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

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ABSTRACT

Small intestine transit time is relatively constantan dishardly in fluenced by the nature of the formulation administered. Studies have shown that, once having left the stomach, the formulation arrives at the ileocaecal junction about 3-4 hrs after dosing. This delivery system consists of a capsule, half of which is non-disintegrating and other half enteric coated. The enteric coat dissolves on entering the small intestine and a hydroplug, stopping the non-disintegrating parts, well saturate determined by the degree of cross linking. After predetermined time (e.g.5hrs.), the hydrogel plugs well so much that it. Becomes ejected from the non-disintegrating bottom half of the capsule there by releasing the drug. It must be noted that the swelling of the hydrogel plug is pH independent. Other reports also appear in the literature on the use of pH dependent timed release system for site specific drug release in the colon. Timed-controlled formulations have also been prepared using water insoluble ethyl cellulose and swellable polymer (Hydroxypropyl Cellulose). Each of the formulations consisted facore, drug, swelling agent and water insoluble membrane. The swelling agent absorbs liquid and ethyl cellulose coated is integrated as the core swells. A lag time of 4±0.5hrs in relation to absorption was found for this formulation in a human bioavailability study and it was not in fluenced by food. However, the site-specific of timed release do sage form is considered poor because of large variation in gastric emptying times and passage across the ileocaecal junction.

Key words: Pantoprazole, Super disintegrants, Entric Coated.

INTRODUCTION

Pantoprazole is a proton pump inhibitor drug used for short-term treatment of erosion and ulceration of the esophagus caused by gastro esophageal reflux disease [1].

Description

Generic name: Pantoprazole

Chemical name: 6-(difluoromethoxy)-2-{[(3,4-dimethoxypyridin-2-yl)methane]sulfinyl}-1H-1,3-benzodiazole

Empirical formula: $C_{16}H_{15}F_2N_3O_4S$

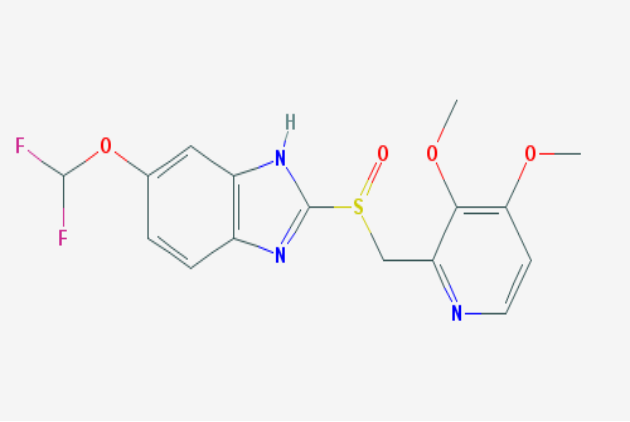
Molecular weight: 383.075133083

Category: Anti-Ulcer Agents, Proton Pump Inhibitors

Mechanism of action

Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid production by forming a covalent bond to two sites of the (H^+,K^+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. This effect is dose- related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus [2].

Structure



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Pharmacokinetics

Absorption

Pantoprazole is well absorbed. It undergoes little first-pass metabolism resulting in an absolute bioavailability of approximately 77%.

Metabolism

Pantoprazole is extensively metabolized in the liver through the cytochrome P450 (CYP) system. The main metabolic pathway is demethylation, by CYP2C19, with subsequent sulfation; other metabolic pathways include oxidation by CYP3A4. There is no evidence that any of the pantoprazole metabolites have significant pharmacologic activity [3].

Elimination

After administration of a single intravenous dose of 14C-labeled pantoprazole to healthy, normal metabolizer subjects, approximately 71% of the dose was excreted in the urine with 18% excreted in the feces through biliary excretion [4].

The aim of the present study is to formulate a pharmaceutically stable and quality improved formulation of Pantoprazole enteric coated tablets. The primary objective of the study is to improve therapeutic efficacy. To achieve this goal various prototype formulation trials will be taken and evaluated with respect to the various quality control tests such as dissolution, assay. The formula will be finalized by using the in vitro dissolution parameter [5].

MATERIALS AND METHODS

Pre Formulation Studies

API Characterization:

Pre formulation studies for Pantoprazole

1. Solubility
2. Drug polymer compatibility studies

1. Solubility

The solubility of a drug may be expressed in number of ways. The U.S. pharmacopoeia and national formularies list the solubility of the drugs as the number of millilitres of solvent in which 1 gram of solute will dissolve. For substance whose solubility are not definitely known, the values are described in the pharmaceutical compendia by the use of certain general terms. One gm. of Pantoprazole was dispersed in the solvent and based on the following table solubility was determined. The solubility of the drug was determined in water, ethanol, methanol, chloroform and acetone.

2. Drug polymer compatibility studies

Study was carried out using FT-IR spectrometer. FT-IR Spectra of Pantoprazole and polymers with Pantoprazole were obtained. The spectrum was studied for specific peaks of drug and polymer. The spectra are shown in figure and the spectral data are shown in table no.

Experimental methods

Analytical methods

Determination of λ max of Pantoprazole

Standard Stock solution

100 mg of Pantoprazole was dissolved in 100 ml of pH 6.8 phosphate buffers (1000 µg/ml).

Scanning: From the stock solution 10µg/ml was prepared in methanol and UV scan was taken between 200 to 400 nm. The absorption maximum was found to be 285 nm and was used for the further analytical studies.

Calibration curve of Pantoprazole in 0.1N HCL

From the standard stock solution (1000 µg/ml), appropriate aliquot were transferred to series of 10 ml volumetric flasks and made up to 10 ml with 0.1 N HCL, so as to get concentration of 4, 8, 12,16 and 20 µg/ml. the absorbance of the solution were measured at 285nm. This procedure was performed in triplicate to validate calibration curve. A calibration graph was plotted and shown in figure no.

Preparation of 6.8pH phosphate buffer

Dissolve 28.80g of disodium hydrogen phosphate and 11.45g of potassium hydrogen phosphate in sufficient water to produce 1000ml.

Calibration curve of Pantoprazole in 6.8pH phosphate buffer

From the standard stock solution (1000 µg/ml), appropriate aliquot were transferred to series of 10 ml volumetric flasks and made up to 10 ml with 6.8pH phosphate buffer so as to get concentration of 4, 8, 12,16 and 20 µg/ml. the absorbance of the solution were measured at 285nm. This procedure was performed in triplicate to validate calibration curve.

Compatibility studies

In the coated tablets, drug is in intimate contact with one or more excipients, which could affect the stability of the drug. Knowledge of drug excipients interactions is therefore essential for selecting appropriate excipients. This was studied using Fourier transform-Infrared spectrophotometry (FT-IR), and Drug – excipient compatibility studies.

Fourier Transform – Infrared Spectroscopy Studies: (FT-IR)

FT-IR is primarily used to determine the functional groups that are present in a specific compound. FT-IR is the best analytical tool for screening and profiling polymer samples. Compatibility studies were performed using FT-IR spectrophotometer. The FT-IR spectrum of pure drug, HPMCP (polymer) and the mixture of drug and polymer were obtained by KBR pellet method [6].

Procedure

The samples of the pure drug and the polymer were selected separately and dispersed in KBr powder. The pellets were made by applying a pressure of 6000 kg/cm^2 using KBr press and analysed. Spectral measurements were obtained by powder diffuse reflectance on a FT-infrared spectrophotometer type, FT IR- 8400-S, Shimadzu, Japan. The Scanning range was 400-4000 cm-

1.

Formulation Development of Pantoprazole Enteric Coated Tablets

Compilation of Pantoprazole core Tablets

An ideal mixture of powder was directly punched into tablets weighing about 200 mg containing 40 mg of Pantoprazole, using rotary tablet compression machine.

Pantoprazole Enteric coated tablets

Pantoprazole enteric coated tablets were prepared by direct compression technique using different excipients as well as with varying concentrations disintegrants.

Manufacturing Process

1. Co-sift Pantoprazole, PVPK30 and Disintegrant through sieve # 30.
2. Sift Mannitol through sieve # 30.
3. Sift the Step 1 and Step 2 materials through # 30 mesh.
4. Load the step 3 materials into blender and mix for 30 mins.
5. Sift Aerosil through sieve # 40 along with a portion of prelubricated blend.
6. Load the step 5 material to the blender and mix for 5 mins.
7. Compress the lubricated blend of step no. 8 into tablets.
8. Disperse coating polymer in Acetone under stirring to prepare clear solution.
9. Add plasticizer and talc to the step no. 10 solution.
10. Add colour which is pre sifted and add to the step no.11
11. Spray coating solutions on tablets using spray gun in coating pan. Warm the enteric-coated tablets in coating pan at 50°C ± 5°C for 20 -30 mins.

Coating Parameters

- ✓ Temperature: 45± 5°C
- ✓ Pan Speed: 3RPM

Tooling

8 mm round shaped, deep concave plain tooling with corresponding dies.

Tablet compression parameters

Weight of the tablet	200 mg
Hardness range	6-7kg/cm^2
Thickness range	2.7 ± 0.3 mm

There are various in process control parameters should be performed. They are

a) During tablet compression:

- ✓ Appearance
- ✓ Average weight
- ✓ Weight uniformity
- ✓ Hardness
- ✓ Thickness
- ✓ Disintegration time

b) During enteric coating:

- ✓ Appearance
- ✓ Average weight of enteric coated tablets
- ✓ Acid resistance

Pantoprazole Enteric coated tablets were prepared by wet granulation method.

Evaluation Parameters

Pre-compression Characteristics

1. Angle of Repose

Angle of repose is used to determine the flow properties of powders, pellets or granules. Angle of repose is the maximum angle possible between the surface of a pile of the blend and the horizontal plane. Fixed funnel method was employed. A funnel that was secured with its tip at a given height above the graph paper was placed on a flat horizontal surface. Granules were carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius and height of the pile were then measured. The angle of repose (θ) for samples were calculated using the following equation [7].

$$\textbf{Tan } \theta = \frac{\text{Height of the heap}}{\text{Radius of the heap}}$$

2. Bulk Density

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring perceived granules into a graduated cylinder via a large funnel and measure the volume and weight [8].

$$\textbf{Bulk Density} = \frac{\text{Weight of granules}}{\text{Bulk volume of granules}}$$

3. Tapped Density

Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the granules in the cylinder and this minimum volume, the tapped density may be computed [9].

$$\textbf{Tapped density} = \frac{\text{Weight of granules}}{\text{Tapped volume of granules}}$$

4. Compressibility Index (CI)

Compressibility index is measured by using the values of bulk density and tapped density. The following equation is used to find the Carr's index [10].

$$\textbf{CI} = \frac{\text{(Tapped density-Bulk density)}}{\text{Tapped density}}$$

5. Hausner's ratio

The ratio of tapped density to bulk density of powders is called the Hausner's ratio. It is calculated by the following equation [11].

$$\textbf{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Post-Compression Characteristics

1. Weight Variation

The USP weight variation test will be run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average [12].

$$\textbf{Weight variation} = \frac{\text{(Weight of tablet-Average weight)}}{\text{Average weight of tablets}} \times 100$$

Weight variation should not be more than 7.5%.

2. Thickness and diameter

The thickness of a tablet will be the only dimensional variable related to the process. 10 tablets were measured for their thickness and diameter with Vernier calipers, Thickness Gauge. Average thickness and diameter were calculated [13].

3. Hardness

Hardness of the tablets will be determined by Varian Hardness Tester and the hardness should be found within the range of 3.5-5.5 kg/cm². A tablet is placed between the anvils and the crushing strength which causes the tablet to break is recorded [14].

4. Friability

The friability of tablets will be determined by Electrolab EF-2, Friabillator. 20 tablets were taken and weighed. After weighing the tablets were placed in the Electrolab EF-2, Friabillator and subjected to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping the tablets from a distance of six inches with each revolution. After operation the tablets were de-dusted and reweighed.

Friability is determined by using below equation:

$$\textbf{F=100(1-Wo/Wt)}$$

Where, Wo= weight of tablets before friability test.

Wt= weight of tablets after friability test.

5. Disintegration Test

Disintegration testing of coated dosage forms was carried out in the six tablet basket rack USP disintegration apparatus. One tablet was introduced into each tube of the basket rack assembly of the disintegration apparatus without disc. The assembly was positioned in the beaker containing 900ml of Water. The disintegration time of each tablet was recorded.

6. Dissolution

Drug release studies were carried out using a USP type II dissolution test apparatus at 50rpm for 2hours in 900ml 0.1N HCl previously maintained at 37°C ± 0.5°C. 5ml of sample was taken and analysed. After 2hrs replaced with pH 6.8 and tested for drug release for 12hrs at same temperature and rotation speed. 5ml of aliquots were withdrawn at pre-determined time intervals and an equal amount of the medium will be replaced to maintain sink conditions. The aliquots were diluted suitably and the amount of drug released will be determined by U.V method.

7. Assay

Ten tablets were weighed individually and powdered; an amount equivalent to100 mg of drug was taken and 50 ml of 95% ethanol was added and was shaken for 30 minutes. Sufficient ethanol (95%) was added to produce 100 ml. The solution was filtered (through 0.45 µm). Drug content was measured at 285 nm using UV/Visible single beam spectrophotometer.

Table 1. List of Equipments

Equipment	Model /Company
Electronic balance	Citizen, India
Tablet compression machine	Cadmach single punch machine
Hardness tester	Monsanto hardness tester
Dissolution test apparatus	Lab India
Disintegration test apparatus	Campbell Electronics
Friability test apparatus	Riche Rich
U.V visible spectrophotometer	Shimadzu UV-1601, Japan
Fourier Transformer Infrared spectrophotometer	Bruker (Tensor 27)
Hot air oven	Lab India
pH meter	Citizen, India

Table 2. Terms of Approximate Solubility

Term	Parts of solvent required for 1 part of solute
Very soluble	Less than 1 parts
Freely soluble	1 to 10 parts
Soluble	10 to 30 parts
Sparingly soluble	30 to 100 parts
Slightly soluble	100 to 1000 parts
Very slightly soluble	1000 to 10,000 parts
Practically insoluble or insoluble	More than 10,000 parts

Table 3. Compilation Of Pantoprazole Core Tablets

Formulation(mg)	F_1	F_2	F_3	F_4	F_5	F_6	F7	F8	F9
Pantoprazole	40	40	40	40	40	40	40	40	40
Explotab	5%			7.5%			10%		
Kollidone		5%			7.5%			10%	
HPMC			5%			7.5%			10%
PVPK 30	4%	4%	4%	4%	4%	4%	4%	4%	4%
Mannitol	qs	qs	qs	qs	qs	qs	qs	qs	qs
Aerosil	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
Magnesium stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%
Total weight	200	200	200	200	200	200	200	200	200

Table 4. Enteric Coating Formulation

Ingredients	EC1	EC2	EC3	EC4	EC5	EC6	EC7	EC8	EC9
Eudragit L 100 (%W/W)	4%	6%	8%	-	-	-	-	-	-
PVAP(%W/W)	-	-	-	4%	6%	8%	-	-	-
Eudragit RS100(%W/W)	-	-	-	-	-	-	4%	6%	8%
PEG	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Acetone	QS	QS	QS	QS	QS	QS	QS	QS	QS

Table 5. Parameters Evaluation

Flow property	Angle of Repose (^oC)	C.I	Hausner's ratio
Excellent	25-30	1-10	1.00-1.11
Good	31-35	11-15	1.12 -1.18
Fair – aid not needed	36-40	16-20	1.19-1.25
Passable – may hang up	41-45	21-25	1.26-1.34
Poor – must agitate	46-55	26-31	1.35-1.45
Very poor	56-65	32-37	1.46-1.59
Very very poor	>66	>38	>1.60

Table 6. Weight Variation Tolerances For Uncoated Tablets

S.No.	Average Weight of Tablets (Mg)	Maximum Percentage Difference Allowed
1	130 or less	10
2	130 to 324	7.5
3	More than 324	5

RESULTS AND DISCUSSIONS

Table 7. UV Concentration And Absorbance Values Of Pantoprazole

Concentration	Absorbance at 285nm
0	0
2	0.202
4	0.395
6	0.558
8	0.745
10	0.912

Table 8. Interpretation Of FTIR Graphs

S.No.	Functional group	Observed Range	Pure drug	Optimized EC8
1	NH	3500-3700	3632.55	3640.43
2	C=O	1670-1820	1758.77	1707.92
3	C=N	1080-1360	1271.15	1265.67

4	C-O	1050-1150	1062.95	1019.72
5	C-F	1000-1400	1150.61	1112.26

Table 9. Evaluation parameters of pantoprazole Enteric Coated Tablets

Formulations	Angle of repose(θ)	Loose Bulk Density(g/ml)	Tapped Bulk Density(g/ml)	% Compressibility	Hausner's ratio
F1	27.58±0.15	0.45±0.04	0.50 ± 0.04	12.23±0.6	1.11±0.04
F2	28.44±0.11	0.45±0.05	0.50 ± 0.1	12.23±0.4	1.11±0.02
F3	28.36±0.13	0.45±0.045	0.52 ± 0.04	12.58±0.8	1.13±0.08
F4	25.35±0.13	0.44±0.044	0.52± 0.01	15.19±0.1	1.15±0.06
F5	26.12±0.12	0.45±0.045	0.51 ± 0.04	15.48±0.6	1.18±0.08
F6	29.69±0.19	0.44±0.044	0.50 ± 0.09	13.48±0.8	1.13±0.09
F7	28.32±0.2	0.521±0.02	0.629±0.05	14.48±0.8	1.15±0.09
F8	25.69±0.14	0.518±0.03	0.627±0.05	17.17±0.05	1.20±0.05
F9	28.52±0.19	0.51±0.045	0.59 ± 0.04	17.38±0.07	1.21±0.06

Table 10. Post Compression Parameters of Core Tablet

Formulation	Weight variation	*Hardness(kg/m^2)*	Thickness (mm)	Friability (%)	Disintegration time	Assay%(w/w)
F1	200	3.42	2.6	0.45	1min 44sec	100.3
F2	202	3.66	2.3	0.46	1min 48sec	100.1
F3	201	3.51	2.9	0.50	1min 07sec	100.8
F4	199	3.42	2.3	0.51	1min 05sec	99.0
F5	200	3.41	2.2	0.30	1min 04sec	98.9
F6	202	3.45	2.2	0.32	1min	99.4
F7	201	3.48	2.6	0.18	48sec	100.6
F8	199	3.51	2.1	0.16	10sec	100.2
F9	201	3.51	2.0	0.28	1min 44sec	99.5

Table 11. Values of In Vitro Dissolution Studies

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
6.8 ph phosphate Buffer									
15min	22.8	38.3	14.5	33.4	58.2	50.8	33.8	54.3	50.2
30min	45.3	52.8	38.9	52.1	75.6	76.1	78.2	92.4	80.1
45 min	62.1	72.6	59.2	66.8	90.9	92.4	91.6	100.6	90.6
60min	75.8	85.1	70.4	79.2	99.8	100.1	98.9	100.5	100.7

Table 12. Absorbance Values of Dissolution Studies

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	0.719	0.121	0.458	0.105	0.184	0.160	0.107	0.171	0.158
30	0.143	0.167	0.123	0.164	0.239	0.240	0.247	0.292	0.253
45	0.196	0.229	0.187	0.211	0.287	0.292	0.289	0.317	0.286
60	0.239	0.269	0.222	0.250	0.315	0.316	0.312	0.317	0.318

Table 13. Evaluation Parameters for Enteric Coated Tablets

Formulations	Weight variation	Hardnessss	Thickness (mm)	Friability (%)	Disintegration time	Acid resistance time	Assay %(w/w)
EC1	208	3.40	2.7	0.44	2min 44sec	2hrs	102.3
EC 2	212	3.60	2.4	0.41	2min 48sec	2hrs	101.1
EC 3	216	3.50	3.0	0.56	1min 57sec	2hrs	102.8
EC 4	207	3.40	2.4	0.58	1min 25sec	2hrs	93.0
EC 5	213	3.4	2.3	0.40	1min 44sec	2hrs	99.9
EC 6	217	3.40	2.3	0.45	1min 30sec	2hrs	98.4
EC 7	205	3.41	2.7	0.48	1min 18sec	2hrs	101.6
EC 8	213	3.52	2.2	0.46	1min 10sec	2hrs	101.2

EC 9	216	3.52	2.1	0.48	2min 44sec	2hrs	99.3

Table 14. Dissolution Study for Enteric Coated Tablets

Time	EC1	EC2	EC3	EC4	EC5	EC6	EC7	EC8	EC9	Aciban
0.1N HCl Acidic Buffer										
1hr	0	0	0	0	0	0	0	0	0	0
2hr	0	0	0	0	0	0	0	0	0	0
6.8pH phosphate buffer										
15min	21.11	35.47	13.43	30.93	53.89	47.04	31.30	50.28	46.49	36.25
30min	41.95	48.89	36.02	48.24	70.01	70.47	72.41	85.56	74.17	54.26
45 min	57.50	67.23	54.82	61.86	84.17	85.56	84.82	100.16	83.90	69.85
60min	70.19	78.80	65.19	73.34	92.41	92.69	91.58	100.16	93.25	86.59
120min	100.2	99.6	98.9	100.5	99.8	100.2	98.9	100.16	100.6	99.25

Table 15. Absorbance Values for Enteric Coated Tablet

Time	EC1	EC2	EC3	EC4	EC5	EC6	EC7	EC8	EC9	Aciban
0.1N HCl Acidic Buffer										
1hr	0	0	0	0	0	0	0	0	0	0
2hr	0	0	0	0	0	0	0	0	0	0
6.8pH phosphate buffer										
15min	0.666	0.112	0.424	0.976	0.170	0.148	0.988	0.159	0.147	0.114
30min	0.132	0.154	0.114	0.152	0.221	0.222	0.228	0.270	0.234	0.171
45 min	0.181	0.212	0.173	0.195	0.266	0.270	0.268	0.316	0.265	0.220
60min	0.221	0.249	0.206	0.231	0.292	0.292	0.289	0.316	0.294	0.273
120min	0.316	0.314	0.312	0.317	0.315	0.316	0.312	0.316	0.317	0.313

Table 16. Stability Data of Optimized Enteric Coated Tablet

S.No	Time points (hrs)	Initial(±)	Cumulative % drug release			
			25C/60 %RH		40C/75% RH	
			1st month	3rd month	1st month	3rd month
1	1hr	0	0	0	0	0
2	2hr	0	0	0	0	0
3	15min	50.28	49.5	47.5	48.5	47.2
4	30min	85.56	84.3	80.9	82.6	80.3
5	45min	100.16	98.7	94.7	96.7	94.0
6	60min	100.16	98.7	94.7	96.7	94.0
7	Assay	99.8	98.5	98.3	99.4	98.5

Fig: 2 Standard Graph Of Pantoprazole (0.1 N HCL)

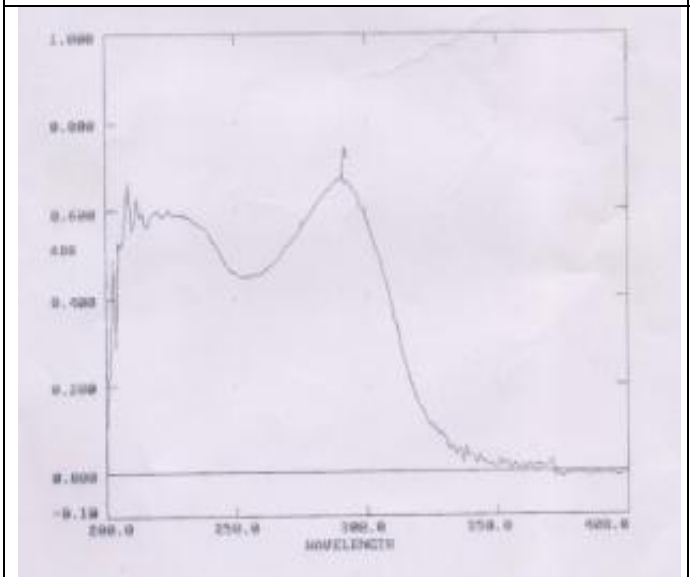


Fig: 3 Calibration Curve For Pantoprazole in 0.1N Hcl at 285nm

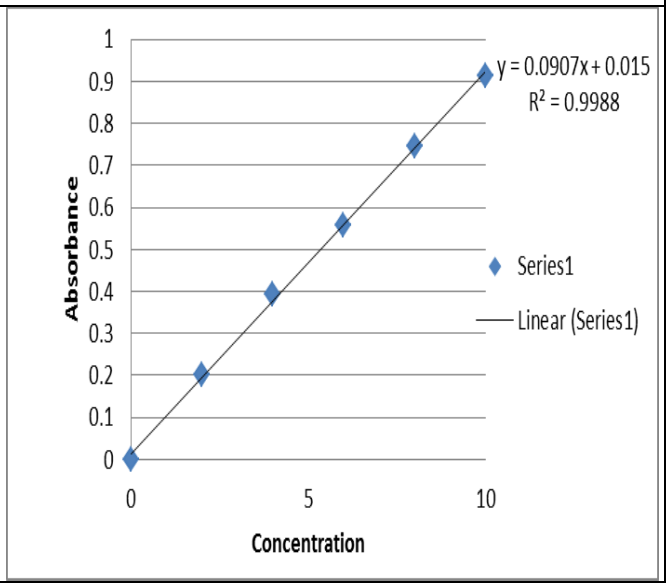


Fig: 7 Comparative In Vitro Drug Dissolution Studies For Best Formulation

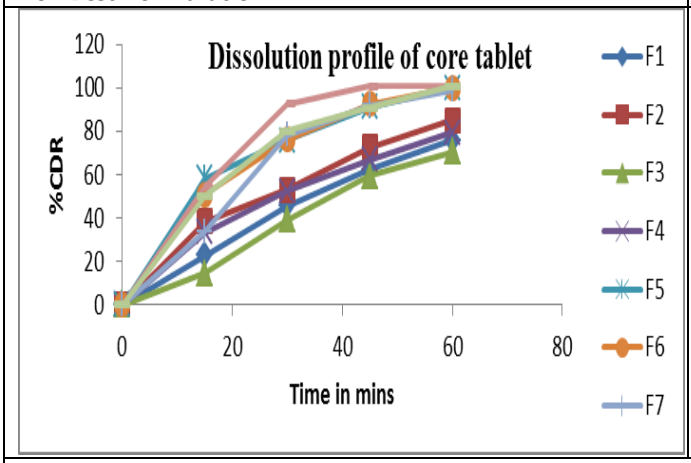


Fig: 8 Cummulative % Drug Release Graph For Formulation EC1-EC9

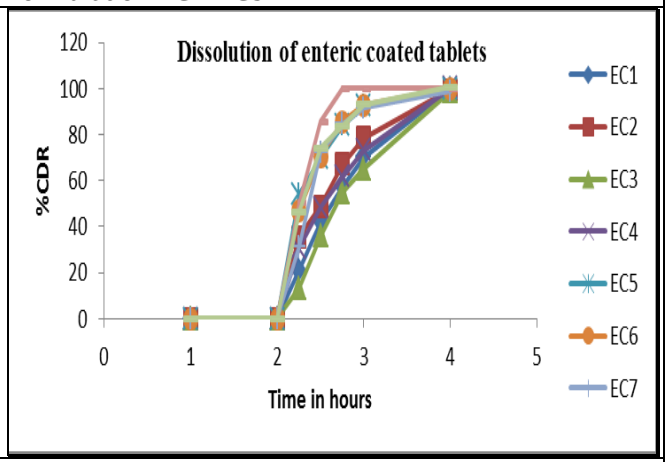


Fig: 5 FTIR Spectra of Pantoprazole

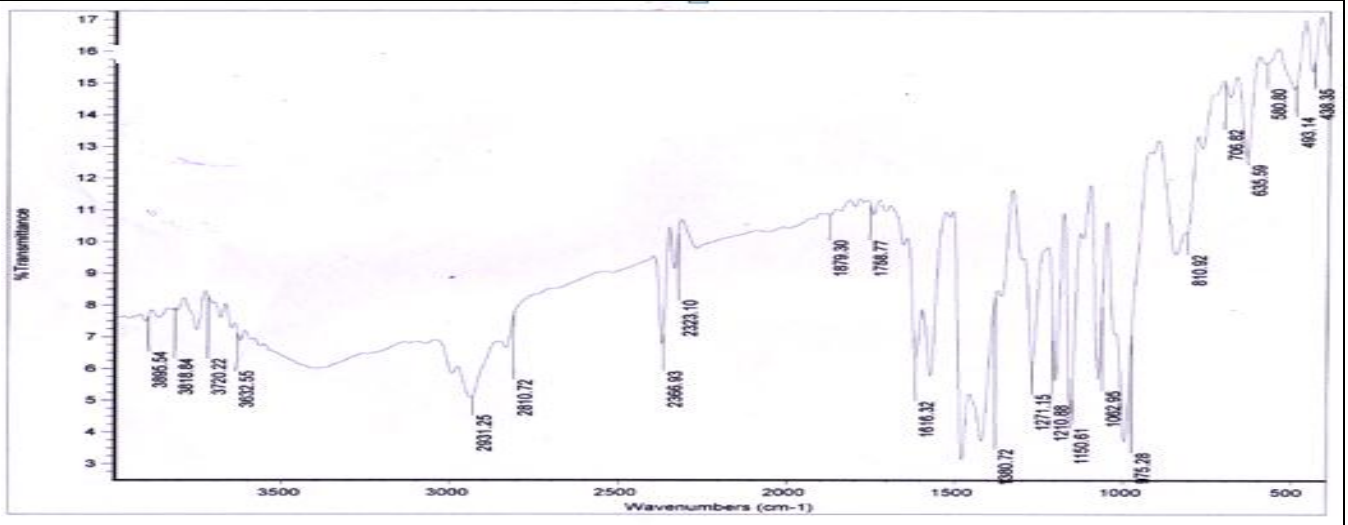
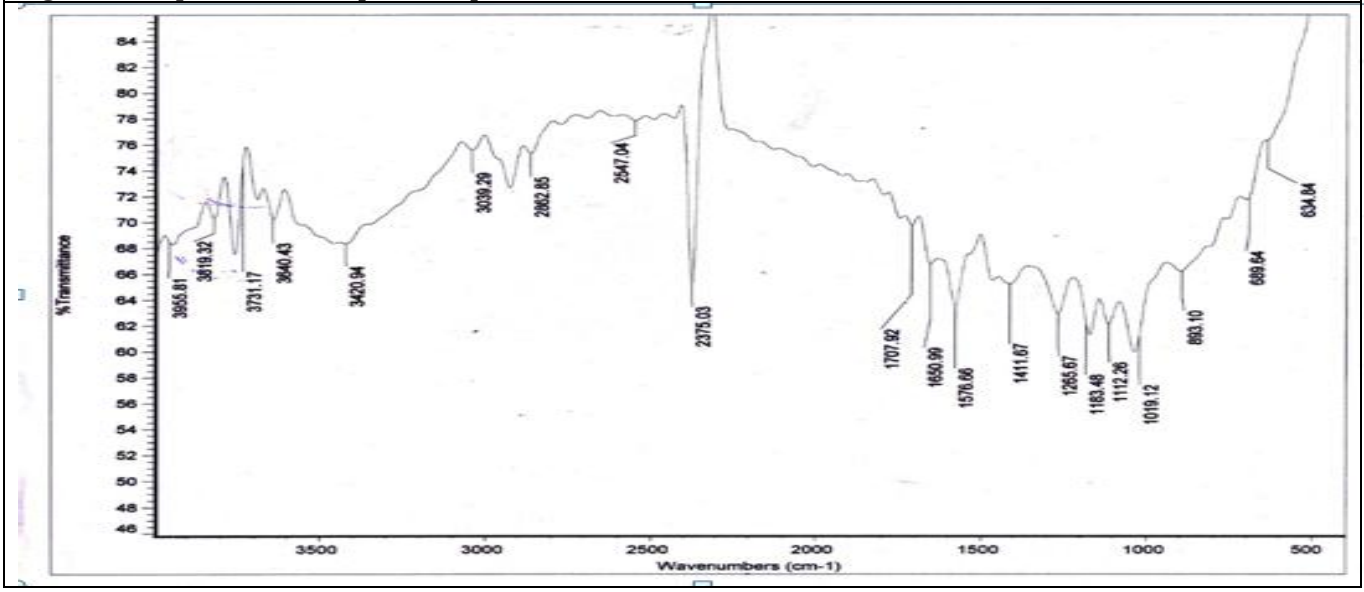


Fig: 6 FTIR Spectra Of Pantoprazole Optimized Formulation



Solubility

Pantoprazole sodium is a white to half-white crystalline powder and is racemic. Pantoprazole has weakly basic and acidic properties. Pantoprazole sodium is freely soluble in water and ethanol, very slightly soluble in

phosphate buffer at pH 7.4, and practically insoluble in n-hexane.
Melting Point: 137.5-145.5°C

Ultraviolet Visible (UV-visible) Spectroscopy

Drug sample showed wave length of maximum absorption (λ-max) 285 nm.

Standard Graph of Pantoprazole (0.1 N HCL)

The standard graph of Pantoprazole has shown good linearity with R^2 values 0.9988 in 0.1 N Hcl and which suggests that it obeys the "Beer-Lambert's law".

Standard Graph of Pantoprazole in 6.8pH phosphate buffer

The standard graph of Pantoprazole has shown good linearity with R^2 values 0.9986 and, which suggests that it obeys the "Beer-Lambert's law".

Angle of repose

Angle of repose values for batch F1 –F9 falls within the range of 25-30, and the flow property was found to be good.

Bulk and Tapped Density

The bulk density value for the formulated blend was found to be within the range of 0.4 to 0.5 gm/ml, where as the tapped density was found to be within the range of around 0.5 to 0.6gm/ml.

Compressibility Index

The percentage compressibility for the batch F1-F9 was found in to be within the range 17 and the flow property was found to be excellent.

Hausner's ratio

The Hausner's ratio value for the batch F1 –F9 falls within the range of 1.11-1.21 and found to have good flow property.

Hardness

The Hardness of the formulated batch F1 to F9 was maintained in the range 3.4 to 3.6 Kg/cm^2.

Percentage friability

The percentage friability for the formulated batches F1 to F9 was found to be within the range i.e., NMT 1% w/w.

Assay

For the entire formulated batch from F1-F8 the assay value was found to be within the limits of 90-110% w/w.

Weight variation

The weight variation values for all the formulated batch F1 to F9 was found to be within the 5% acceptable limits.

Disintegration time

For the formulated batches F1- F9 using different super disintegrants the disintegration time varies from 1min 48sec to 10sec by varying the concentration of the disintegrate.

***In Vitro* Dissolution Studies**

In F8 formulation the concentration of kollidone was optimized and found to have good flow property and releases 100.6% of drug with in 45 min.

Evaluation Parameters For Enteric Coated Tablets

F8 formulation with highest drug release was selected for coating. Three different coating polymers were used in three different concentrations.

***In Vitro* Drug Release Studies**

Dissolution studies of all the formulations were carried out using dissolution apparatus USP type I. The dissolution studies were conducted by using dissolution media 0.1 N HCl for 2hrs and 6.8 pH phosphate buffers for next two hours. The results of the In-vitro dissolution studies of formulations EC1 – EC9**,** showed in Table no.6.6.The plots of Cumulative percentage drug release Vs Time. Figure.6.7 shows the comparison of % CDR for formulations EC1–EC9.The formulations EC8 showed a maximum release of 100.16 with in 45 mins in 6.8pH Phosphate buffer after hours of acid resistance. Among all formulations EC 8 shows maximum drug release in 45 mins when compared with other formulations.

CONCLUSION

The aim of the present study is to formulate a stable and quality improved formulation of Pantoprazole enteric coated tablets. In this study Pantoprazole enteric coated tablets were prepared by using three different enteric coating polymers. Drug-Excipients compatibility studies were performed by FT-IR spectroscopy Powder was evaluated for tests such as angle of repose, Bulk Density, Tapped Density, Carr's Index and Hausner's ratio. The core tablets were prepared by Wet granulation method. Nine formulations of Pantoprazole were developed by preparing core tablets using mannitol as diluent and kollidone, HPMC, Explotab as super disintegrants of which F8 formulation with kollidone as super disintegrant with concentration of 10% was selected as best formulation as it has shown maximum drug release of 100.16% within 45 mins. The F8 core formulation was selected and coated with three different enteric coating polymers i.e. Eudragit RS 100, Eudragit L 100 and PVAP in three different concentrations each of 4%, 6% and 8%. EC 8 formulation with Eudragit RS 100 as coating polymer with concentration of 6% was optimized. Tablets were tested for Weight Variation, Hardness, Friability, Thickness, Disintegration Test, Assay, and Dissolution. EC8 was found to be best of all the enteric coated formulations. Further the EC8 formulation was subjected to comparison with marketed formulation.

REFERENCES

1. Nitesh SC, Roopa K, Firdous BG, Sajal KJ, Uday RS. Studies on Colon Targeted Drug Delivery System for Tinidazole in the Treatment of Amoebiasis. *Journal of Pharmacy Research*, 2(5), 2009, 862-867.
2. Salunkhe KS, Raosaheb SS, Kulkarni M. Formulation and in-vitro Evaluation of Dextrin Matrix Tablet of Albendazole for Colon Specific Drug Delivery. *Journal of Pharmacy Research*, 2(3), 2009, 429-431.
3. Vikas J and Ranjit S. Dicyclomine-loaded Eudragit®-based Micro sponge with Potential For Colonic Delivery: Preparation And Characterization. *Tropical Journal of Pharmaceutical Research*, 9(1), 2010, 67-72.
4. Mei-Juan Z, Gang C, Hirokazu Okamoto, Xiu-Hua H, Feng A, Fu-De C, Kazumi D. Colon-Specific Drug Delivery Systems based on Cyclodextrin prodrugs, in vivo Evaluation of 5-Aminosalicylic Acid from its Cyclodextrin Conjugates. *World Journal of Gastroenterology*, 11(47), 2005, 7457-7460.
5. Mohanad NS, Shaymaa AA, Alaa AAR. Design and in vitro Evaluation of Prednisolone Tablets as a Potential Colon Delivery System. *Asian Journal of Pharmaceutical and Clinical Research*, 2(4), 2009, 84-91.
6. Arun R, Theja I, Ashok KCK, Lavanya Y, Ravindra RP, Vamsee KS. Synthesis, Hydrolysis Studies and Pharmacodynamic Profile of Novel Colon-Specific Mutual Prodrug of Aceclofenac with Amino acids. *Der Pharma Chemica*, 1(2), 2009, 59-71.
7. Muhammed SA, Jakir AC, Ishrat N, Muhammed RI, Muhammed HR. *In vitro* Evaluvation of Dissolution Behaviour of Time and pH Dependent Colon Specific Drug Delivery for Aceclofenac Coated Tablets. *Bangladesh Pharmaceutical Journal*, 13(1), 2010, 60-62.
8. Naikwade SR, Kulkarni PP, Jathar SR, Bajaj AN. Development of Time and pH Dependent Controlled Release Colon Specific Delivery of Tinidazole. *DARU, Journal of Pharmaceutical Sciences*, 16(3), 2008, 119-127.
9. Gang C, Feng A, Mei-Juan Z, Jin S, Xiu-Hua H, Yun-Xia H. Time and pH-dependent Colon Specific Drug Delivery for Orally Administered Diclofenac sodium and 5-Aminosalicylic Acid. *World Journal Of Gastroenterology*, 10(12), 2004, 1769-177.
10. Thiruganesh R, Uma Devi SK, Suresh S. Preparation and characterization of pectin pellets of Aceclofenac for colon targeted drug delivery. *J. Chem. Pharm. Res*., 2(1), 2010, 361-74.
11. Chetan Singh Chauhan, Pushpendra Singh Naruka, Rajendrapal Singh Rathore, Viralkumar Badadwal. Formulation and evaluation of Prednisolone tablet for colon targeted drug delivery system. *J. Chem. Pharm. Res*., 2(4), 2010, 993-8.
12. Aswar PB, Khadabadi SS, Kuchekar BS, Wane TP, Matake N. Development and *in-vitro* evaluation of colon-specific formulations for orally administered Diclofenac sodium. *Arch Pharm Sci and Res*., 1(1), 2009, 48-53.
13. Ghule prashant J, Karle Ganesh D, Saumya Das. Formulation and *In-vitro* evaluation of colon targeted drug delivery of Aceclofenac. *Journal of Pharmacy Research*, 3(5), 2010, 1082-86.
14. Rasika D Bhalke, Raosaheb S Shendge, Fatima J Sayyad, Kishore S Salunkhe. Development of colon specific drug delivery of Aceclofenac by using effective binder system of ethyl cellulose. *International Journal of Pharma and Biosciences*, 1(3), 2010, 1-5.