Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2011; 3(2): 45-47

Research Article ISSN 0975 1556

Pantoprazole and Its Enteric Coating Polymer Concentration for Stable Coating in Acid Media in Stomach

Chanchal Kumar Mishra[1*], Anil Goyal[2], Mukesh Sahu[1], Asha Rani[2], D. Sasmal[3], Rajesh Kumar Nema[4]

[1]*Arya College of Pharmacy, Kukas, Jaipur, Rajasthan, India*
[2]*Govt. Pharmacy Institute, Bariatu, Ranchi, Jharkhand, India*
[3]*Department of Pharmaceutical Sciences, Birla Institute of Technology, Mesra, Ranchi, Jharkhand, India*
[4]*Rishiraj College of Pharmacy, Indore, Madhya Pradesh, India*

ABSTRACT
Pantoprazole and its enteric coating polymer concentration for stable coating in acid media which is an orally administered benzimidazole anti-ulcer drugs. To achieve this goal, various prototype trials were taken and evaluated with respect to the various quality parameters such as disintegration, tablet weight, thickness; diameter, gastric resistance test, drug uniformity and dissolution also determine optimum polymer concentration for enteric coating. Pantoprazole enteric coated tablets prepared by direct compression. Because of its unstability in acidic environment decided to give it alkaline environment with the help of alkaliser and also protective seal coating between core tablet and acid resistant enteric coat. The primary aim of using delayed release is to protect the drug from an unfavourable environment in the gastrointestinal tract, to protect the gastrointestinal tract from high, local concentrations of an irritating drug compound, or to target a specific region of absorption or action. Delayed release products are typically enteric coated or colon targeted system. Formulation can be evaluated by Acid resistant test and *In vitro* drug release test. Delayed release dosage form has an enteric polymeric coating with characteristic pH-dependant solubility (or stability) to prevent release of the active ingredient in the stomach at low acidic pH (i.e. 1-3). Once the delayed release product leaves the stomach, the enteric coating dissolves subsequent *in-vivo* drugs release and then generally follow the same course as for an immediate release product. Applied different parameters of enteric coated tablets evaluation and IR spectral analysis of Pantoprazole that justified the enteric coating polymer concentration for stable coating in acid media in stomach.

Keywords: Pantoprazole, anti-ulcer drugs, pH-dependant solubility.

INTRODUCTION

Pantoprazole is a Proton Pump Inhibitor (PPI), which inactivates the final step in the gastric acid secretion pathway in gastric parietal cells in a dose-dependent manner. Pantoprazole also exhibits antibacterial activity against Helicobacter pylori *in-vitro.*

17 years of clinical experiences, worldwide have shown pantoprazole to be an effective and well-tolerated treatment option in the management of acid-related disorders, including gastric and duodenal ulcers and Gastro-oesophageal reflux disease (GERD) and the treatment or prevention of gastro-duodenal lesions induced by NSAID'S. Pantoprazole also effective in combination with different regimens for H. pylori eradication and is included in the first-line PPI-based options for this purpose. [1-3]

Common disk-shaped tablet is a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid dosage form. [4]

The main objective of the work is to develop a stable, pharmaceutically equivalent, robust and delayed release tablet formulation of pantoprazole and its enteric coating polymer concentration for stable coating in acid media, which is an orally administered benzimidazole anti-ulcer drug.

METHOD & MATERIALS

Table 1: Pre-formulation Studies: - (a) API Pantoprazole sodium Sesquihydrate

S. No.	TEST	SPECIFICATION	RESULTS
1	Characters	White to 0ff white crystalline powder	Complies
2	Solubility	Freely soluble in methanol, water and soluble in ethanol.	Complies
3	Identification A) HPLC B) UV	Retention time of sample with standard Absorption of 0.01 w/v sol. in methanol in 210nm-360nm range	Complies Complies

***Corresponding author: Ms. Chanchal Kumar Mishra,** Arya College of Pharmacy, Kukas, Jaipur, Rajasthan, India; **E-mail:** nema_pharmacy@yahoo.co.in

		shows maxima at about 289nm.	
4	Colour and clarity	Solution should clear and absorption of above identification solution at 420nmis not more than 0.125.	Complies
5	pH	Between 9.0 and 11.5	10.21
	Related substances by HPLC		
6	i.) Individual impurity	NMT 0.5%	0.17%
	ii.) Total impurity	NMT 1.0%	0.35%
7	Heavy metals	NMT 20ppm	Complies
8	Water content by KF	NLT 4.5% AND NMT 8.0%	4.62%
9	Assay by HPLC	NLT 98.0% and NMT 101.0%	99.23%
10	IR spectrum	Comparison of spectra of sample in KBr dispersion by pellet technique with pantoprazole working standard under same conditions and parameters.	Matches with the standard spectrum

Table 1: (b) Drug Excipients Compatibility Study

Test	Observations
Organoleptic properties	Off white, bitter and odourless blend.
pH	9.61(10% aq. solution)
a. Bulk density	0.55 gm/cm^3
b. Tapped density	0.46 gm/cm^3
Water content by IR	3.03% (at 60^{0}C for 10 min.)
Funnel test	Passed
IR spectrum	Comparison of spectra of sample in KBr dispersion by pellet technique with blend of Pantoprazole working standard under same conditions and parameters.
Assay by HPLC	101.93%

MANUFACTURING FORMULA

Table 2: Manufacturing formula for the Pantaprazole and its enteric coating polymers

Ingredients	F1 (200mg)	F2 (180 mg)	Category
Pantoprazole Sodium Sesquihydrate	52.42	52.42	Proton Pump Inhibitor
Disodium Hydrogen Phosphate	4.00	4.00	Alkalinizing Agent
Microcrystalline Cellulose (pH 200)	122.08	102.08	Diluent
Sodium Lauryl Sulphate	2.00	2.00	Wetting Agent
Sodium Starch Glycollate	8.00	8.00	Disintegrant
Crospovidon	2.00	2.00	Disintegrant
Talc	6.00	6.00	Glidant
Colloidal Silicon Dioxide	1.50	1.50	Lubricant
Magnesium Stearate	2.00	2.00	Lubricant

***Temperature is maintained at 25±2°C and Relative Humidity is maintained at 40±5%**

45.1 mg of Pantoprazole Sodium Sesquihydrate is equivalent to 40.0 mg of Pantoprazole

Calculation for Pantoprazole:

*Pantoprazole (A) = $\frac{\text{Std. Quantity X 100 X 100}}{\text{Assay (100 – LOD)}}$ = $\frac{\text{45.1X 100 X 100}}{\text{Assay (100 – LOD)}}$

Sodium Sesquihydrate

Table 3: Evaluation of enteric coating parameters:

Parameters	F5	F6	F7	F8
Organoleptic properties	Brown colour, Circular, Biconvex	Brown colour, Circular, Biconvex	Brown colour, Circular Biconvex	Brown colour, Circular Biconvex
Wt. variation(mg)	3818.8	3889.2	3965.6	4036
Thickness(mm)	3.79- 3.81	3.80- 3.83	3.82- 3.86	3.87- 3.93
Diameter(mm)	8.05	8.07	8.09	8.12
Hardness(kg/cm^2)	5.5	7.0	7.5	9.0
Disintegration test i.) In 0.1 N HCl solution (2 hr)	Fail (50 min)	Fail (75 min)	Fail (105 min)	Pass (18 min)
ii.)In mixed PO4 buffer soln. (pH 6.8) (within 1hr)				
Dissolution i.) In 0.1 N HCl soln. ii.) In mixed PO4 buffer soln. (pH 6.8)				Result Awaited
Assay(%purity)	94.58	97.88	95.66	101.75

Table 4: Enteric coated tablet parameters in which Pantoprazole delayed release tablets evaluated

Description	Browne coloured, round, biconvex, enteric coated tablet
Avg. Weight of core tablet	202 mg/tab (± 7.5% 217.15.5-181.8 mg)
Weight of 20 tablet	4.04gm (± 2% ,3.96gm-4.12 gm)
Diameter	8.10 -8.20 mm
Thickness	3.80- 4.00 mm
Hardness	NLT 3 kg/cm^2
Disintegration time	Tablet should be intact in 0.1N HCL 37^{o}C ± 2 ^{o}C For 120 mins., Mixed phosphate buffer ph 6.8,Tablets disintegrate with in 60 mins.
Assay	90-110% (Release Limit- NLT 98%)

IR Spectral Analysis

Weighed amount of the drug (3 mg) was mixed with 100 mg of Potassium bromide (dried at 40°-50°C), which was then compressed under 10-ton pressure in a hydraulic press to form a transparent pellet.

Using FTIR 410 PC spectrometer carried out the compatibility studies between the drugs and the polymers. There was no appearance or disappearance of any characteristic peaks, which confirmed the absence of any chemical interactions between the drug and polymer.

Table 5: Data for IR Spectral analysis in different wavelengths

FREQUENCY (cm^{-1})	ASSIGNMENTS
3235	N-H stretches
2984	C-H stretches(CH_2)
1579	C=N, C=C stretches
1456	CH_2bending
1254	S=O stretches
1173	Sp^2 C-O aromatic ether stretches
1038	CH-O stretches
857	C-H bending of the pyridine ring hydrogen's

RESULT & DISCUSION

Pantoprazole drug is rapidly degraded in gastric environment, so due to this there is very poor bioavailability of drug in stomach. So we have prepared the delayed release tablets. Dissolution study performed in 0.1 N HCl it passes limit i.e., not more than 10 % released in acid media. Also in pH 7.4 phosphate buffer passed limit it released drug 90 –110 % within 45 min.

Finally stability batch was taken and charged for 3 months in stability chambers in different temp and humidity conditions. Tablets tested for physical and chemical parameters and were found for trial and stability batch, satisfactory.

REFERENCES

1. "Guidelines for the design and evaluation of oral prolonged release dosage forms" by Ministry of Health and Welfare, Japan, March 11, 1988.
2. Ghebre-Sellassie, in Pharmaceutical Pellitization Technology (Ghebre – Sellassie, I., ed.), Marcel Dekker, 1989, 1-13,

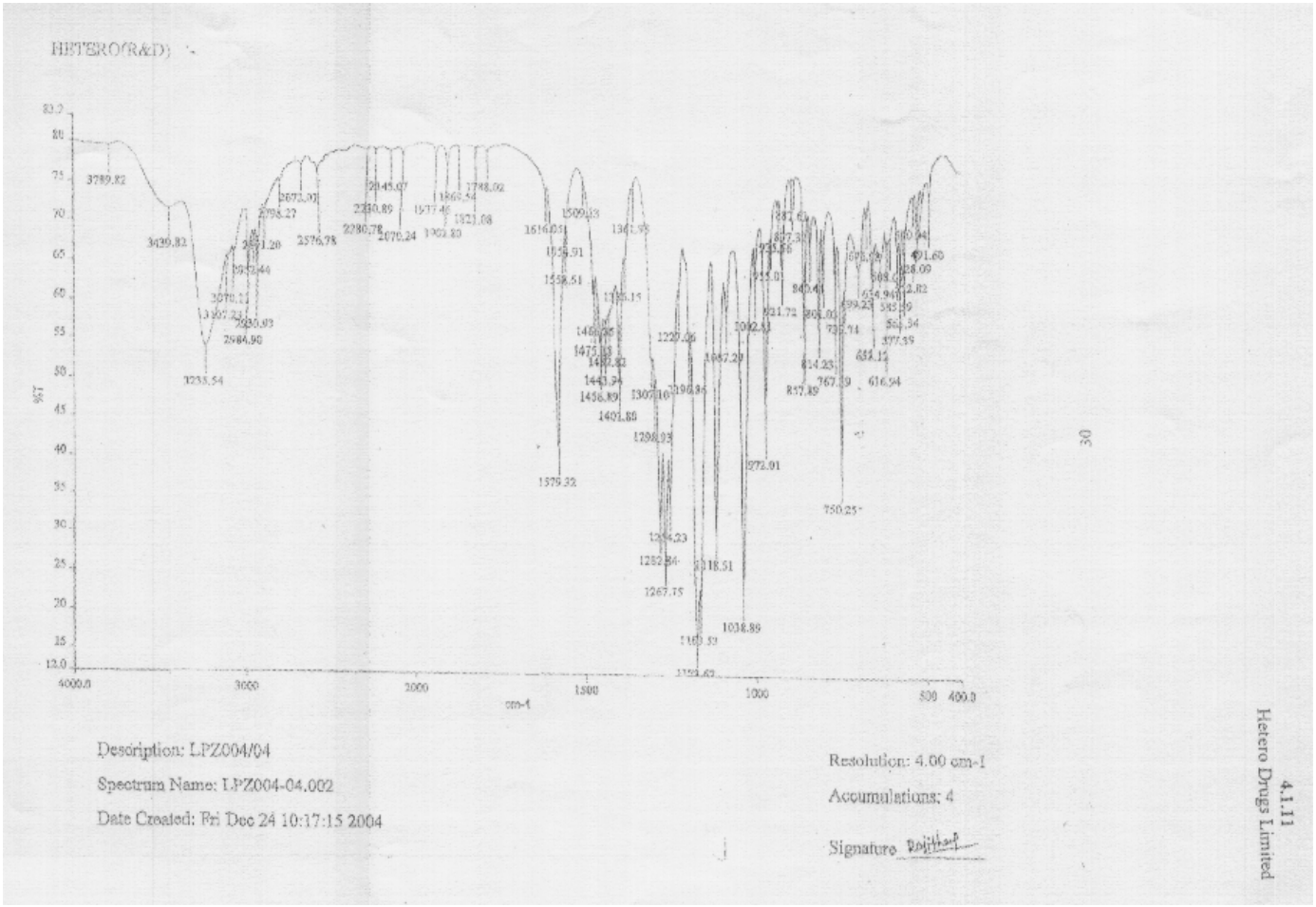

Fig.: -IR Spectral analysis peak of Pantoprazole in different wavelengths

3. Saltiel E, Fask A. Prevalence of potential proton-pump inhibitor drug interactions:A retrospective review of prescriptions in community pharmacies. Clin Ther. 1999; 21(10):1812-19.
4. US Patent By Chen P.N.6.726927 B2 “Preparation of enteric pharmaceutical dosage forms for omeprazole and lansoprazole”, 2004.