Development and In Vitro Evaluation of Pantoprazole Sodium Enteric Coated Tablets Using Different Super Disintegrants

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ABSTRACT :
The present study was aimed at the development and in vitro evaluation of Pantoprazole Sodium enteric coated tablets using different superdisintegrants to enhance disintegration and drug release characteristics. Pantoprazole Sodium, a proton pump inhibitor, is highly acid-labile and thus requires enteric coating to prevent degradation in the gastric environment and ensure drug release in the intestinal region. Core tablets were prepared by direct compression method employing various superdisintegrants such as Crospovidone, Croscarmellose sodium, and Sodium starch glycolate in different concentrations. The formulated core tablets were then coated with HPMC as seal coat and Eudragit as enteric coating polymer to provide acid resistance. The prepared formulations were evaluated for pre-compression parameters (angle of repose, bulk density, tapped density, and compressibility index) and post-compression parameters (hardness, friability, disintegration time, drug content, and weight variation). In vitro dissolution studies were performed in phosphate buffer pH 6.8 to assess the drug release profile. Among all the formulations, the batch containing Crospovidone (4%) exhibited the least disintegration time and the highest cumulative drug release, meeting official pharmacopoeial requirements. The results indicated that the selection of a suitable superdisintegrant and enteric coating polymer significantly influenced tablet performance and drug release. The optimized formulation demonstrated rapid disintegration in intestinal pH, excellent acid resistance, and controlled release of Pantoprazole Sodium, suggesting its potential for effective gastro-resistant oral delivery.
Keywords: Pantoprazole Sodium, Enteric coating, Superdisintegrants, Crospovidone, Eudragit L100, In vitro evaluation.

I.INTRODUCTION

Oral solid dosage forms remain the most preferred route of drug administration due to their convenience, cost-effectiveness, stability, and patient compliance. Among them, tablets are widely used, however, the therapeutic efficacy of orally administered drugs is often limited by factors such as poor stability in gastric pH, delayed onset of action, and variable bioavailability.[1] These challenges are particularly significant for acid-labile drugs that undergo degradation in the acidic environment of the stomach, necessitating formulation strategies that protect the drug until it reaches the intended site of absorption.[2] Pantoprazole sodium is a proton pump inhibitor (PPI) widely prescribed for the management of acid-related gastrointestinal disorders such as gastroesophageal reflux disease (GERD), peptic ulcer disease, and Zollinger–Ellison syndrome.[3] To overcome this limitation, enteric coating of pantoprazole tablets is essential to prevent drug release in the stomach and ensure delivery to the intestine, where the drug remains stable and can be effectively absorbed.[4] Enteric-coated tablets are designed to resist the acidic gastric environment while rapidly disintegrating and releasing the drug in the higher pH of the intestinal fluid. The performance of such formulations largely depends on the formulation composition, particularly the choice and concentration of excipients used in the core tablet.[5] Super disintegrants play a crucial role in enhancing the disintegration and dissolution characteristics of tablets by facilitating rapid breakup of the dosage form upon contact with gastrointestinal fluids. In vitro evaluation of enteric-coated tablets provides essential information regarding physicochemical properties, acid resistance, disintegration time, and dissolution behavior, which are key indicators of formulation performance and quality[6]. Studying the effect of different super disintegrants on the in vitro characteristics of pantoprazole sodium enteric-coated tablets can help optimize the formulation to achieve enhanced dissolution, consistent drug release, and improved bioavailability.[7] Hence, the present study aims to develop and evaluate pantoprazole sodium enteric-coated tablets using different super disintegrants and to assess their influence on tablet properties and in vitro drug release behavior, with the objective of identifying an optimized formulation that ensures gastric protection and effective intestinal drug delivery.

II. EXPERIMENTAL WORK

Materials

Pantoprazole Sodium was procured from Hetero Labs, Hyderabad. Croscarmellose and Sodium starch glycolate were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Methodology

Fourier Transform Infrared Spectroscopy: Fourier Transform Infrared (FTIR) spectroscopy was performed to identify functional groups of pantoprazole sodium and to check for any possible interactions between the drug and excipients. Initially, 1–2 mg of the pure drug or drug-excipient mixture was thoroughly mixed with 100–200 mg of dry, IR-grade potassium bromide (KBr) and ground to obtain a fine, homogeneous powder. The mixture was then compressed into a thin, transparent pellet using a hydraulic press.[8]

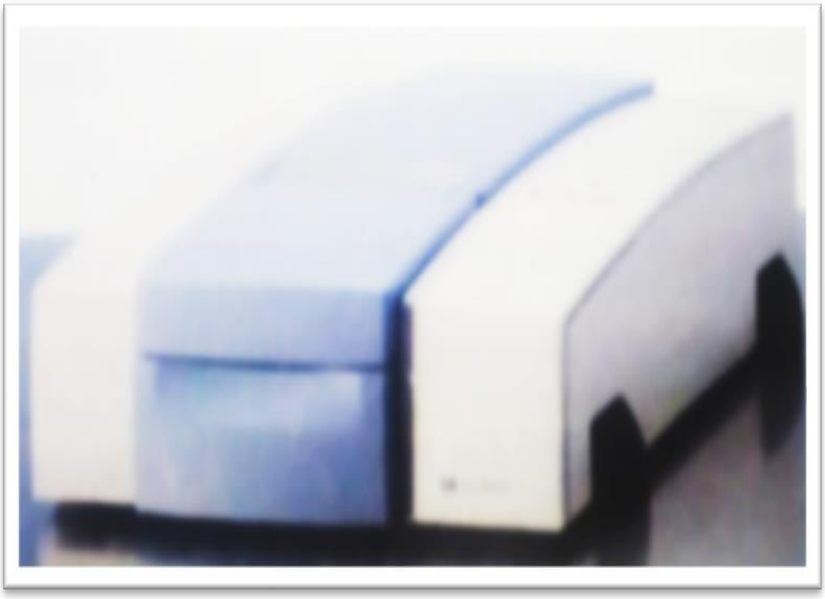

Fig-1: FTIR Instrument

Formulation of pantoprazole core tablet

Table-1: Formulation development

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8
Pantoprazole	40	40	40	40	40	40	40	40
Croscarmellose	10	20	30	40	-	-	-	-
SSG	-	-	-	-	10	20	30	40
Lactose	40	30	20	10	-	-	10	20
MCC	-	-	-	-	-	-	-	-
Talc	5	5	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5	5	5
Total wt	100	100	100	100	100	100	100	100

Formulation of enteric coating suspension

Table-2: Formulation of enteric coating suspension

Ingredients	Quantity
Eudragit RS 100	100
HPMC	100
PEG	0.2
Iso propyl alcohol	0.1ml

Water	0.2
Yellow iron oxide	1

Procedure for Preparation of Pantoprazole Enteric-Coated Tablets[9,10]

1. Mixing and Granulation:

- Pantoprazole sodium and excipients (diluent, binder, superdisintegrant) are accurately weighed.
- The dry powders are blended thoroughly in a mortar or blender to obtain a uniform mixture.
- A binder solution (polymers in water) may be added to the mixture to form a wet mass.
- The wet mass is passed through a sieve to obtain uniform granules.
- Granules are dried at 40–50°C until a constant weight is achieved.

2. Lubrication:

Dried granules are blended with lubricants (magnesium stearate) and glidants (talc) to ensure smooth tablet compression.

3. Compression:

The lubricated granules are compressed into core tablets using a tablet press.
Tablets are checked for weight variation, hardness, and friability before coating.

4. Enteric Coating:

Core tablets are coated with an enteric polymer solution using a pan coating method.
Coating is done until the desired weight gain is achieved (usually 5–10%).
Coated tablets are dried to remove residual solvents.

Evaluation of core tablets [11,12,13]

Weight variation test: The weight variation test was performed to ensure uniformity of the tablet weight and content. For this, 20 tablets were randomly selected from each batch. Each tablet was weighed individually using a digital analytical balance, and the average weight of the batch was calculated.

Friability Test: Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This in-process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. It is usually measured by the use of the Roche Friabilator. Ten tablets are weighed (W1) and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed (W2) and the weight is compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. Normally, when capping occurs, friability values are not calculated. The percent friability was determined using the following formula.

$$\text{Friability} = w1 - w2 / w1 * 100$$

Where,
W1 = weight of ten tablets before test
W2 = weight of ten tablets after test

Hardness test: Hardness, which is now more appropriately called crushing strength determinations are made during tablet production and are used to determine the need for pressure adjustment on tablet machine. If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specifications; if it is too soft, it may not be able to withstand the handling during subsequent processing such as coating or packaging and shipping operations. The force required to break the tablet is measured in kilograms/cm2 and a crushing strength of 4 kg/cm2 is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10 kg; However, hypodermic and chewable tablets are usually much softer (3 kg/cm2) and some sustained release tablets are much harder (10 -20 kg/cm2). Hardness (diametric crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The force is measured in kilograms. The hardness was tested using Monsanto Tester. The tablets were placed horizontally in contact with the lower plunger of the

Monsanto Hardness Tester and zero reading was adjusted. The tablet was then compressed by forcing the upper plunger until the tablets breaks. This force was noted.

Thickness, width and length: Control of physical dimension of the tablets such as thickness, width and length is essential for consumer acceptance and to maintain tablet to tablet uniformly. The dimensional specifications were measured using digital micrometre callipers. The thickness of the tablet is mostly related to the tablet hardness which can be used as initial control parameter.

Drug content uniformity: To ensure the consistency of dosage units, each unit in a batch should have active substance content within a narrow range around the label claim. Dosage units are defined as dosage forms containing a single dose or a part of a dose of an active substance in each dosage unit. The term "Uniformity of dosage unit" is defined as the degree of uniformity for substance among dosage units. The test for content uniformity is based on the assay of the active medicament of content uniformity is necessary the quantity of the active medicament is within the limit in the formulation. Procedure From each batch of the formulation, 10 tablets were collected randomly and powered using a mortar and pestle. A quantity of the powder equivalent to the weight of one tablet (300mg drug) was transferred to a 100ml volumetric flask. To this, about 50ml of distilled water was added and subjected to sonication for 15 minutes. The volume was then made up to 100ml with the same solution. This solution was suitably diluted using distilled water to get a concentration between 5µg/ml to 25µg/ml. These solutions are then analyzed by UV spectrometer as per the calibration graph method by recording the absorbance at 222.6 nm.

In vitro Drug release studies: In vitro drug release of the samples was carried out using USP– type II dissolution apparatus (paddle type). The dissolution medium, 900 ml 0.1N HCl solution, was placed into the dissolution flask maintaining the temperature of 37 + 0.5oC and rpm of 50. One film coated tablet was placed in each paddle of dissolution apparatus. The apparatus was allowed to run for 12hours. Samples measuring 1 ml were withdrawn at regular intervals up to 12 hours using 1 ml syringe. The fresh dissolution medium (37oC) was replaced every time with the same quantity (1ml) of dissolution medium. Collected samples were suitably diluted with 0.1N HCl and analyzed at 222.6 nm using 0.1N HCl as blank. The cumulative percentage drug release was calculated.

Disintegration time: The disintegration time of the coated tablets was determined using the The USP model disintegration appatatus (EI). Six tablets were placed in the basket rack assembly, and was run for 2 hours in 0.1 N HCl media with the discs.The tablets were removed from the solution, gently dried by bloating. The test was then continued by placing the tablets in phosphate buffer ph 6.8, for 1 h, maintaining the temperature at 37±2 oC

Dissolution of Pantoprazole from coated tablets : Thein vitro drug dissolution studies was conducted in an eight stage dissolution apparatus (TDT-08L, Electrolab) using an rotating paddle, at 50 rpm, in 900 ml of silulated gastric fluid, maintained at 37± 0.5 oC. Samples were withdrawn of the gastric media at 2 h and then, the vessel was drained off the acid and was replaced with 900 ml of phosphate buffer pH 6.8.The samples were withdrawn at regular intervals, filtered and suitably diluted. The concentration in acid media and phosphatebuffer was measured with a spectrophotometer (Lambda 25, Perkin Elmer) at 283 and 289 nm, respectively, by comparison to a calibration curve1

Drug release kinetics: [14]The results of in vitro release data obtained for all formulations were fitted in four popular models of data treatments as follows:
1. Zero-order kinetic model (cumulative percentage drug release versus time),
2. First-order kinetic model (log cumulative percentage drug remaining versus time),
3. Higuchi's equation (cumulative percentage drug release versus square root time).
4. Korsmeyer-Peppa's equation (log cumulative percentage drug release versus log time

Zero-order kinetics
When the rate of release of drug is independent of the amount of the drug remaining in the dosage form and constant over a period of time, it is said to be zero-order release. This is expressed mathematically as follows:
$dc/dt=K_r^0$
Where,
C = concentration of undissolved drug,
K0 r = zero order release constant,

t = time
Since "C" is constant, X the amount of drug release is identified as:
dc/dt=K
Integration of the equation (2) yield: $k_t=k_t$+constant
If the data from a release studies followed a zero order release, a plot of X verses t, results in straight line plots with slope equal to K, the value of K would indicate the amount of drug that is releasing per unit time and intercept of the line at zero is equal to the constant in the equation (3).

First-order kinetics
When the rate of release is proportional to the first power of drug in the dosage form and expressed mathematically in the form of equation (4), then the release is said to be first order with respect to drug in the dosage form.
dc/c=K1dt
Where, K1=first order rate constant which on integration yields in natural logarithm form.
lnC= K1t+constant
or in common logarithm form
log C= K1t/2.303
Both equation (5) and (6) will be recognized as producing straight lines if In C and log C is plotted against t, this is an identifying characteristic of a release in which the release is proportional to the concentration of the drug present in the dosage form
The log percentage drug remaining was plotted against time to obtain first order release patterns.

Higuchi's equation
Drug release from the matrix devices by diffusion has been described by following Higuchi's classical diffusion equation.
$Q=(DE/T\ (2A-EC_s))C_{st}$
Where,
Q = Amount of drug release at time t
D = Diffusion coefficient of the drug in the matrix
A = Total amount of drug in unit volume of matrix
Cs = the solubility of the drug in the matrix
E = Porosity of the matrix
T = Time in hrs at which q is the amount of drug is release Equation-3 may be simplified if one assumes that D, Cs and A are constant. Then equation-3 becomes
Q=Kt ½
When the data is plotted according to equation-4 i.e. cumulative drug release versus Square root of time yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to k.

Korsmeyer-Peppa's equation
In order to understand the mode of release of drug from swellable matrices, the data were fitted to the following equation
Log (Mt/Mf)=Log k+n Log t
Where,
Mt is the amount of drug release at time t;
Mf is the amount of drug release after infinite time;
K is a release rate constant incorporating structural and geometric characteristics of the drug release.
The log value of percentage drug dissolved is plotted against log time for each formulation according to equation.
n= diffusion release exponent indicative of release mechanism.

Stability Testing: [15] To evaluate the stability of enteric coated tablets of Pantoprazole and naproxen, the optimized formulations were packed in polyethylene bottles. Accelerated stability studies were conducted by reserving the tablets at room temperature 40± 2 °C and 75± 5 % RH, in a humidity chamber. The samples were withdrawn at the intervals of 0, 1, 2 and 3 months from the date of packing. The physical appearance, assay and the percentage drug release were evaluated to assess the constancy of the tablets.

III.RESULTS AND DISCUSSION

FTIR Studies

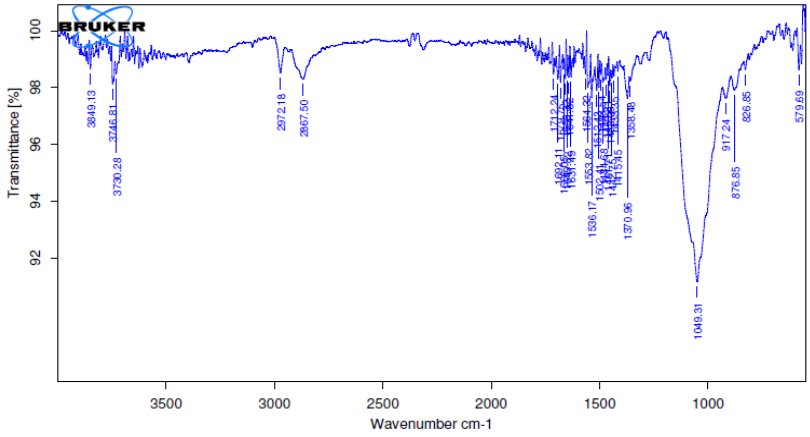

Fig-2: FTIR Studies of Pantoprazole

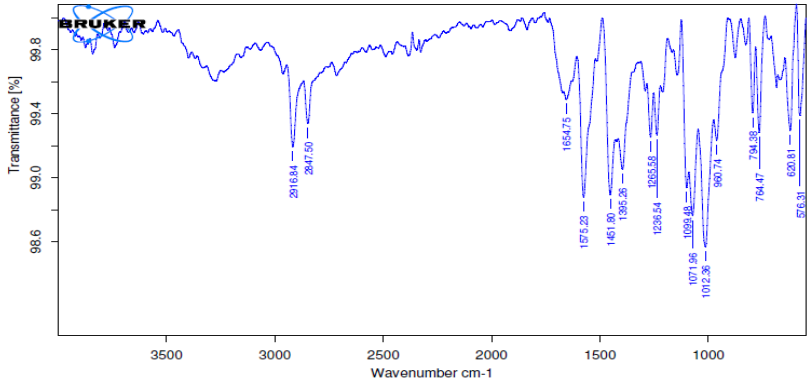

Fig-3: FTIR Studies of Physical mixture of drug and excipients

Evaluation studies

Weight Variation:

The weight of tablets ranged from 199 to 202 mg, which is very close to the theoretical weight of 200 mg. This indicates that the tablets are uniform in weight, reflecting good flow and compressibility of the powder blends, and ensuring consistent drug dosing.

Thickness:

Thickness varied between 1.3 mm and 2.3 mm across the formulations. Minor variations in thickness are acceptable and do not significantly affect tablet performance. Thinner tablets (F7, F8) may be easier to swallow, while slightly thicker tablets (F1) may have higher mechanical strength.

Hardness:

Hardness values ranged from 3.1 to 3.8 kg/cm², which is within the acceptable range for immediate-release tablets. Adequate hardness ensures mechanical stability during handling and packaging, but is not too high to delay disintegration.

Friability:

Friability values were between 0.22% and 0.31%, well below the 1% limit set by pharmacopoeial standards. This indicates that the tablets are mechanically strong and resistant to abrasion, suitable for transport and storage.

Drug Content (%):

Drug content ranged from 89.33% to 94.28%, indicating acceptable uniformity. Slight variations may be due to mixing efficiency or the presence of different superdisintegrants. All values are within the pharmacopoeial limit of 85–115%, confirming content uniformity.

Disintegration Time:
Disintegration times varied from 11 to 19 minutes, depending on the type and concentration of superdisintegrant used.Formulations F2, F3, F5, F6, F7, and F8 disintegrated within 12–14 minutes, which is acceptable for immediate-release enteric-coated tablets in intestinal pH.Longer disintegration times (F1, F4) may be due to lower superdisintegrant efficiency or higher tablet thickness.

Table-3: Evaluation parameters of delayed release tablets

F. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)	Disintegration time(min)
F1	200	2.3	3.5	0.25	89.33	17
F2	199	1.5	3.4	0.22	92.55	12
F3	201	2.0	3.8	0.24	90.22	11
F4	200	1.8	3.1	0.26	89.57	19
F5	202	1.7	3.7	0.30	92.46	12
F6	199	1.5	3.6	0.29	93.47	13
F7	200	1.4	3.5	0.30	94.28	14
F8	201	1.3	3.2	0.31	90.85	12

In-vitro Dissolution Study
All the 8 formulation of prepared delayed release matrix tablets of naproxen and Pantoprazole were subjected to in-vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for the 8 hrs.

Table-4: Dissolution Profile of F1 to F8

Time (hrs.)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	26.72	26.50	25.22	24.59	25.19	26.93	28.30	27.59
2	35.63	31.15	32.81	31.22	32.56	33.22	32.42	33.65
3	40.92	38.65	39.90	35.65	42.39	43.59	41.18	43.19
4	52.65	48.23	53.41	55.98	56.39	52.36	50.90	51.37
5	61.25	59.95	65.50	66.49	65.81	65.24	63.82	65.91
6	73.12	72.82	74.84	75.82	76.83	75.66	73.86	75.89
7	80.19	81.84	83.90	84.69	85.10	83.65	84.82	85.20
8	91.16	92.32	93.25	94.56	93.22	97.81	98.12	97.53

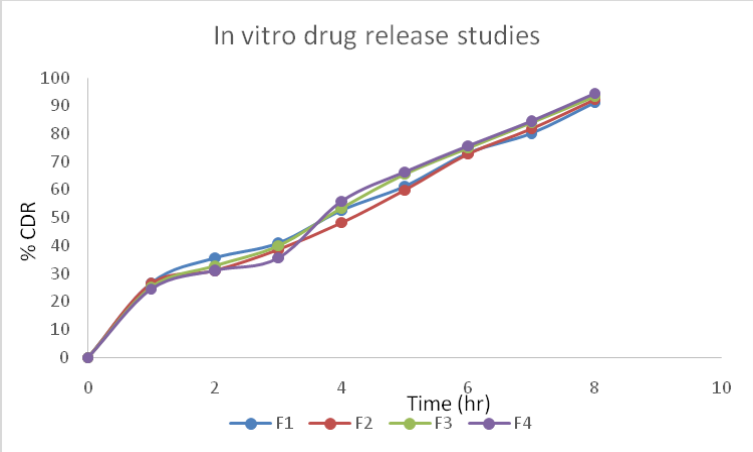

Fig-4: In vitro drug release studies of F1-F4 formulations

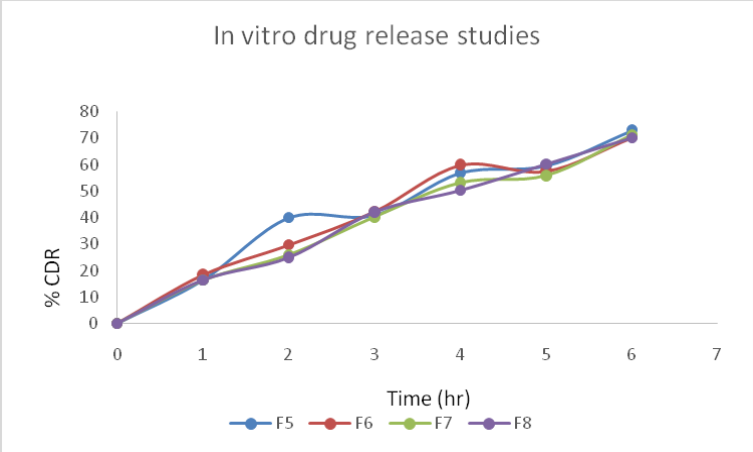

Fig-5: In vitro drug release studies of F5-F8 formulations

Release order kinetics:

Zero order kinetics:

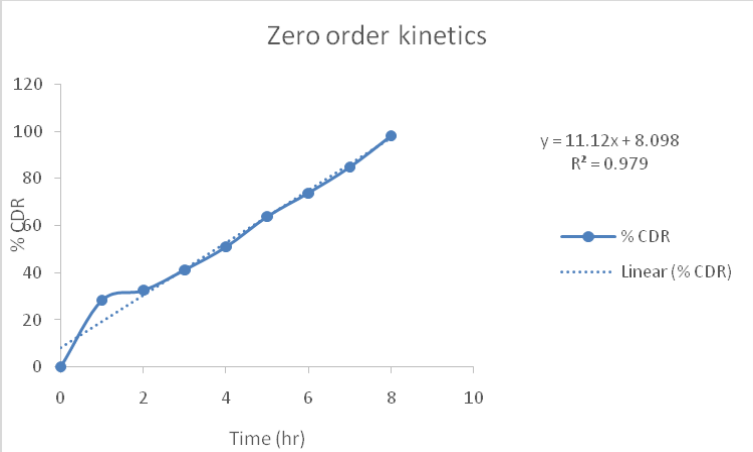

Fig-6: Zero order plot for optimized formula

First order kinetics

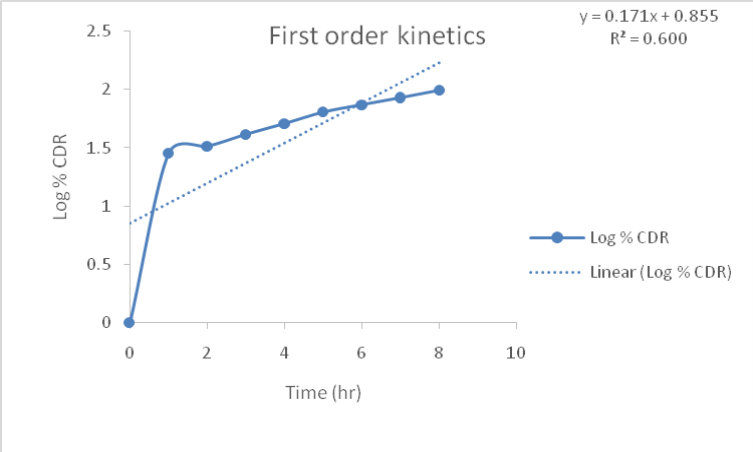

Fig-7: First order for optimized formula

Higuchi plot

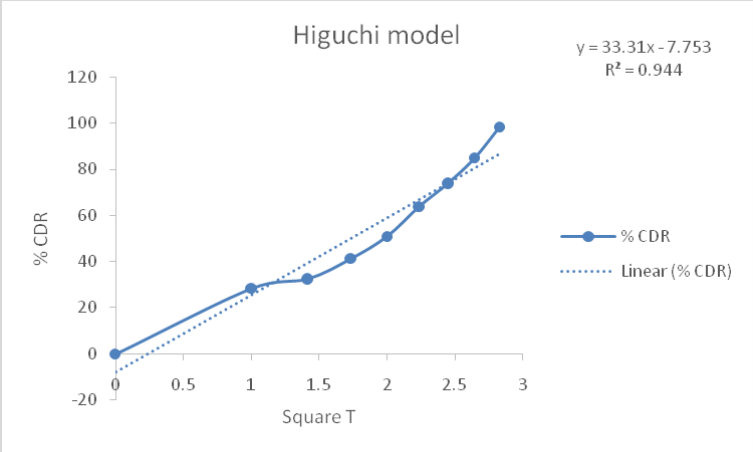

Fig-8: Higuchi plot for optimized formula

Korsmeyer peppas

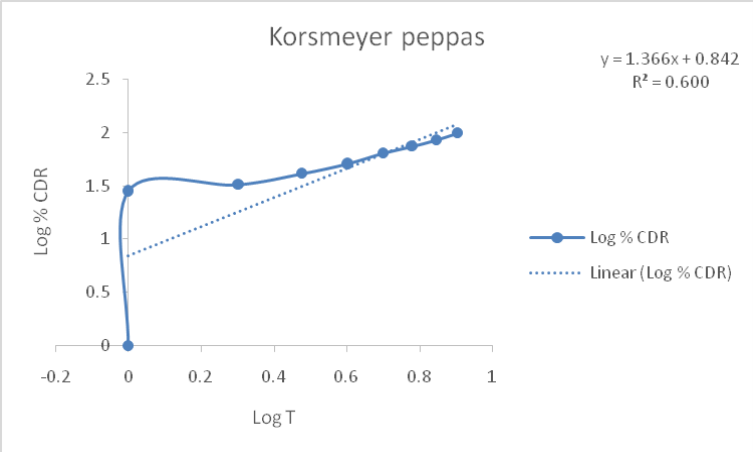

Fig-9: Korsmeyer peppas plot for optimized formulation

Stability studies

DR tablets formulated in the present study were subjected to accelerated stability studies. Stability studies of the prepared formulations were performed at ambient humidity conditions, at room temperature, at 25, 30, 40°c and 2-8°c for a period up to 90 days.

Table-4: Results of stability studies of optimized formulation F-7

F. Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-7	25°C/60%RH % Release	98.12	97.86	96.17	96.55	Not less than 85 %
F-7	30°C/75% RH % Release	98.12	97.52	96.18	96.28	Not less than 85 %
F-7	40°C/75% RH % Release	98.12	97.16	96.33	96.20	Not less than 85 %

CONCLUSION

Pantoprazole Sodium enteric-coated tablets were successfully formulated with different superdisintegrants, and all batches exhibited acceptable pre- and post-compression properties, ensuring uniformity, mechanical strength, and drug content. The enteric coating protected the acid-labile drug, and formulations with crospovidone

(F6 and F7) showed optimal disintegration and potential for enhanced bioavailability.These findings indicate that the developed pantoprazole enteric-coated tablets are suitable for oral administration, with improved therapeutic efficacy and patient compliance, and can be further considered for commercial formulation and clinical use.

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