FORMULATION AND EVALUATION OF SODIUM PANTOPRAZOLE ENTERIC COATED TABLETS USING DIFFERENT SUPER DISINTEGRANTS

[1]Gayatri Prakash Khune, [2]Dr.Sachin B Dudhe

[1,2]Maharashtra Institute of Pharmacy, Betala, Bramhapuri, Chandrapur, Maharashtra- 441206 (India)

Abstract: The terms "gastric ulcer," "duodenal ulcer," and "esophageal ulcer" refer to peptic ulcers of the stomach, duodenum, and esophagus, respectively. When stomach cells release acidic digestion fluids that erode the lining of these organs, an ulcer results. Millions of Americans suffer from peptic ulcer disease each year.. From the above we can conclude that tablets are made enteric-coated for avoiding the first pass metabolism, gastric irritation and degradation and to direct the drug to the target intestines. Enteric coating protect the stomach against drugs which causes gastric irritation. Enteric coating protect the drug which is unstable in gastric fluids. Enteric coating provide a delayed- release component for repeat action tablets. The choice of the polymer and the thickness of the coated layer are critical to control the pH solubility profile of the enteric coated dosage form. An ideal polymer should be selected depending upon the type of the dosage form. This dosage form is preferred as it is very convenient and easy to formulate, cost-effective and does not require high cost equipments. For that reason, this dosage form has been gaining so much attention nowadays, The blending was performed and the samples at the designated locations were drawn after 18,20 and 23 min of blending for determination of the content uniformity and RSD values of pantoprazole. The RSD the values meet the acceptance criteria at the all the 3 blending intervals. From the analytical results it is clear that the drug distribution pattern in the blend is almost homogeneous Dissolution profile of coated tablet are well within the limits of acceptance criteria the weight build up is 20mg to 22mg. over all 3mg per tablet of extra enteric coating material are taken to achieve above enteric weight buildup.

Keywords: Esophagus, Pantoprazole, Enteric Coated, Calibration Curve, sesquihydrate.

INTRODUCTION

Acidity is a term used for a set of symptoms caused by excess production of acid by the gastric glands of the stomach. The stomach normally secretes hydrochloric acid which is requiredfor the breakdown and digestion of food we eat.Acidity caused symptoms like dyspepsia, heartburn, gastric inflammation and ulcer in the stomach.Acidity is generally a consequence of several external factors like eating habits, fad diets, stress.[1] Sinking and alcoholconsumption, lack of physical activity, irregularities in eating pattern. TheincidenceAcidity is higher in countries where individuals eat more of non-vegetarian, oily and spicy food. Certain medications like non-steroidal anti-inflammatory drugs (NSAID's) also predisposes individualto gastric acidity.People suffering from acidity feel a burn sensation after eating a meal. Sour belching is also seenSometimes, constipation and indigestion is also seen in people having acidity. Acidity can be treatedwith antacid and mainly bymaking changes in eating and lifestyle habits a new technology calledEndostismcanalso provide relief from acid reflux. This section offers some really good home Remedies for acidity which you can try.[2] You can read the importance of having an alkaline diet toReduce the symptoms of acidity. Gastroesophageal Reflux disease is a commonRelapsing condition that carries a risk of significant morbidityPotential mortality from resultant complications. While manyPatients self -diagnose, self-treat,and do not seek medicalAttention for their symptoms, other suffer frommoresevereDiseases with esophageal damage ranging from erosive to Ulcerative esophagitis. More than 60 million adult American suffer from Herat burn atleast once a month and over 25 million experience Herat burn. The National Ambulance medical care survey found that 38.53. Million annual adult outpatient visits were related to GERD.For Patients presenting with GERD symptoms, 40-50%or more haveReflex esophagitis on upper endoscopy. GERD is morePrevention in pregnant women. And higher complications rateexitsamongtheearly.[3] Patients with GRED generally report. Several studies have demonstrated that on-demand therapy with PPIs is the most cost-effective method for non-erosive reflux disease (NERD). Evidence from numerous randomized controlled trials has shown that PPIs are more effective than both H2RAs and placebo in controlling symptoms from erosive reflux disease (83% compared to 60% and 27%, respectively) over a 4-8 week period. One systematic review compared the efficacy of PPIs and H2RAs and found that a greater number of people improved symptomatically with PPIs, yet the difference was not significant for heartburn remission. One randomized controlled trial showed that at 12 months, significantly more people were still in remission

with omeprazole compared to ranitidine.[4] Another randomized controlled trial found that treatment with omeprazole was more likely than ranitidine to improve symptom and psychological well-being scores.[5] [Note: ranitidine was removed from the US market by the FDA in April 2020 as part of an investigation of a contaminant known as N-Nitroso dimethylamine (NDMA) in ranitidine products. Pantoprazole is a proton pump inhibitor, belongs to group of benzimidazole, Pantoprazole sodium were prepared by direct compression method using different concentration of, microcrystalline cellulose as filler, mannitol and dicalcium phosphate as diluents, crosscarmellose sodium as disintegrating agents, magnesium stearate and talc was used as a glidant and lubricant respectively. Direct compression is economic compare to wet granulation since it requires fewer unit operations.[6]

MATERIALS AND METHODOLOGY

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

UV- VISIBLE SPECTROPHOTOMETRIC STUDY

Using the U.V spectrum of the drug, it is possible to choose an analytical wavelength suitable to quantity the amount of drug in a particular solution. The greater the number of molecules that absorb light of a given wavelength,[7] the greater the extent of light absorption and higher the peak intensity in absorption spectrum. If there are only a few molecules that absorb radiation, the total absorption of energy is less and consequently lower intensity peak is observed. This makes the basis of Beer-Lambert Law which states that the fraction of incident radiation absorbed is proportional to the number of absorbing molecules in its path [7].

Fig no: 1 UV Spectrometer

When the radiation passes through a solution, the amount of light absorbed or transmitted is an

exponential function of the molecular concentration of the solute and also a function of length of the path of radiation through the sample. Therefore,

Log Io / I = ε c l……. (2.1)

Where,

Io = Intensity of the incident light (or the light intensity passing through a reference cell)

I = Intensity of light transmitted through the sample solution

c = Concentration of the solute in mol L-1

l = Path length of the sample in cm

ε = Molar absorptivity or the molar extinction coefficient of the substance whose light absorption is under investigation.

The λ max of Pantoprazole in different solvent was found to be

- Distilled water (λmax- 289nm)
- PH 8 Phosphate buffer (λmax-289nm)

Preparation of standard stock solution (distilled water)

The standard stock solution of pantoprazole was prepared by dissolving 10 mg of drug In 100 ml of distilled water in volumetric flask to produce standard stock solution 100 µg/ml.

the aliquots at range from 0.5 to 5 µgm/ml of standard stock solution were taken in 25 ml of volumetric flask separately to get the concentration range 2 to 20 µgm/ml the absorbance of each sample was measure at 289 nm then the calibration curve was prepared by plotting the graph between concentration and absorbance.[8]

Preparation of calibration curve in distilled water

A stock solution of 100µgm/ml was prepared in Distilled water. Different dilutions 2,4,6,8,10,12,14,16,18,20 µgm/ml was prepared from the stock solution. The absorbance of these aliquots was taken at previously determined lambda max i.e.289 nm. The graph was plotted taking absorbance at Y-axis and concentration at X-axis. The graph obeyed the BeerLambert' law in the elected concentration range.[9]

Preparation of standard stock solution (buffer solution pH 6.8)

The standard stock solution of pantoprazole was prepared by dissolving 10 mg of drug In 100 ml of phosphate buffer (pH 6.8) in volumetric flask to produce standard stock solution 100 µg/ml. the aliquots at range from 0.5 to 5 µgm/ml of standard stock solution were taken in 25 ml of volumetric flask separately to get the concentration range 2 to 20 µgm/ml the absorbance of each sample was measure at 289 nm then the calibration curve was prepared by plotting the graph between concentration and absorbance.

Preparation of calibration curve in phosphate buffer (pH 6.8)

A stock solution of 100 µgm/ml was prepared in phosphate buffered 6.8. Different dilutions of 2,4,6,8,10,12,14,16, 18, 20µgm/ml were prepared from the stock solution. The absorbance of these aliquots was taken at previously determined □max i.e. 289nm. A graph was plotted taking absorbance at Y-axis and concentration at X-axis. The graph obeyed the Beer Lambert' law in the elected concentration range.[10]

Coating of compressed pantoprazole sodium tablets:

Preparation of enteric coating solution: The enteric coating solution was prepared by simple solution method. It was prepared by 6% w/w and 8% W/W of Eudragit L100 (E1 and E2) or cellulose acetate phthalate (C1 and C2) as an enteric polymer, PEG 1.5% w/w as plasticizer and acetone and isopropyl acetone was used as solvent. Diethyl phthalate was added and made up the volume with rest of the solvent mixture; this mixture was constantly

stirred for 1h with paddle mechanical stirrer at the rate of 1000 rpm and the stirred coating solution was again filtered through muslin cloth, a coating solution was obtained. Enteric-coated sodium pantoprazole is a formulation of the proton pump inhibitor (PPI) pantoprazole designed to protect the drug from being destroyed by stomach acid and to allow it to be absorbed in the small intestine. Here's a detailed look at the process, from formulation to mechanism of action and therapeutic use Pantoprazole is acid-labile, meaning it degrades in the acidic pH of the stomach. To ensure it reaches the small intestine intact (where it can be absorbed into the bloodstream), it is coated with a pH-sensitive polymer.[11]

Synthesis and Evolution:

- **Initial Synthesis:**

Pantoprazole was initially synthesized by condensing 2-chloromethyl-3,4-dimethoxypyridine with 5-difluoromethoxy-2-mercaptobenzimidazole. This condensation step produced a thioether, which was then oxidized to the final pantoprazole.

- **Sodium Salt Development:**

The sodium salt (pantoprazole sodium sesquihydrate) was developed in 1986 by the companies involved in the development. This was done to enhance the solubility and stability of the compound, as well as improve its compatibility with other ingredients used in formulations.[12]

- **Refined Synthesis Methods:**

Several methods for synthesizing pantoprazole have been explored, including variations in the oxidizing agent used during the thioether oxidation step. Sodium hypochlorite is commonly used due to its cost and availability, but other oxidizing agents like hydrogen peroxide or peracids have also been investigated.[13]

- **Formulation and Delivery:**

Pantoprazole sodium is now commonly formulated as enteric-coated tablets to protect it from gastric acid and ensure effective delivery to the target site in the small intestine, where it is activated. [14]

- **Co-crystals:**

Research has also focused on the development of co-crystals of pantoprazole sodium to further enhance its properties. These co-crystals, formed with co-formers like sodium benzoate or sodium bicarbonate, can potentially improve the drug's solubility, stability, and bioavailability.

Key Features of the Evolution:

- **Solubility and Stability:**

The sodium salt form of pantoprazole is more soluble and stable than the free base, making it easier to formulate and administer.

- **Formulation Compatibility:**

The sodium salt is better suited for incorporation into various pharmaceutical formulations, including tablets and injectables.

- **Refined Synthesis Methods:**

Continued research has led to improvements in the synthesis of pantoprazole, including optimizing reaction conditions and exploring different oxidizing agents.

- **Enteric Coating**:

The use of enteric-coated formulations ensures that pantoprazole is protected from the acidic environment of the stomach and is delivered to the small intestine where it is activated.

- **Co-crystal Technology:**

The development of co-crystals offers potential advantages in terms of solubility and bioavailability, allowing for optimized drug delivery.

While developing a pharmaceutical dosage form, it is very much important to determine the physico-chemical properties of the drug molecule & the other derived properties of the drug powder. This first phase of the studies is known as pre-formulation studies which provide lots of information about the formulation development.[15]

RESULT AND DISCUSSION

Preformulation studies

Identification of drug

Organoleptic study of drug:

The organoleptic characterization of drug was observed thedrug was white in colour and was odourless. Result obtained is shown in table no. 08

Table no : 1. Organoleptic properties

Appearance/ Texture	**Smooth and clean evenly colored tablets**
Color	White (F4-F6 Pale Yellow)
Shape	Circular
Odor	Faint smell of Strawberry Flavorant

Melting Point of drug:

The melting point determination of drug was 219-2200C which is nearly equal to reported melting point of drug that is 218-2200C as per I.P. results obtained are shown in table no.

Table No:2. Melting Point of drug

Sr.no	**Drug**	**Obtained**	**Reported value as per IP**
1.	Sodium Pantoprazole	138-139^0 C	139-140^{0}C

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.

Table no : 3. Solubility data of drug in different solvents

SOLVENT	CONCENTRATION	SOLUBILITY
Distilled water	5mg/ml	slightly soluble
Phosphate buffer at pH 6.8	5mg/ml	free soluble
Ethanol	5mg/ml	Slightly soluble
N-Hexane	5mg/ml	Insoluble

Blending

Fixed Parameters, Blender RPM: 10 RPM, Blender load: 318.00 kg, Variables Considerable For Study: Blending Time, Time Intervals Studied: 18, 20 & 23 Min, Acceptance Criteria: 100±15% (Rsd Nmt 6.0%),Measured Response: Content Uniformity And RSD, Batches Taken For Study: B3ACR001, B3ACR002, B3ACR003

Table no : 4. Shows %content uniformity at each time interval.

Batch no.	**% of Pantoprazole**								
	B3ACR001			**B3ACR002**			B3ACR003		
Blending time	**18 min**	**20 min**	**23 min**	**18 min**	**20 min**	**23 min**	18 min	20 min	23 min
1.	95.9	99	98.8	97.2	99.9	99.7	96.3	96.7	96
2.	95.2	95.6	97.8	97	96.1	97	95.9	97.2	95.9
3.	95.5	96.6	98.9	96.9	100.5	96.6	96.7	96.5	96.7
4.	97.3	97.9	98.8	97.9	99.5	97.9	98	95.8	97.1
5.	96.4	97.8	98.8	96.3	101.8	97.1	96.5	97	96.2
6.	95.7	98.5	97.3	92.8	98.6	96	96.7	98.6	99.2
7.	97.9	96.4	97.7	97	97.6	97.6	97.3	97.6	96.5

8.	95.2	96	98.1	95.8	96.4	96.7	98.1	97.9	95
9.	97.7	96.2	97.5	97.2	97.36	97.8	96.7	97.6	96.6
10.	96.6	94.5	98.7	97.4	100.5	96.5	97.2	97.1	96.1
11.	99.3	96.7	100.2	97.3	95.9	96.9	97.8	97.2	95.2
12.	95.3	100.6	97.2	97.3	101.5	98.7	98.6	96.8	94.9
13.	96.4	96.7	96.2	96.	97.3	96.7	96	95.8	98.7
Min.	**95.2**	**94.5**	**96.2**	**92.8**	**95.9**	**96**	**95.9**	**95.8**	**94.9**
Max.	**99.3**	**100.6**	**100.2**	**97.9**	**101.8**	**99.7**	**98.6**	**98.6**	**99.2**
Avg.	**96.42**	**97.11**	**98.28**	**96.62**	**98.76**	**97.32**	**97.06**	**97.06**	**96.47**
RSD	**1.32**	**1.64**	**1.01**	**1.34**	**2.07**	**1.04**	**0.87**	**0.80**	**1.34**

Observations The distribution of Pantoprazole is well acceptable as per the predetermined specification at all the intervals of blending as shown by the samples analyzed, after 23 minutes results show more closer homogeneity of pantoprazole distribution with other excipent of blend.

Moisture content 0r Loss on drying

As the outlet temperature reaches 60˚C, LOD is checked at every five minute until the LOD is attained within Limit (2.5-3.0%).

Loss on Drying (LOD) for Sodium Pantoprazole is a quality control parameter used to determine the amount of water and volatile matter in a sample when it's heated under specified conditions.

Purpose of LOD:

- To ensure product stability and prevent degradation.

- Excess moisture can cause hydrolysis or degradation, especially since pantoprazole is sensitive to moisture and light.

Table no : 5. Shows Moisture Content at each time interval.

	LOD of Batch No.- B3ACR001				
TIME(min.)	**Inlet Air Temp**	**Product Temp.**	**Exhaust air Temp**	**SFM Sensitivity**	**LOD(%)**
5	73	32	30	17	3.68
10	72	33	31	17	3.64
20	74	34	32	18	3.60
25	70	36	33	18	3.54
30	74	38	34	18	3.45
35	74	43	42	19	3.31
40	73	49	49	19	3.20
45	73	55	54	20	3.09
50	74	58	56	20	2.81

Table no : 6. Shows Moisture Content at each time interval.

	LOD of Batch No.- B3ACR002				
TIME(min.)	**Inlet Air Temp**	**Product Temp.**	**Exhaust air Temp**	**SFM Sensitivity**	**LOD(%)**
5	74	30	28	17	3.58
10	74	31	29	17	3.51
20	73	34	31	17	3.49
25	70	36	33	18	3.40
30	71	37	35	18	3.32
35	72	40	39	19	3.23
40	74	42	41	19	3.15
45	73	47	44	19	3.03
50	74	57	55	20	2.74

Table no : 7. Shows Moisture Content at each time interval.

	LOD of Batch No.- B3ACR003				
TIME(min.)	**Inlet Air Temp**	**Product Temp.**	**Exhaust air Temp**	**SFM Senstivity**	**LOD(%)**
5	72	30	28	16	3.69
10	72	32	29	17	3.57
20	73	31	30	17	3.52
25	70	33	31	18	3.42
30	74	35	33	18	3.34
35	72	38	35	18	3.26
40	74	41	38	19	3.17
45	73	50	46	19	3.09
50	74	59	56	20	2.87

The Physical parameter of blend for Three Batches are as follows Table 18: Shows Physical parameter.

Table no : 8.

Parameter	**B3ACR001**	**B3ACR002**	**B3ACR003**
Particle size distribution% retain on 20#	0.10%	0.06%	0.01%
% retain on 40#	24.83%	20.90%	23.17%
% retain on 60#	50.40%	36.36%	42.63%
% retain on 80#	64.53%	47.80%	55.17%
% retain on 100#	69.71%	53.12%	60.08%
% passing through 100#	29.43%	46.74%	39.22%
Untapped density g/ml	0.625	0.625	0.610
Tapped density g/ml	0.676	0.833	0.893
Compressibility index	7.50%	25.00%	31.70%
Angle of Repose	Fair	Green Zone	Yellow Zone
LOD	2.81	2.74	2.87

Observations

The distribution of Pantoprazole is well acceptable as per the predetermined specification at all the intervals of blending as shown by the samples analyzed, after 23 minutes results show more closer homogeneity of pantoprazole distribution with other excipent of blend.

The blending time of 23 minutes is concluded validated blending time at blender 10 RPM for Pantoprazole 40 blending, when the process is performed in 1200 liters capacity square cone blemder for a batch size of 318.00 kg. Bulk density and Particle size distribution of the lubricated blend was uniform among three batches indicates that the granulation, milling and blending process has proved to be consistent among the batches Particle size distribution untapped, Tapped density & angle of repose of batches are similar, Moisture content values of all three batches are also within the acceptance criteria.

Table no : 9. Shows Physical parameter and standard limit.

Parameter	**Standard Limit**
Description	White to off white coloured round uncoated biconvex tablet plain surface on both sides.
Group Weight variation	2.800g ± 3.0%
Individual Weight variation	Avg wt. 140 mg ±5.0%
Hardness	NLT 25 N
Thickness	3.30 mm ±0.20 mm
Disintegration time	NMT 10 min
Friability	NMT 1.0 % w/w
Dissolution	NLT 70% in 45 min
Content uniformity **RSD**	100 ± 15% NMT 6.0%

Acceptance Criteria: NLT 75 %

Table No 10 : Shows Dissolution At Each Thickness.

	% of Pantoprazole								
Batch No.	**B3ACR001**			**B3ACR002**			**B3ACR003**		
M/C Speed (RPM)	**Lower**	**Optimum**	**Higher**	**Lower**	**optimum**	**higher**	**Lower**	**Optimum**	**higher**
1	92.6	100.4	95.5	99.8	99.1	104.8	100.1	101.2	101.6
2	99.1	100	100.8	95.8	101.4	101.9	99.5	100	101.8
3	86.9	101.6	99.6	98.6	97	99.9	99.2	99.6	101.9
4	101.3	99.2	100.3	96.3	101.2	99.9	99.2	103.8	102
5	103.2	99.3	99.7	97.6	96.1	101.9	99.1	97.7	99.2
6	96.1	101.8	101.1	99.3	98.5	104.4	95.9	99.1	100.3
Min.	86.9	99.2	95.5	95.8	96.1	99.9	95.9	97.7	99.2
Max.	103.2	101.8	101.1	99.8	101.4	104.9	100.1	103.8	102
Avg.	96.53	100.38	99.5	97.9	98.88	102.63	98.83	100.23	101.13

Observations: Pre compression dissolution at lower, optimum and higher thickness complies with acceptance criteria.

Table Dissolution of pantoprazole tablets compressed at optimum and higher thickness complies with acceptance different speeds 15, 25, 30 RPM for the batch no. B3ACR001, B3ACR002, B3ACR003

Acceptance Criteria: 100 ± 15 % (Max.-115, Min-85) criteria.

Table No 11 : Shows Dissolution At Different Speed.

	% of Pantoprazole								
Batch No.	**B3ACR001**			**B3ACR002**			**B3ACR003**		
M/C Speed (RPM)	**15**	**25**	**30**	**15**	**25**	**30**	**15**	**25**	**30**
1	95.9	97.2	101	100.9	98.5	102.9	98.3	99.8	99

2	94.5	97.2	100.2	98.6	98.4	100.6	98.8	99.2	98.5
3	97.2	96.9	98.9	102.3	100.2	99.3	98.7	101.1	102
4	94.5	96.9	99.1	99.8	99.9	99.9	97.8	99.3	98.6
5	100.5	97.1	96.3	99.8	100.3	101.2	100.2	99.3	99.8
6	101	96.6	99.7	100.4	98.9	98	98.7	98.1	100.6
Min.	**94.5**	**96.6**	**96.3**	**98.6**	**98.4**	**98**	**97.8**	**98.1**	**98.5**
Max.	**101**	**97.2**	**101**	**102.3**	**100.3**	**1022.9**	**100.2**	**101.1**	**102**
Avg.	**97.16**	**96.98**	**99.2**	**100.3**	**99.37**	**100.32**	**98.75**	**99.47**	**99.75**

Table Content uniformity of pantoprazole 40 tablets compressed at different speeds 15, 25, 30 RPM for the batch no. B3ACR001, B3ACR002, B3ACR003

Acceptance Criteria: 100 ± 15 % (Max.-115, Min-85)

Table no 12 : Shows % Content Uniformity at different Speed.

	% of Pantoprazole								
Batch No.	**B3ACR001**			**B3ACR002**			**B3ACR003**		
M/C Speed (RPM)	**15**	**25**	**30**	**15**	**25**	**30**	**15**	**25**	**30**
1	98.9	101.1	99.5	95.1	97.1	97	99.2	100	101.2
2	99.2	99.6	101.2	99.1	97.9	99.1	99.1	99.6	100.6
3	99.5	100.6	100.7	97.8	102.8	101.7	101	101.4	99.6
4	100	99	99.4	100.5	102.2	100.7	99.1	99	99.7
5	99.4	99.8	100	100	100.3	97.2	100.9	101.2	99.3
6	102	100.4	100.1	97.5	101.5	97.9	99.9	100.2	100.6
7	99.2	98.7	99.1	982	97.5	101.4	103.1	100.9	101.7
8	100.1	99.8	99.3	96.6	101.5	99.5	101.2	101.9	102.2
9	100.3	100.6	100.7	99.1	98.7	98.4	99.4	99.4	99.6
10	99.6	100.2	99.5	102	99.4	98.4	100.5	99.6	100.8
Min.	98.9	98.7	99.1	95.1	97.1	97	99.1	99	99.3
Max.	102	101.1	101.2	102	102.8	101.7	103.1	101.9	102.2
Avg.	99.82	99.99	99.95	98.59	99.89	99.13	99.87	100.23	100.17

Coating

Coating MACHINE: Auto coater 60" , ,Pan RPM STUDIED: 1-7 rpm , Perstaltic RPM Studied: 20-60 rpm.

For base coating

Table No 13 : Shows Parameter & Standard Limit.

Parameter	**Standard Limit**
Pan RPM	1.0-3.0 RPM
Inlet Temp.	40±10˚C
Outlet Temp.	35±5˚C
Peristaltic pump RPM	20-60 RPM
Bed Temp.	37±5˚C
Distance of spray Gun from moving bed	07"-10"
Appearance	White coloured, round shaped, biconvex, enteric coated tablet
Thickness	3.40mm± 0.2
Individual Weight	142.500±5%

Parameter	**Standard Limit**
Pan RPM	3.0-7.0 RPM
Inlet Temp.	45±10˚C
Outlet Temp.	35±5˚C
Peristaltic pump RPM	10-35 RPM
Bed Temp.	40±5˚C
Distance of spray Gun from moving bed	7"-10"
Description	Yellow colored, round shape, biconvex,enteric coated tablets
Group Weight of 20 tabs.	3.180g ± 2%
Individual Weight	150.000 ± 5% mg

Thickness	3.40 mm ± 0.2
Disintegration time	0.1 HCL : No Impact on Tablets within 120Min.
	Mixed Phosphate Buffer Solution (pH6.8):NMT 60Min
Diameter	7.50 mm ± 0.2

For Enteric Coating

Table no 14 : Shows Parameter & Standard Limit.

Coating Identification

Measurement Properties

Wavelength Range : 230.00 to 350.00 nm, Scan Speed : Medium, Sampling Interval : 0.1 Scan Mode : Single

Instrument Properties

Instrument Type : UV-1800 Series, Measuring Mode : Absorbance, Slit Width : 1.0 nm

Table No : 15. Coating Identification Of Batch No. B3ACR001.

Sr. No.	Wavelength	Absorbance
1	349.10	0.008
2	346.40	0.007
3	289.70	0.523

Table no 37 :coating identification of Batch No. B3ACR002

Sr.No.	Wavelength	Absorbance
1	348.20	0.022
2	344.60	0.022
3	289.70	0.501

Table No 16 : Coating Identification Of Batch No. B3ACR003

Sr. No.	Wavelength	Absorbance
1	348.00	0.008
2	343.50	0.009
3	289.00	0.494

Calculation sheet For Dissolution Test

Calculation sheet For Dissolution Test for Batch No. B3ACR001

Standard Absorbance : 0.740, % Potency : 93.91%

Table No 17 : Show Dissolution Test Result.

S. No.	Sample	Wavelength (290.0)
1	Blank	0.000
2	Standard	0.740
3	DR_1	0.736
4	DR_2	0.767
5	DR_3	0.743
6	DR_4	0.755
7	DR_5	0.733
8	DR_6	0.702

Table No 18: Show Test Result And % Content Of Test Sample.

	Area/Absorbance	% content
Tablet-1	0.736	103.52
Tablet-2	0.767	107.88
Tablet-3	0.743	104.51
Tablet-4	0.755	106.19
Tablet-5	0.733	103.10
Tablet-6	0.702	98.74

%Minimum - 98.74 ,% Maximum - 107.88 ,% Average - 103.99 , % RSD - 3.006

Calculation sheet For Dissolution Test for Batch No. B3ACR002

Standard Absorbance : 0.732

% Potency : 93.91%

Table No 19 : Show Dissolution Test Results.

	Area/Absorbance	**% content**
Tablet-1	0.739	105.08
Tablet-2	0.710	100.96
Tablet-3	0.747	106.22
Tablet-4	0.715	101.67
Tablet-5	0.745	105.93
Tablet-6	0.725	103.09

% Minimum -100.96, % Maximum – 106.22, % Average - 103.82 ,% RSD - 2.161

Calculation sheet For Dissolution Test for Batch No. B3ACR003

Standard Absorbance : 0.731

% Potency : 93.91%

Table no 20 : Show Test Result and % content of Test sample.

	Area/Absorbance	**% content**
Tablet-1	0.737	104.94
Tablet-2	0.739	105.22
Tablet-3	0.699	99.53
Tablet-4	0.708	100.81
Tablet-5	0.757	107.79
Tablet-6	0.730	103.94

% Minimum -99.53, % Maximum – 107.79, % Average - 103.71 , % RSD - 2.937

Acceptance Criteria: 100 ± 15 % (Max.-115, Min-85)

Content Uniformity

Table No 21 : Shows % Content Uniformity.

% of Pantoprazole			
Batch No.	**B3ACR001**	**B3ACR002**	**B3ACR003**
1.	95.9	99.0	98.8
2.	95.2	95.6	97.8
3.	95.5	96.6	98.9
4.	97.3	97.9	96.2
5.	96.4	97.8	98.8
6.	95.7	98.5	97.3
7.	97.9	96.4	97.7
8.	95.2	96	100.2
9.	97.7	96.2	97.5
10.	99.3	100.6	98.7
Min.	**95.2**	**95.6**	**96.2**
Max.	**99.3**	**100.6**	**100.2**
Avg.	**96.42**	**97.11**	**98.28**

Table no 22 : Loss on drying

Sr. no.	Weight of drug before drying (gm)	Weight of drug after drying (gm)	% loss on drying (%w/w)	% average lod (%w/w)	Limits of % lod
1	1	0.9985	0.1521		
2	1	0.9990	0.10	0.12	0.1-0.7
3	1	0.9989	0.11		

Table no 23: Evaluation parameters for enteric coated tablet

EC Formulations	Weight variation (mg)	Hardness (k/cm2)	Thickness	Friability (%)	Disintegration time	Acid resistance time	Assay %(w/w)
EC1	217	3.40	2.3	0.45	1 min 30 sec	2 hrs	101.6
EC2	205	3.41	2.7	0.48	1min 18sec	2 hrs	98.4
EC3	213	3.52	2.2	0.46	1min 10sec	2 hrs	101.2
EC4	216	3.52	201	0.48	3min 44sec	2 hrs	99.3

Table No 24 : Dissolution Of Enteric Coated Tablet

Formulation	Parameter				
	Bulk density	Tapped density	Carr's index	Hausner's ratio	Angle of repose
F1	0.3896	0.4152	6.165	1.065	29.10
F2	0.4219	0.4456	5.318	1.056	27.90
F3	0.4265	0.4585	6.979	1.075	29.46
F4	0.3899	0.4514	13.624	1.157	28.66
F5	0.4198	0.4500	6.711	1.071	29.26
F6	0.4156	0.4521	8.073	1.087	29.95
F7	0.4269	0.4801	11.081	1.124	26.99
F8	0.4345	0.4756	8.641	1.094	29.32
F9	0.4235	0.4896	13.500	1.156	32.15
F10	0.3876	0.4690	17.461	1.219	33.11

Table no 25 :Enteric coated Formulations in cumulative % drug release in 0.1N HCl Acidic Buffer

Time (hrs)	EC1	EC2	EC3	EC4
1 hr	0	0	0	0
2 hr	0	0	0	0
6.8 pH phosphate buffer				
15 min	47.04	31.30	50.28	46.49
30min	70.47	72.41	85.56	74.17
45min	85.56	84.82	100.16	83.90
60min	92.69	91.58	100.16	93.25

Table No 26 : In Vitro Drug Release Of Sodium Pantoprazole

Time (min)	Absorbance	Conc. in 900 mL (mg /mL)	Loss	Loss Cumulative	Cumulative drug released	Cumulative percentage drug released
0	0	0	0	0	0	0
15	0	0	0	0	0	0
30	0	0	0	0	0	0
45	0	0	0	0	0	0
60	0	0	0	0	0	0
75	0	0	0	0	0	0
90	0	0	0	0	0	0
105	0.024	0.6469	5.822	0	5.822	14.62+0.52
120	0.06	14.555	0.0064	0.0064	14.561	36.58+0.40
135	0.091	2.	21.496	0.0226	21.518	05+0.90
150	0.1213	28.582	0.0238	0.0465	28.629	71.91+0.39
165	0.142	33.543	0.0317	0.0782	33.621	84.46+0.17
180	0.162	38.267	0.0372	0.1155	38.383	96.42+0.40

Table no 27 : Calibration curve data of pantoprazole in distilled water

Sr no	Concentration (µgm/ml)	ABSORBANCE
1	2	0.041
2	4	0.156
3	6	0.343
4	8	0.494
5	10	0.662
6	12	0.831
7	14	0.981
8	16	1.115
9	18	1.322
10	20	1.494

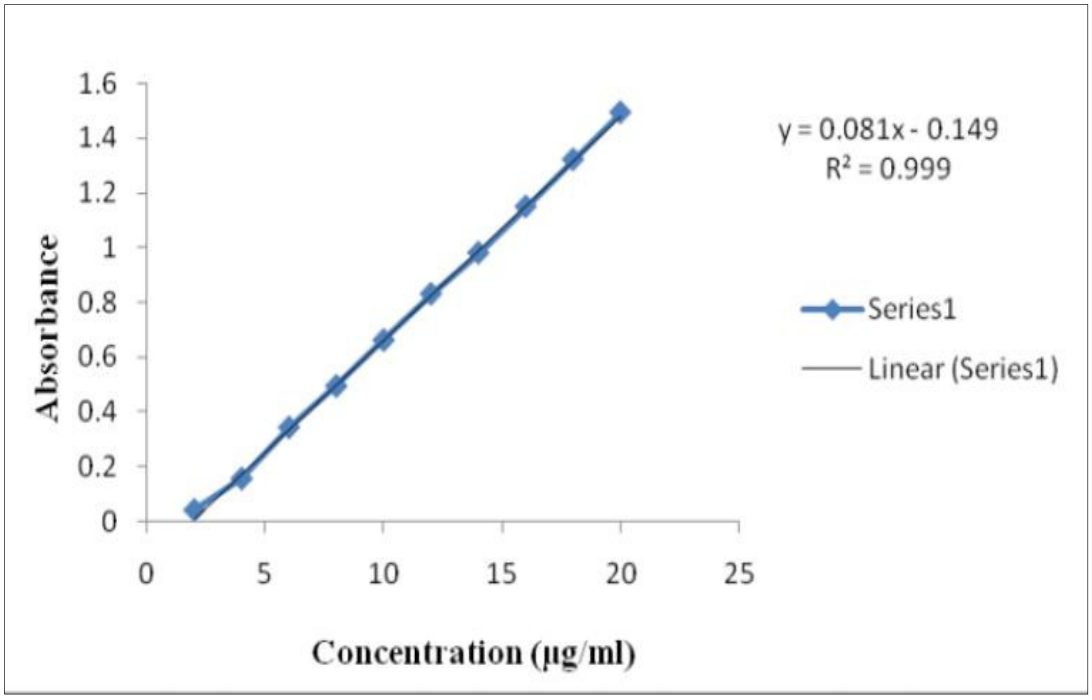

Figure no.2.standard curve of pantoprazole in distilled water

Table no.28 : Calibration curve data of pantoprazole in phosphate buffer

Sr no	Concentration (µgm/ml)	ABSORBANCE
1	2	0.072
2	4	0.132
3	6	0.223
4	8	0.299
5	10	0.362
6	12	0.462
7	14	0.539
8	16	0.620
9	18	0.692
10	20	0.782

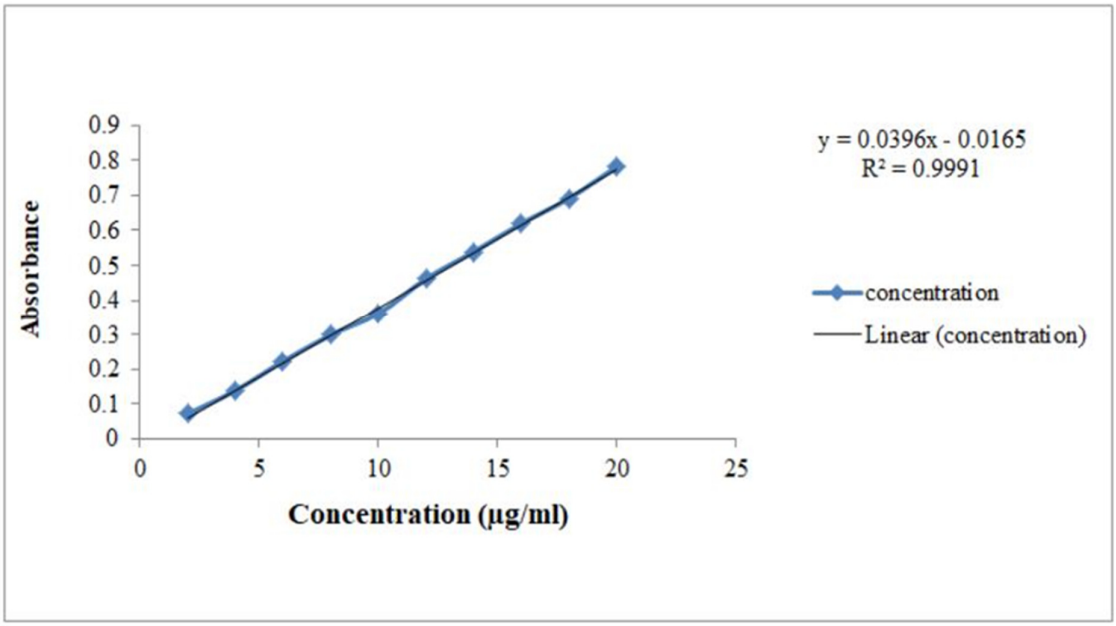

Figure No 3 : Standard Curve Of Pantoprazole In Phosphate Buffer

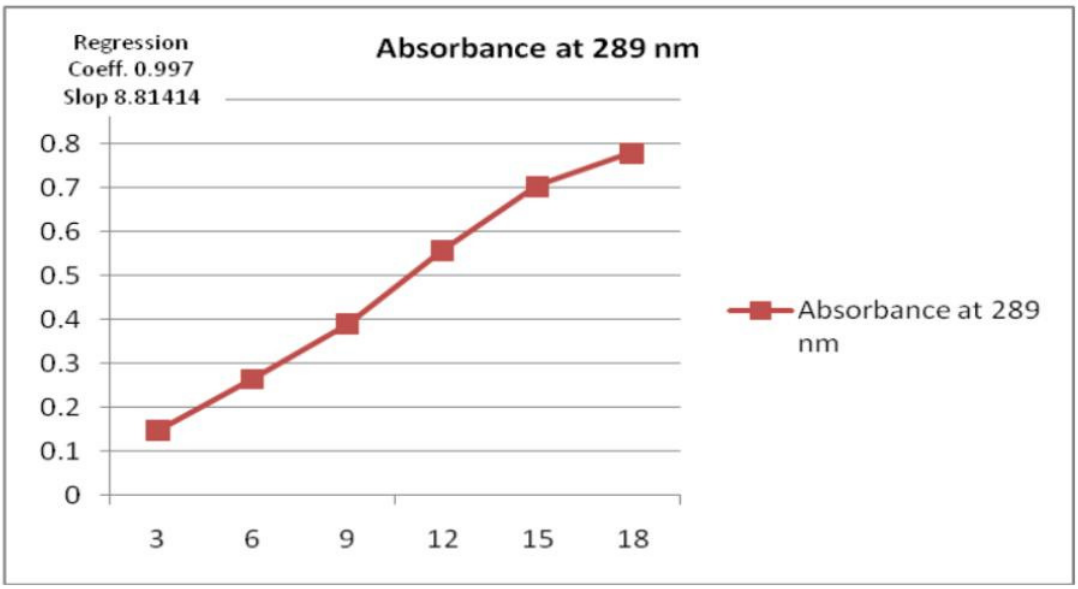

Figure No 4 : Calibration Curve For Pantoprazole Sodium At 298nm

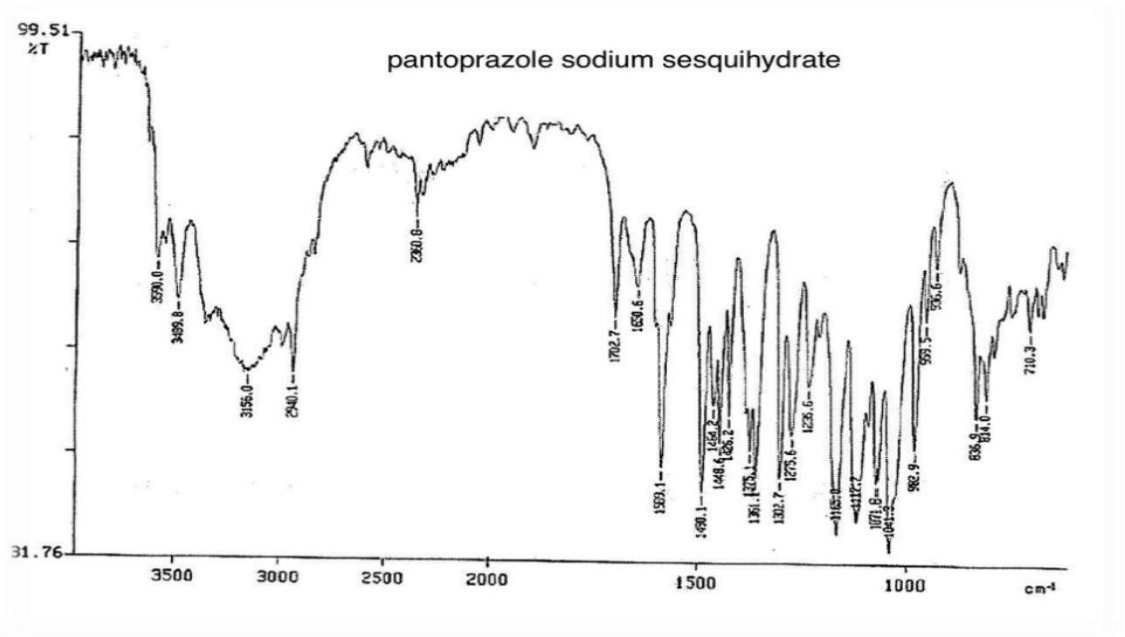

Figure No 5 : FTIR Graph Showing Pantoprazole Sodium Sesquihydrate Peaks

FORMULATION STUDIES:

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.

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 : 29 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)	4	6	8	4	6	8	4	6	8
Microcrystalline cellulose(mg)	25	23	20	28	24	46	58	46	22
Mannitol (mg)	50	75	100	50	84	50	43	50	73
Dicalcium phosphate (mg)	75	50	26	72	40	50	49	52	52
Talc (mg)	2	2	2	2	2	2	2	2	2
Magnesium stearate (mg)	4	4	4	4	4	4	4	4	4
Total weight (mg)	200	200	200	200	200	200	200	200	200

Coating of compressed pantoprazole sodium tablets:

Preparation of enteric coating solution: The enteric coating solution was prepared by simple

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

Table no : 30 Composition of coating solution

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

Enteric coating of pantoprazole sodium compressed tablets by dipping method:

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

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.

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.

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.

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