug was maintained in the physical mixtures.

Evaluations

Pre-compression parameters

Table 6: 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 $\pm$ 0.03	0.384 $\pm$ 0.05	7.03 $\pm$ 0.09	1.075 $\pm$ 0.04	28.31 $\pm$ 0.26
F2	0.312 $\pm$ 0.04	0.335 $\pm$ 0.02	6.86 $\pm$ 0.15	1.073 $\pm$ 0.05	27.20 $\pm$ 0.14
F3	0.306 $\pm$ 0.03	0.326 $\pm$ 0.03	6.13 $\pm$ 0.12	1.065 $\pm$ 0.02	29.13 $\pm$ 0.34
F4	0.312 $\pm$ 0.03	0.334 $\pm$ 0.06	6.58 $\pm$ 0.14	1.070 $\pm$ 0.06	26.13 $\pm$ 0.26
F5	0.306 $\pm$ 0.03	0.334 $\pm$ 0.05	8.38 $\pm$ 0.17	1.091 $\pm$ 0.08	26.78 $\pm$ 0.18
F6	0.384 $\pm$ 0.04	0.429 $\pm$ 0.05	10.48 $\pm$ 0.20	1.117 $\pm$ 0.07	25.79 $\pm$ 0.24
F7	0.358 $\pm$ 0.05	0.385 $\pm$ 0.04	7.01 $\pm$ 0.13	1.075 $\pm$ 0.03	29.52 $\pm$ 0.14
F8	0.286 $\pm$ 0.05	0.313 $\pm$ 0.04	8.62 $\pm$ 0.07	1.094 $\pm$ 0.03	26.95 $\pm$ 0.15
F9	0.348 $\pm$ 0.08	0.328 $\pm$ 0.05	5.74 $\pm$ 0.13	1.06 $\pm$ 0.08	26.13 $\pm$ 0.26

*Mean $\pm$ SD; n=3

DOI: 10.2016-19146535/ ; <https://doi-ds.org/doi/10.2025-76127896/ASIO-JDD/7/11/VT>

The prepared pantoprazole powder blend for tableting 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 in Table 6.

The bulk densities of the granules were found to be in the range of 0.306 $\pm$ 0.03 to 0.384 $\pm$ 0.04gm/mL, while the tapped densities were ranged between 0.313 $\pm$ 0.04to0.429 $\pm$ 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 $\pm$ 0.13 to 10.48 $\pm$ 0.20%) signify good flowability. The angle of repose of all formulation was less than 30 ° (25.79 $\pm$ 0.24 to 29.52 $\pm$ 0.14) also indicate the good flowability of the prepared granules.

Formulation studies

Preparation of pantoprazole sodium tablets

The pantoprazole sodium sesquihydrate tablets were prepared by direct compression method A total of nine formulations (F1-F9) by using a rotary tablet compression machine (8 mm diameter, Riddhi 10 station mini tablet press RDB4-10, Rimek, Ahmedabad, India). Compositions of the pantoprazole sodium sesquihydrate tablets are shown in Table 1.

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 7).

Hardness has to be controlled to ensure that the product is firm enough to with and 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 ± 0.15 to $100.34 \pm 0.13\%$. 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 7: 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 $\pm$ 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 pH 6.8 and insoluble in pH 1.2 (Table 8).

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 9. The weight variation was found to be between $0.211 \pm 0.024\%$ to 214 ± 0.021 mg. The drug content was found to be between $93.47 \pm 0.23\%$ to $98.45 \pm 0.12\%$. The hardness was found to be from 5.2 ± 0.11 to 6.5 ± 0.15 Kg/ cm².

Table 8: 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 L100	Insoluble	Soluble	0.24 ± 0.08

*Mean $\pm$ SD, n=3

Table 9: 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**

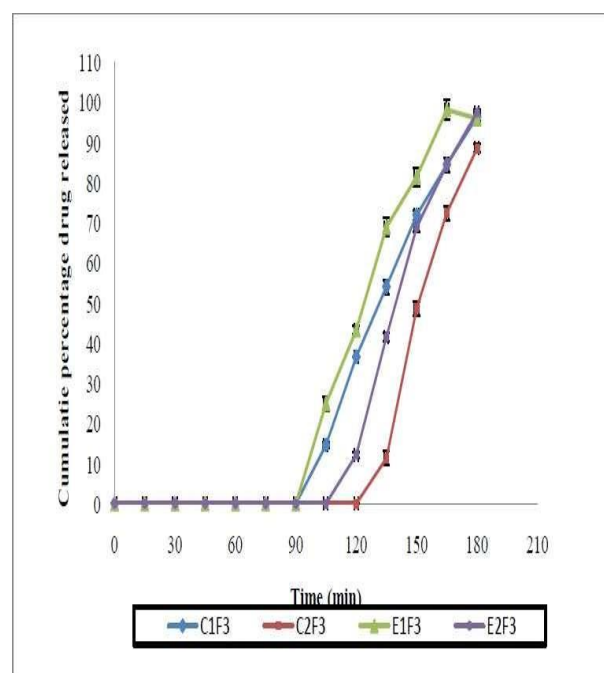
The *in vitro* release of pantoprazole sodium from the prepared tablets was studied in pH 1.2 for 2 h and in phosphate buffer pH 6.8 for 1 h. *In vitro* dissolution studies were performed using USP Type II rotating paddle dissolution apparatus (Electrolab TDT-08L, India) by using 1.2 N HCl and phosphate 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, C1F3-90 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, E1F9-90 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 10 and Figure 7 & 8.

Table 10: *In vitro* drug release of pantoprazole sodium (C2F9)

Time (min)	Cumulative percentage drug released*
0	0
15	0
30	0
45	0
60	0
75	0
90	0
105	0
120	0
135	32.18±0.34
150	58.44±0.58
165	82.94±0.18
180	99.72±0.46

*Mean±SD, n=3

Figure 7: *In vitro* drug release of pantoprazole sodium (C1F3 to E2F3)

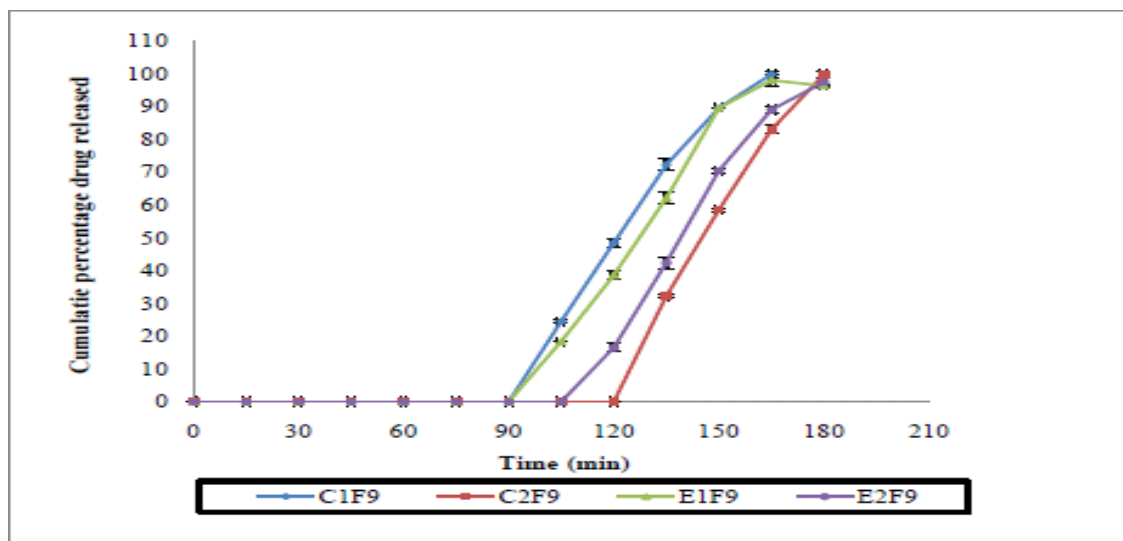


Figure 8: *In vitro* drug release of pantoprazole sodium (C1F9 to E2F9)

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 in stability. Among the three enteric coated formulations, C2F9 was selected for stability studies based on the physicochemical characterization of coating films and release characteristics.

The stability studies were carried out at $40 \pm 2^\circ\text{C}$ with $75 \pm 5\%$ RH which shown in **Table 11**. 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 months.

Table 11: Stability studies of cellulose acetate phthalate coated tablet formulation C2F9

Evaluation parameters	Observation in month			
	Initial	1 st month	2 nd month	3 rd 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

*Mean± SD, n=3

The aim of the present study was to formulate and evaluate of enteric coated pantoprazole sodium sesquihydrate tablets by using manitol, dicalcium phosphate, microcrystalline cellulose, crossrmelose sodium, magnesium stearate and talc.

FT-IR study was carried out to check any possible interactions between the drug and the excipients manitol, dicalcium phosphate, microcrystalline cellulose, crosscarmellose sodium, Pantoprazole sodium sesquihydrate were prepared by direct

compression method using different concentration of, Avicel PH (MCC) 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. The granules were evaluated for the pre-compression parameters like angle of repose, bulk density, tapped density and compressibility index. The flow characteristics of the granules were assessed by determining their angle of repose and Carr's Index. The values

of compressibility index and angle of repose signify good flowability of the granules for all the batches. This shows that the granules had smooth flow properties ensuring homogenous filling of the die cavity during the compression (punching) of tablets.

Coating materials like CAP and Eudragit L100 with the difference concentration. The *in vitro* dissolution studies were carried out for compressed and coated tablets using USP dissolution apparatus type II. The cumulative percentage of drug release from the tablets varied and depends on the type of polymer used and its concentration. Formulation 3 and formulation 9 was selected for the coating. CAP and Eudragit L 100 were used for the coating polymer. In this present study coating material was used with 6 and 8 percentage on the above mentioned formulation.

The stability study indicated that the prepared formulation was stable retained their pharmaceutical properties at room temperature and 40°C/75% RH over a period of 1 month. The coated tablets did not release the drug in hostile acidic environment (pH 1.2) due to protective polymer coating and released the drug in the intestinal environment (pH 6.8). Formulation 9, coated with 8% CAP was found to be best formulation, based on release time of the drug in the intestine.

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. 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 buffers. The formulation which is said to the best formulation is C2F9, which is formulation no.9 and coated with 8% CAP. Therefore the study proved that 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

1. Anne W, Allison G, in Ross, Wilson. Anatomy and Physiology in Health and Illness. 9th Ed: Churchill Livingstone, Spain; 2001; 296.
2. Rang HP, Dale MM, Ritter JM, Morre PK. Pharmacology. 5th Ed: Churchill Livingstone, 2005; 374.
3. Laurence L, John S, Keith L, in Goodman & Gilman's The pharmacological basis of therapeutics. 11th Ed, McGraw-Hill, 2006: 623- 634.
4. Heinz L, Albrecht Z, Klaus M. Color Atlas of Pharmacology. 2nd Ed. Thieme Stuttgart, NewYork- 2000;166
5. Tripathi KD. Essential of Medical Pharmacology. 5th Ed. Jaypee Brothers Medical Publishers (P) Ltd. New Delhi: 2003; 631
6. Joseph T, Robert L, Gary C, Gary R, Barbara G, L. Michael. Pharmacotherapy: A Pathophysiologic Approach, 6th Ed. 613-615.
7. Nicole GM. Clinical effects of proton pump inhibitors. Erasmus University. 2010; 1-2.
8. Richard F, Michelle A, Luigi X. Lippincott's Illustrated Reviews: Pharmacology, 4th Ed. Lippincott Williams & Wilkins. 2009; 331.
9. Bertram GK, Susan B. Masters, Anthony J. Trevor. Basic & Clinical Pharmacology, 11th Ed. by The McGraw-Hill Companies, 2009; 1479.
10. Jayesh P, Manish R. Tablet Formulation Design and Manufacture: Oral Immediate Release Application. Pharma Times April 2019; 41(4): 22.
11. Karl T, Karoline B, Enteric coated hard gelatin capsules. Department of Pharmaceutical Technology, Ludwig Maximilian University, 8000 Munich 2, Germany. Capsugel Library. 1-3.
12. Liberman, Lachman L. The Theory and Practice of Industrial Pharmacy. 3rd Ed, Verghese Publication House. 1987; 293.
13. Neelam DK, Prafulla SC, Rajesh J. Innovations In Tablet Coating Technology: A Review. IJABPT. Jan-Mar - 2021; 2(1): 214-217.
14. Salam W. Dumitru L. Directly Compressible Adjuvants-A Pharmaceutical Approach. Farmacia. 2008; Vol LV16:591-593.
15. Rabia B, Muhammad H, Nousheen A. Formulation Development and Optimization Of Ibuprofen Tablets By Direct Compression Method. Pak. J. Pharm. Sci. April 2018; 21(2) : 113.
16. Rakesh P, Mansi B, Directly Compressible Materials via Co-Processing International Journal of PharmTech

- Research. 2019; 1(3): 745-748.
17. Olowosulu AK, Avosuahi O, Isah AB. Formulation and Evaluation of Novel Coprocessed Excipients of Maize Starch and Acacia Gum (StarAc) For Direct Compression Tableting. International Journal of Pharmaceutical Research and Innovation. 2011; 2: 39-40.
18. Herbert A. Lieberman, Leon Lachman, Joseph B. Schwartz. Pharmaceutical Dosage Forms: Tablets. 2nd Ed.. Marcel Dekker. 1989; 214.
19. British Pharmacopoeia. London: The stationary office. 2003; (1).
20. Indian Pharmacopoeia. Delhi: The controller of publications. 1996; (1).
21. Pantoprazole sodium sesquihydrate available at: <http://www.Rxlist.com>.
22. Raymond C, Paul J, Marian E. Handbook of pharmaceutical excipients. 6th Ed. London: The Pharmaceutical Press. 2009; 94, 129, 206, 404, 424, 928.
23. Sumit C, Sibaji S, Sujit D. Formulation Development and Evaluation of Pantoprazole Enteric Coated Tablets. Int. J. Chem Tech Res. 2019; 1(3): 663-666.
24. 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. 2010; 1(4).
25. Saffar M, Rajeev S, Sophia D. Comparative in vitro evaluation of commercially available pantoprazole tablets. Kathmandu University Journal Of Science, Engineering And Technology. 2017; 1(3): 1-7
26. 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. 2011; 3(2): 45-47.
27. 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. 2021; 01 (06): 106-111.
28. Bozdog S, Çalis S, Sumnu M. Formulation and stability evaluation of enteric-coated omeprazole formulations. S.T.P. Pharma Sciences. 1999; 9 (4): 321-327.
29. 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. 2019; 5(9): 1190-1194.
30. Devraj, Bhatt DC. Studies on enteric coated sustained timed-release tablets of metronidazole. J. Chem. Pharm. Res. 2010; 2(2): 226-232.
31. Bankim Chandra Nandy, A. K. Gupta, A brief review on recent advances of extended release technology employed to design the oral dosage forms, International Journal of Medical and Biomedical Studies, 1(6)., Vol 1 No 6 (2017), 1-15.
32. Durriya H, Fahim M, Harris S, Zafar M, Rabia B, Rabial Y. Development of enteric coated flurbiprofen tablets using opadry/acryleze system-a technical note. AAPS PharmSciTech. 2018; 9(1): 116-121.
33. Senthil K, Ashokkumar S, Ezhilmuthu RP. Formulation and evaluation of didanosine enteric coated sustained release tablet. J Biomed Sci and Res. 2010; 2(3): 126-131.
34. Muhammad A, Syed S, Naqvi, Shahnaz G. Development of co-processed microgranules for direct compression. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; 3(2): 64-69.
35. Vivek U, Haranadh S, Sreerama T, Seetha D, P Teja. KPR Chowdary. Formulation and in vitro evaluation of enteric coated tablets of didanosine. Pharamnest - An International Journal of Advances in Pharmaceutical Sciences. 2011; 2 (1): 40-45.
36. 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 2009; 2(1): 443-449.
37. 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. 2010; 2(8): 126-135.
38. Rabia B, Muhammad Shoaib, Nousheen A, Zafar M, Durriya H. Enteric coating of ibuprofen tablets (200 mg) using an aqueous dispersion system. Brazilian Journal of Pharmaceutical Sciences. 2010; 46(1): 99-107.
39. Mominur Md, Saiful Md, Nahid S, Jakir C, Reza-ul J. Preparation and evaluation of cellulose acetate phthalate and ethyl cellulose based microcapsules of diclofenac sodium using emulsification and solvent evaporation method. Dhaka Univ. J. Pharm. Sci. 2010; 9(1): 39-46.
40. Rakesh T, Prashant P. Rabiprazole sodium delayed release multi-particulates: Effect of enteric coating layer on product performance. Journal of Advance Pharmaceutical Technology & Research. 2011; 2(3): 184-191.
41. B. C. Nandy, Bhaskar Mazumder, Three Levels Face Centered Central Composite Design of Colon Targeted Micro-Particulates System of Celecoxib: Screening of Formulations Variables and in Vivo Studies, Current Drug Delivery, 2014, 11(1), 1-7.
42. Gohel MC, Pranav J. A review of co-processed directly compressible excipients. J Pharm Pharmaceut Sci. 2005; 8(1): 76-93: 76-93.
43. Rajeshwar a, vijayj, ripudaman s. Development and evaluation of gastro-resistant microspheres of pantoprazole. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; 2(3): 112-116.
44. Martin A. Micromeritics. In: Martin A, ed. Physical Pharmacy. Baltimores, MD: Lippincott Williams and Wilkins. 2001; 423-454.
45. Liberman H, Lachman L. The Theory and Practice of Industrial Pharmacy. 3rd Ed. Bombay: Verghese Publication House. 1991; 171-193.
46. Bankim Chandra Nandy, Bhaskar Mazumder. Optimization and Characterizations of Delayed Release Multi-Particulates System of Indomethacin: Screening of Formulations Variables and In Vitro Investigations, ASIO Journal of Pharmaceutical & Herbal Medicines Research, 2015, 1(1): 25-40.
47. Bankim Chandra Nandy, Bhaskar Mazumder, Preparation and Evaluations of Multi-Particulates System of Celecoxib: Optimization by Response Surface Methodology, ASIO Journal of Drug Delivery (ASIO-JDD), 2015, 1(1): 11-25.