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Formulation Development and Characterization of Enteric Coated Tablets of Lansoprazole

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ABSTRACT

The current study is an endeavor to formulate and assess hindered release enteric coated tablets of Lansoprazole by means of dissimilar enteric coated polymers like Eudragit L30D55, Hydroxy propyl methyl cellulose phthalate and Cellulose acetate phthalate. Tablets can be prepared by using approved excipients, which were proved compatible with the active ingredient by IR studies. Core tablets were primed by wet granulation and, gauged for physical parameters like hardness, friability, thickness, and disintegration time. Core tablets were sub-coated expending Hydroxy propyl methyl cellulose with buildup of 3%w/w and enteric coating with either of polymers with an average weight buildup of 5% & 8% w/w. The disintegration of enteric coated tablets i.e. formulations thru 5% weight buildup (F5a to F5c) in 0.1N HCl might not permit the test. Though, formulations with 8% weight accumulation (F5d to F5f) showed no disintegration in 0.1N HCl for a period of 2hrs. Dissolution of enteric coated tablets (F5d to F5f) in 0.1N HCl and monitored by pH6.8 phosphate buffer was adequate. Amongst the polymers verified, Eudragit L30D55 with 8% (F5d) weight buildup exhibited least release in 0.1N HCl and the comprehensive release in pH 6.8 phosphate buffer. Auxiliary, the plasticizer outcome on Eudragit L30D55 was similarly premeditated (F5d, F5d1 and F5d2) and institute, with proliferation in concentration of plasticizer there is diminished drug release in both 0.1 N HCl and 6.8 pH phosphate buffer. Based on the tablets assessment outcomes, the formulation F5d was designated as the optimized formulation which was constant throughout the study period (90 days).

Keywords: Lansoprazole; sub-coating; Enteric coating; Eudragit L 30 D55;Hydroxy propyl methyl cellulose phthalate; Cellulose acetate phthalate.

Abbreviations: Conc.: Concentration; °C: Degree Centigrade; hr: Hour; mg: milligram; min: Minute; mL: milliliter; mM: millimolar; nm: nanometer; mm: millimeter; rpm: Revolution per minute; Sec: Second; IP: Indian Pharmacopoeia; BP: British Pharmacopoeia; USP: United States Pharmacopoeia; UV: Ultraviolet; FTIR: Fourier Transform Infrared; HPMC: Hydroxy propyl methyl cellulose; HPMCP: Hydroxy propyl methyl cellulose Phthalate; CAP: Cellulose acetate phthalate; PPI: Proton Pump Inhibitor.

INTRODUCTION

Oral administration of medications has remained the extreme conjoint and anticipated course for delivery of supreme salutary proxies. The reputation of the oral route is ascribed to patient consent and affluence of administration. Orally administered drug requisite be enthralled over the gut which be contingent on diverse facets such as gastric emptying, intestinal motility, mucosal surface area, degradation of drug in the stomach and first pass effect. The absorption rate diverges from the stomach to the intestine owed to the improved surface area (about 4500 cm^2), the intestinal mucosa and superior blood flow (1000 ml/min) over the intestinal capillaries paralleled to the gastric capillaries. It is also acknowledged that specific drugs retaining pH dependent constancy which is not stable in acidic environment (in the stomach) [1].

Innumerable practices have been established to astound this stability problem. One obtainable of them is advance of enteric coated products. These enteric-coated dosage forms repel the acidic environment of the stomach and consent disintegration in the upper pH environment of the intestinal fluid. The enteric coating on a solid dosage form can also be used for site-specific drug delivery of a therapeutic agent to the intestinal region. The principal intension is to delay the release of drugs which are incapacitated by the stomach contents or might source nausea or bleeding by irritation of gastric mucosa.

Important reasons for enteric coating are as follows:

- Safeguard acid-liable drugs from the gastric fluid
- Defend gastric grief or nausea due to annoyance from drug
- Distribute drugs projected for local accomplishment in the intestine
- Deliver drug that are optimally absorbed in the small intestine to their principal absorption site in their utmost concentrated form.
- Afford a delayed release constituent to reprise activities
- Shield the drugs from destructive consequence of the gastric contents; selected drugs are disposed to to be hydrolyzed in acid media (E.g. Lansoprazole, omeprazole & pantaprazole)

Peptic ulcers are exposed eruptions or attritions on the gut lining of the stomach, duodenum, or esophagus. A peptic ulcer of the stomach is called a gastric ulcer; of the duodenum, a duodenal ulcer; and of the esophagus, an esophageal ulcer [2]. An ulcer ensues once the covering of these organs is blemished by the acidic digestive juices which are stowed by the stomach cells.

Peptic ulcer disease (PUD) can flinch after the protective obstacle that lines the stomach or intestines is injured, divulging the essential tissue

to stomach acid. Assortments of things can impairment the shielding lining of the stomach or intestine [3]. The origins are enumerated beneath;

a. Helicobacter pylori (H. pylori): A bacterial organism, is liable for utmost ulcers. This entity flags the defending coating of the stomach and duodenum and authorities the harming digestive juices to exacerbate the profound lining beneath.

b. Non-steroidal anti-inflammatory drugs (NSAIDs: Enduring practice of this class of medications is the subsequent utmost collective source of ulcers. These drugs (which embrace aspirin, ibuprofen, naproxen, diclofenac, tolmetin, piroxicam, fenoprofen and indomethacin) are acidic. They wedge prostaglandins constituents in the stomach that comfort sustain blood flow and shield the extent from injury.

c. *Zollinger-Ellison syndrome:* Individuals thru this unusual ailment have tumors in the pancreas and duodenum that produce gastrin, a hormone that excites gastric acid production. Prior heritages of ulcers are circumstantial that can upshot in undeviating impairment to the wall of the stomach or duodenum, such as heavy use of alcohol, radiation therapy, burns, and physical injury [4].

Treatment of peptic ulcers [5]:

Following are the slants used for the management of peptic ulcer disease;

- Proton pump inhibitors, including omeprazole, lansoprazole, pantoprazole, rabeprazole and esomeprazole, decreases gastric acid secretion. This is the best medications for treating ulcers.
- H_2 blockers, such as cimetidine, ranitidine, nizatidine and famotidine, reduce gastric acid secretion.
- Anticholinergic, these are of little importance in the treatment of ulcers. They reduce acid secretions by 35-40%. These are used along with antacids.
- Sucralfate makes a coating over the ulcer, protecting it from further damage.
- Antacids may relieve heartburn or indigestion but will not treat ulcer.

MATERIALS AND METHODS

Lansoprazole was attained from Nice Chemicals, HPMC, Eudragit, HPMC Pthalate, CAP are obtained from Finar Chemicals. Hyderabad.

Preformulation studies

Infrared absorption spectrum (FTIR): FTIR of Lansoprazole was detailed with a KBr disc over the wave No. 4000 to 400 cm^{-1}.

Preparation of standard calibration curve

Preparation of calibration curve of Lansoprazole in 0.1 N HCl: 50mg of Lansoprazole was engaged in 50ml volumetric flask and

dissolved with little drops of methanol and prepared up the volume to 50ml with 0.1 N Hydrochloric acid to contribute the concentration of 1000 µg/ml. 1ml of beyond was diluted to 10ml with 0.1 N HCl to give concentration of 100µg/ml. From the beyond stock solution, aliquots of 0.5, 1, 1.5, 2, 2. 5 and 3 ml were shifted to 10 ml volumetric flasks and made up to the mark with 0.1 N Hcl. This solution was perused in UV-Visible Spectrophotometer. The absorbance of these solutions was restrained at 304 nm and a graph of concentration versus absorbance was plotted.

Preparation of calibration curve of Lansoprazole in phosphate buffer of pH 6.8: 50mg of Lansoprazole was taken in 50ml volumetric flask and dissolved with few drops of methanol and made up the volume to 50ml with phosphate buffer pH6.8 to give the concentration of 1000µg/ml. 1ml of SS1 was diluted to 10ml with phosphate buffer to give concentration of 100µg/ml. From the above stock solution, aliquots of 0.5, 1, 1.5, 2, 2.5, and 3 ml were transferred to 10 ml volumetric flasks and made up to the mark with phosphate buffer pH 6.8. The absorbance of these solutions was measured at 300 nm and a graph of concentration versus absorbance was plotted.

Compatibility studies of drug and polymers

FTIR Studies: Compatibility of the Lansoprazole with superdisintegrants and other polymers used to formulate where studied by FTIR analysis by KBr pellet method [6].

Formulation Development: Lansoprazole enteric coated tablets were arranged by wet granulation process and enteric coated with diverse sorts of polymers as revealed in table 1. The compression practice was executed by expending sixteen station rotary compression machines.

Preparation of core tablets: Dummy granules for tablets were arranged by wet granulation technique. The particular elements (polymer, and additives) were delivered through a sieve no. 60 (250 µm) and unified with a turbula mixer. Instigation of PVP K-30 was finished exhausting isopropyl alcohol and the primed granules were dried. The dried granules were assorted with drug and compressed on a 16-station tablet machine exhausting 5 mm biconvex round shaped die and punches [7].

Preparation of seal coating solution: exactly weighed the vital extent of HPMC 5cps. Commotion the water with the aid of a propeller and so that a vortex molded deprived of depiction of any air into the liquid [8]. Currently, HPMC was auxiliary to the vortex leisurely so that powder initiation on the vortex can be eluded.

Preparation of enteric coating solution: the solvents, water for Eudragit L30 D55 and a mixture of isopropyl alcohol and dichloromethane (1:1) for HPMCP and CAP were reserved in a mingling vessel. The identified expanse of dibutyl phthalate was added and agitated for 30 min to get undeviating dispersion of coating material [9]. The sub-coated tablets were coated expending beyond primed solutions in conservative coating pan.

Table 1: Formulation Table

Sl.No	Ingredients	Formulations qty./ tab (mg)				
		F1	**F2**	**F3**	**F4**	**F5**
1	Lansoprazole	30	30	30	30	30
2	Mannitol	39	-	19.5	38	37
3	Dibasic calcium phosphate	-	39	19.5	-	-
4	Sodium bicarbonate	33	33	33	33	33
5	Polyvinyl pyrrolidone(K30)	7	7	7	7	7
6	Croscarmellose sodium	4	4	4	5	6
7	Magnesium stearate	3	3	3	3	3

8	Talc	4	4	4	4	4
9	Isopropyl alcohol	Q.s	Q.s	Q.s	Q.s	Q.s
10	**Total weight**	120	120	120	120	120

Selected formulation (Core tablets) for enteric coating

S.No	Ingredients	Qty/tab (mg)	%w/w	Qty/100 tablets
1	Lansoprazole	30	25	3000
2	Mannitol	37	30.83	3700
3	Dibasic calcium phosphate	-	-	-
4	Sodium bicarbonate	33	27.5	3300
5	Polyvinyl pyrrolidone (K30)	7	5.83	700
6	Croscarmellose sodium	6	5	600
7	Magnesium stearate	3	2.5	300
8	Talc	4	3.33	400
9	Isopropyl alcohol	Q.s	Q.s	Q.s
10	**Total weight**	120	100	12000

Enteric coating (5% and 8% weight buildup)

S.No	Ingredients	Formulations					
		5% wt gain			8% wt gain		
		F5a	F5b	F5c	F5d	F5e	F5f
1	Eudragit L 30 D 55	5	-	-	5	-	-
2	HPMCP	-	5	-	-	5	-
3	CAP	-	-	5	-	-	5
4	Dibutyl Pthalate	0.5	0.5	0.5	0.5	0.5	0.5
5	Talc	0.75	0.75	0.75	0.75	0.75	0.75
6	Isopropyl alcohol	-	50	50	-	50	50
7	Dichloromethane	-	50	50	-	50	50
8	Water	100	-	-	100	-	-

Enteric coating (8% weight buildup, Plasticizer effect)

S.No	Ingredients	Formulations		
		F5d	F5d1	F5d2
1	Eudragit L 30 D 55	5	5	5
2	Dibutyl Pthalate	0.5	0.75	1
3	Talc	0.75	0.75	0.75
4	Water	100	100	100

Evaluation Parameters [10, 11, 12]

Pre Compression Parameters for pure drug

Bulk Density (BD)

Bulk density = Weight of powder / Bulk volume

Tapped density (TD)

Tapped Density = Weight of powder / Tapped volume

Carr's Index: It is a meek test to assess the BD and TD of a powder and the rate at which it is crowded down. The formula for Carr's Index is as beneath:

Carr's Index (%) = [(TD-BD) x100]/TD

Hausner's Ratio: The Hausner's ratio is a digit that is interrelated to the flowability of a powder or granular material and their standard values are given in table 2.

Hausner's Ratio = TD / BD

Table 2: Effect of Carr's Index and Hausner's Ratio and Angle of repose on flow property

Flow Character	Carr's Index (%)	Hausner's Ratio	Angle of repose
Excellent	≤10	1.00-1.11	<20
Good	11-15	1.12-1.18	20-30
Fair	16-20	1.19-1.25	-----
Passable	21-25	1.26-1.34	30-34
Poor	26-31	1.35-1.45	-------
Very poor	32-27	1.46-1.59	>35
Very very poor	>38	>1.6	-------

Angle of repose

$$\tan \theta = h/r$$

Where, h and r are the height and radius of the powder cone correspondingly.

Post-compressional Studies

Shape and appearance: Tablets were scrutinized underneath a lens for the shape of the tablet, and color was perceived by observance the tablets in light [13].

Uniformity of thickness: Thickness and diameter of mutually core tablets and coated tablets were restrained using a calibrated dial calipers. Three tablets of apiece formulation were chosen arbitrarily and extents were indomitable. It is articulated in mm and standard deviation was also premeditated [14].

Weight variation test: To revise weight variation, 20 tablets of each pulse dose formulation were weighed independently exhausting a Sartorius electronic balance and the test was accomplished conferring to the endorsed technique. The average weight was illustrious and standard deviation was premeditated. The tablet permits the test if not more than two tablets fall separate the percentage bound and none of the tablet diverges by more than double the percentage limit [15].

Hardness test: Hardness signposts the capacity of a tablet to endure mechanical shudders while handling. Hardness of core tablets was indomitable using an endorsed dial type hardness tester. It is articulated in kg/cm^2. Three tablets were erratically picked from respectively batch and considered for hardness. The mean and standard deviation were also premeditated [16].

Friability test: For each pulse dose tablet formulation, the friability of 6 tablets was indomitable using the Roche friabilator [17]. Friability can be determined by ensuing equation:

$$F = \left[\frac{Wt_{Initial} - Wt_{Final}}{Wt_{Initial}}\right] \times 100$$

Disintegration time: The *in-vitro* disintegration time was resolute by using disintegration test apparatus [18]. The tablets were employed in each of the six tubes of the apparatus. The circumstances for enteric-coated tablets are:

a) All the six tablets tested should not disintegrate in 2 hour in 0.1N HCl and should not show any sign of cracks or swelling.

b) All the six tablets tested in 0.1N HCl for 2 hour should disintegrate within 30 min in phosphate buffer pH 6.8.

In vitro dissolution studies: Dissolution was carried out in 0.1N HCl for 2 hour and phosphate buffer pH 6.8 for 45 min. in 900ml volume of type 2 paddle apparatus with rotation Speed 75 rpm and at temperature: 37^0 C $\pm$ 0.5^0 C [19]. The percentage drug release can be calculated by following equation;

$$\textbf{\% drug content} = \frac{AT \times WS \times DT \times P \times 100}{AS \times DS \times 1 \times 100 \times LC}$$

Similarity Factor (f_2): This is used for the Performance difference between the Two Identical Dosage Compunds. If the value further than 50 it is similar (f2) and less than 50 it is Dissimilar (f1).

Release kinetics: In edict to apprehend the mechanism and kinetics of drug release, the results of the in vitro drug release study were fitted with various kinetic equations namely zero order (% release vs time), first order (log% unreleased vs time), and Higuchi matrix (% release vs square root of time). In order to delineate a model which will epitomise a better fit for the formulation, drug release data advance considered by Peppas equation, $Mt/M\infty = ktn$, where Mt is the amount of drug released at time t and $M\infty$ is the amount released at time ∞, the $Mt/M\infty$ is the fraction of drug released at time t, k is the kinetic constant and n is the diffusion exponent, a degree of the primary mechanism of drug release. Regression coefficient (r^2) values were premeditated for the linear curves acquired by regression analysis of the above plots [20].

Stability Studies: the stability studies were conceded out as per ICH guidelines at refrigerator & work bench for the ensuing particular formulation for 3 months. Subsequently indicated time intervals, parameters like physical appearance, disintegration time, drug content, related substances and dissolution were evaluated rendering to the procedure designated as formerly [21].

RESULTS AND DISCUSSION

Preformulation Studies: In preformulation studies, characterization of API (identification test by FTIR,) was executed and it was institute that all are within the range detailed in the pharmacopoeia.

Characterization of Active pharmaceutical ingredient were performed Calibration Curve of Lansoprazol

Table 3: Calibration curve of Lansoprazole

0.1 N HCl		
S.No	**Concentration of Lansoprazole in mcg/ml**	**Absorbance (304nm)**
1	0	0

2	5	0.22 ± 0.02
3	10	0.42 ± 0.02
4	15	0.632 ± 0.004
5	20	0.862 ± 0.007
6	25	1.109 ± 0.01
Phosphate buffer of pH 6.8		
1	0	0
2	3	0.065± 0.004
3	5	0.091 ± 0.002
4	10	0.202 ± 0.43
5	15	0.303 ± 0.006
6	20	0.399 ± 0.003
7	25	0.51 ± 0.03
8	30	0.594 ± 0.004

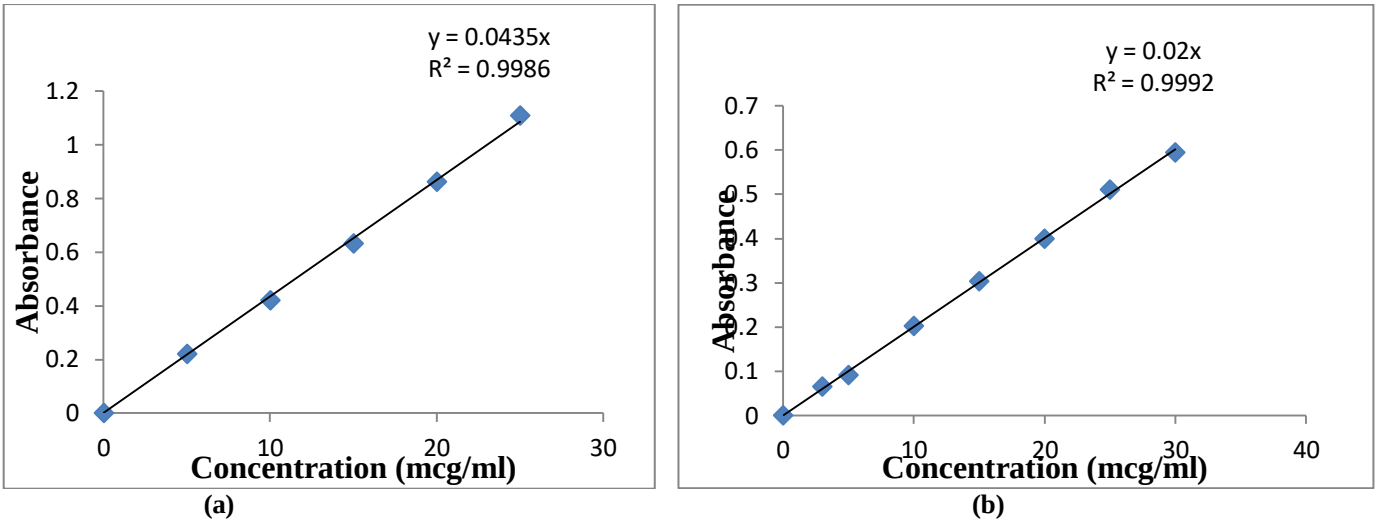


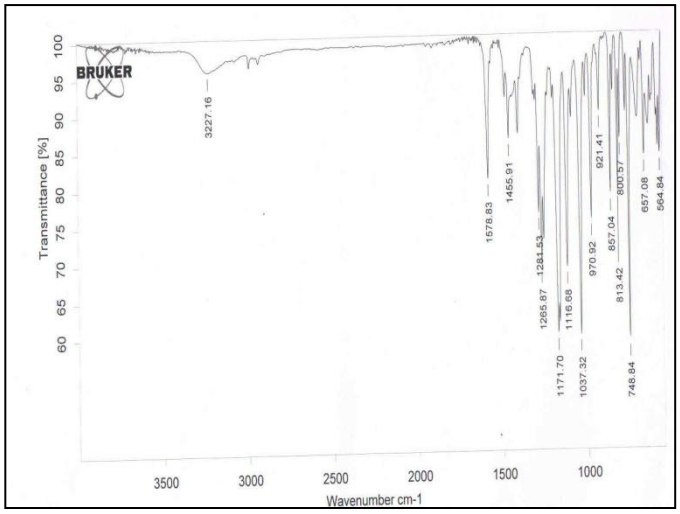
Figure 1: Calibration curve of Lansoprazole (a) in 0.1 N HCl (b) in Phosphate buffer of pH 6.8

Compatibility studies

Table 4: Values of FTIR spectra

IR Spectra	**Peak of Functional groups [Wave length (cm-1)]**						
	C=C	**N-H**	**C=N**	**S=O**	**C-O**	**C-CH_3**	**C-CF_3**
Lansoprazole	1456	3227	1579	1456	1266	1172	1037
Lansoprazole + all excipients	1455	3231	1579	1455	1266	1172	1037
Lansoprazole + HPMC	1455	3228	1579	1455	1266	1172	1037
Lansoprazole + Eudragit L30 D55	-	-	-	-	-	-	-
Lansoprazole + HPMCP	-	3231	1579	1455	1266	1171	1037
Lansoprazole + CAP	-	-	1579	-	1252	1172	1037

The drug-excipient compatibility study was conceded out using FTIR. The spectral data acquired that Lansoprazole is compatible with all the excipients used in the formulation except enteric polymers (i.e. hydroxy propyl methylcellulose phthalate, Cellulose acetate pthalate & Eudragit L 30 D 55) which origins degradation of Lansoprazole. So throughout formulation sub-coat is assumed prior to enteric coating in order to dodge interaction amongst enteric polymers and Lansoprazole.



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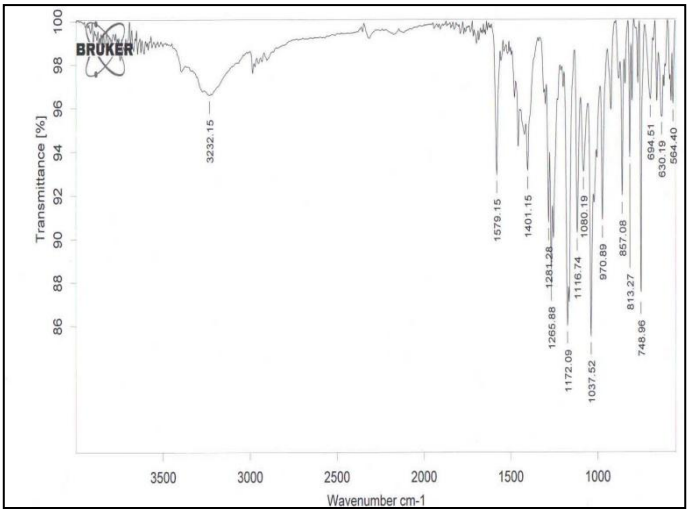

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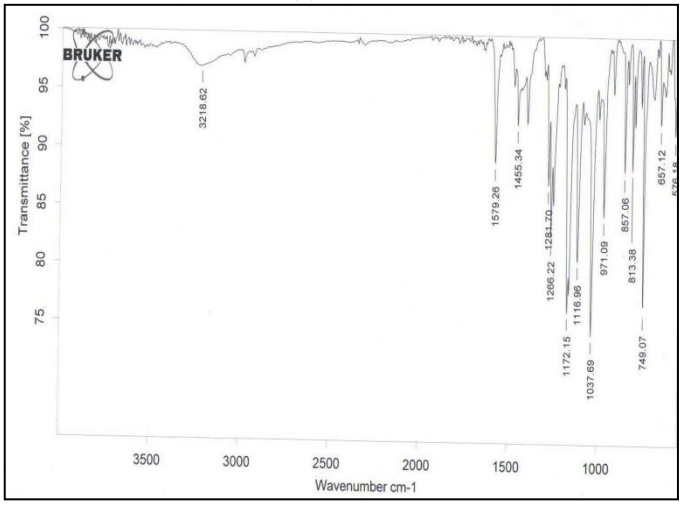

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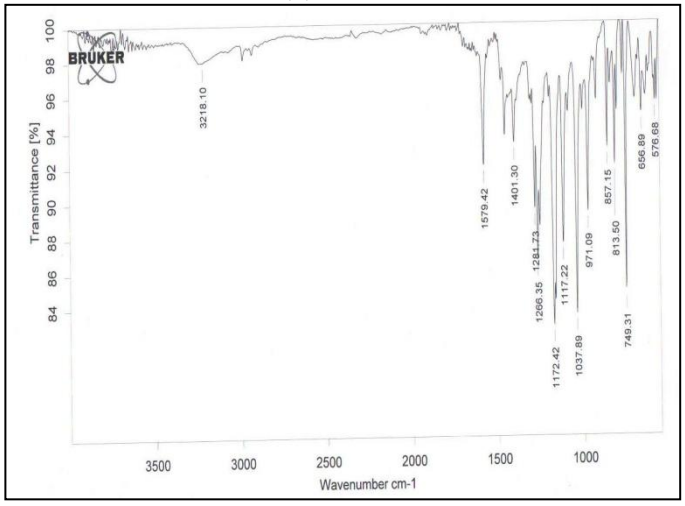

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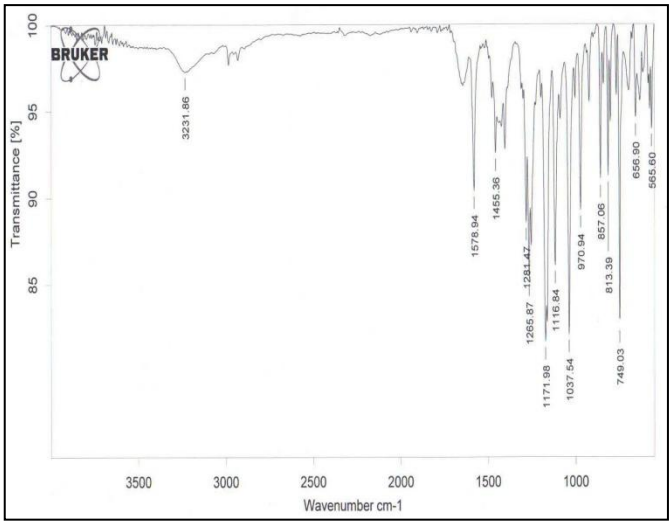
BRUKER
Transmittance [%]
Wavenumber cm-1
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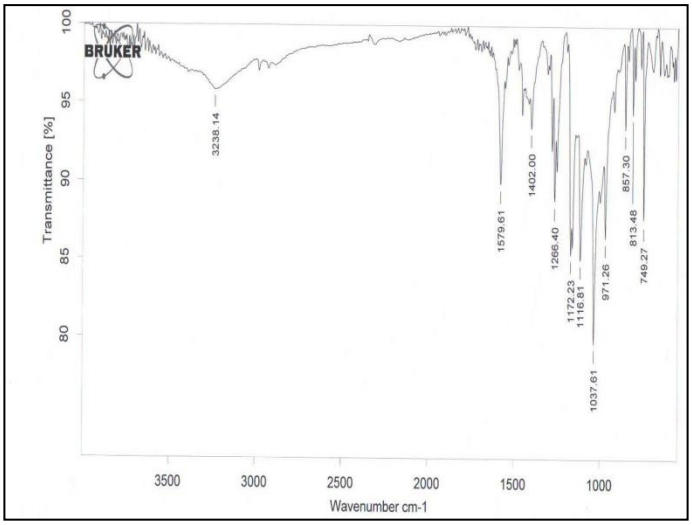
1578.94
1455.36
1281.47
1265.87
1171.98
1116.84
1037.54
970.94
857.06
813.39
749.03
656.90
565.60

(e)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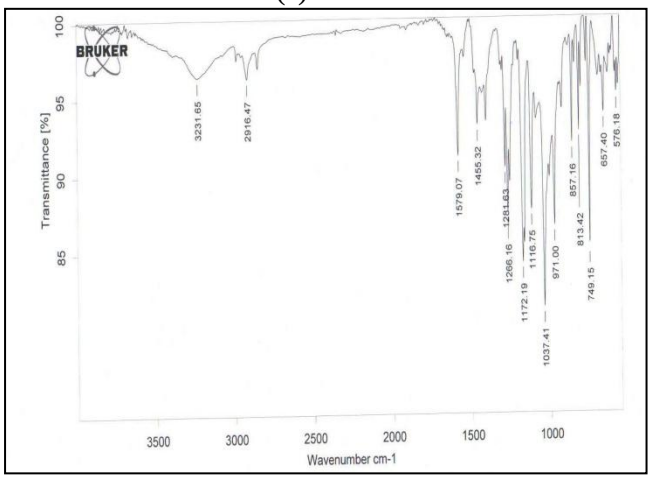
(f)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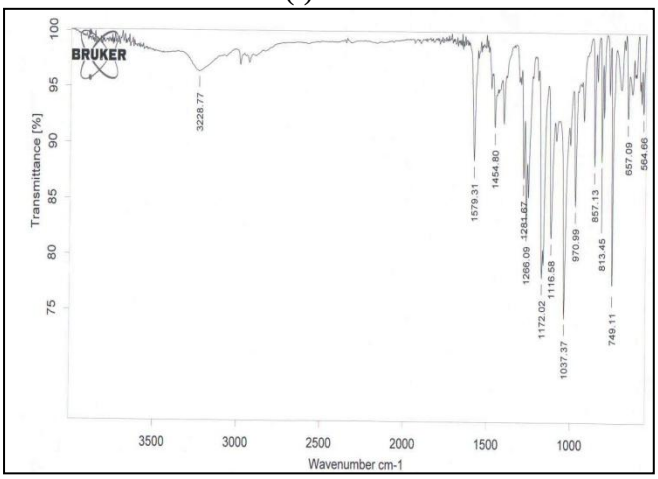
1579.07
1455.32
1281.63
1266.16
1172.19
1116.75
1037.41
971.00
857.16
813.42
749.15
657.40
576.18

(g)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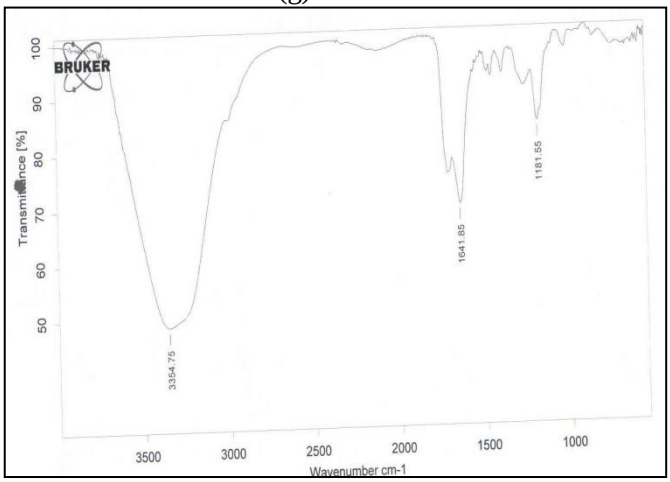
857.13
813.45
749.11
657.09
564.66

(h)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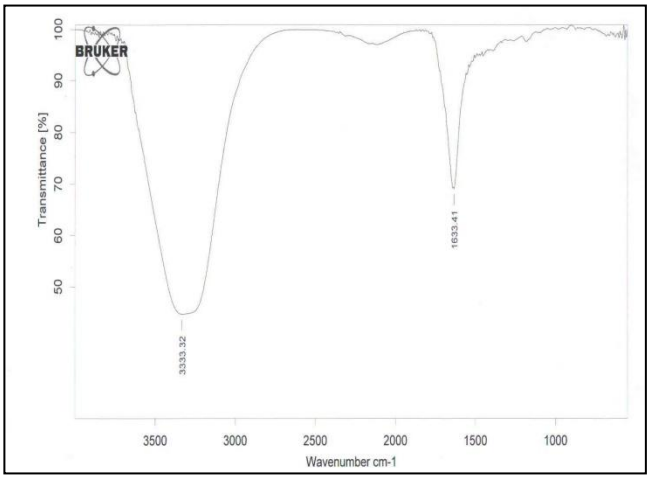
1181.55

(i)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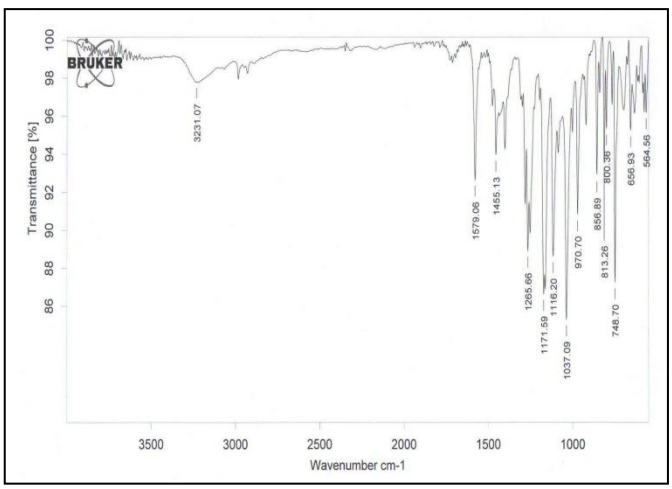

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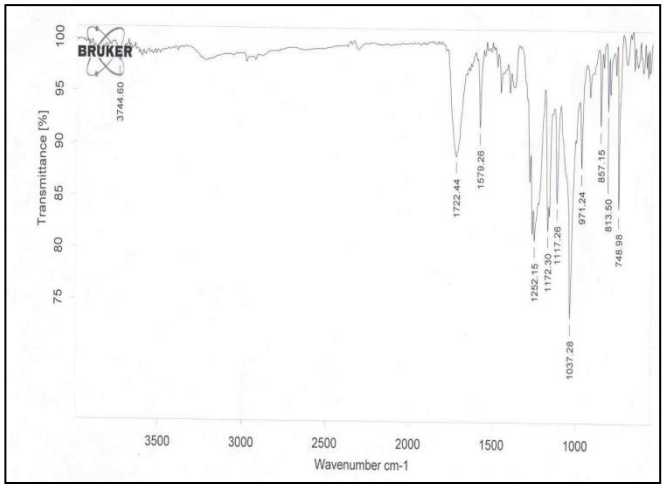

(l)

Figure 2: IR spectra of (a) Lansoprazole (b) Lansoprazole + Mannitol (c) Lansoprazole + Dicalciumphosphate (d) Lansoprazole + Sodiumbicarbonate (e) Lansoprazole + PVP K 30 (f) Lansoprazole + Croscarmellose Sodium (g) Lansoprazole + All excipients of the core tablet (h) Lansoprazole + HPMC (i) Eudragit L30 D55 (j) Lansoprazole + Eudragit L30 D55 (k) Lansoprazole + HPMCP (l) Lansoprazole + CAP

Pre-Compression Parameters

The pre-compression constraints like bulk density, angle of repose, tapped density; Carr's index and hausner ratio have been executed. The Carr's index & Hausner ratio for formulation F1- F3 were in the range of 19-16 & 1.22-1.19 correspondingly, which signpost a fair flow property of the powders. Likewise for F4 &F5 it was institute to be in the range of 15-12 & 1.17-1.14 correspondingly, which signpost a good flow property of the powders.

Post Compression Parameters (Core tablets)

Table 5: Pre-compression and Post compression parameters

Pre-Compression Parameters					
Parameters	**Formulations**				
	F1	**F2**	**F3**	**F4**	**F5**
Angle of repose	23.39±0.02	25.06±1.06	24.93±0.19	24.72±0.15	23.31±0.04
Bulk density (g/cc)	0.453±0.01	0.48±0.015	0.456±0.005	0.463±0.015	0.446±0.01
Tapped density (g/cc)	0.59±0.016	0.556±0.015	0.543±0.015	0.526±0.015	0.53±0.02
Carr's index (%)	16.53±1.38	19.78±2.6	18.41±3.82	15.2±3.56	13.56±0.73
Hausner ratio	1.227±0.04	1.229±0.05	1.19±0.022	1.17±0.05	1.14±0.01
Post Compression Parameters					
Physical properties of tablet formulation F1-F5					
Physical properties	**Formulations**				

	F1	F2	F3	F4	F5
Average weight (mg)	122.5±0.01	123±0.15	121.5±0.05	122±0.15	122.5±0.1
Hardness (N)	3.5±1.52	4.0±1.15	3.5±1.25	3.5±1.12	3.5±1.1
Friability (%)	0.27±0.01	0.39±0.03	0.24±0.02	0.3±0.005	0.28±0.03
Thickness (mm)	4.31±0.005	4.41±0.01	4.32±0.03	4.38±0.02	4.22±0.02
Disintegration test(min)	4.18± 0.34	5.08± 0.42	5.36± 0.3	3.53± 0.23	3.23± 0.11

Physical properties of enteric coated formulations (F5a-F5f)

Physical properties	Formulations					
	F5a	F5b	F5c	F5d	F5e	F5f
Thickness (mm)	4.75±0.06	4.76±0.03	4.75±0.01	4.79±0.06	4.78±0.02	4.78±0.06
Disintegration test (0.1 N HCl)	Failed	Failed	Failed	Passed	Passed	Passed
Disintegration test (Phosphate buffer 6.8)	8.50 ± 0.34	9.21±0.55	9.47± 0.82	10.37±0.62	12.25 ± 0.28	12.40 ± 0.36

Physical properties of enteric coated formulations (F5d-F5d2)

Physical properties	Formulations		
	F5d	F5d1	F5d2
Thickness (mm)	4.79±0.06	4.79±0.03	4.78±0.01
Disintegration test (0.1 N HCl)	Passed	Passed	Passed
Disintegration test (Phosphate buffer 6.8)	10.37 ± 0.62	10.21 ±0.55	10.1 ± 0.62

***** Each value is the mean ± SD (n=3)

The shape and size of the prepared tablets were institute to be within the limit. The average weight was institute to be within the recommended limit. The hardness of the tablets was found to be in the range of 3.5±1.1 to 4.0±1.15 (kg/cm^2). Thicknesses of the tablets were found to be in the range of 4.22±0.02 to 4.41±0.01 mm for core tablets and 4.75±0.01 to 4.79±0.06 mm for coated tablets. The friability of the tablets was found to be less than 0.5 %.

Physical Properties of Enteric Coated Tablets

Disintegration test was engaged as a tool to assess the functional qualities of the enteric coat during acquaintance to simulated gastric fluid. Proximately after simulated gastric fluid acquaintance, each tablet was visually scrutinized for any confirmation, which would signpost inadequate function of the enteric coat then reassigned to a phosphate buffer media. All the enteric coated tablets gladly passed the USP enteric coated disintegration test excluding the formulations F5a, F5b & F5c with 5% weight buildup in 0.1N HCl. The alteration in the disintegration test was pragmatic for the formulations F5d, F5e and F5f, when assessed in phosphate buffer pH 6.8 and they were in the range of 8.50 ± 0.34 to 12.40 ± 0.36. The alteration in disintegration time may be due to the difference in the type of the enteric coating polymer.

In vitro dissolution studies

Table 6: *In vitro* dissolution studies

***In vitro* dissolution studies for F5d, F5e & F5f**				
Sample time	**Cumulative drug release (%) ± SD (n=3)**			
	Innovators product	**F5d**	**F5e**	**F5f**
2hr (0.1N HCL)	0.34 ± 0.11	5.11±0.36	6.36±1.4	8.123±0.49
10	70.03±0.99	73.61±1.23	65.70±1.06	62.1±1.2
20	86.63±1.26	83±1.1	74.57±0.92	70.23±0.89
30	93.46±1.07	91.53±1.21	86.85±1.39	80.43±0.5
40	95.2±1.42	95.23±1.35	90.46±1.07	88.3±1.43
50	98.76±0.59	97.55±0.51	92.2±1.42	91.6±1.06
60	99.89±0.1	99.13 ±0.69	95.13 ±0.7	94.85 ±0.81
***In vitro* dissolution studies for F5d, F5d1 & F5d2**				
Sample time	**Innovators product**	**F5d**	**F5d1**	**F5d2**
2hr(0.1N HCL)	0.34 ± 0.11	5.11±0.36	4.28±0.64	3.39±0.69
10	70.03±0.99	73.61±1.23	70.12±1.54	67.7±0.53
20	86.63±1.26	83±1.1	81.32±0.25	79.63±0.45
30	93.46±1.07	91.53±1.21	88.34±0.54	86.7±1.1
40	95.2±1.42	95.23±1.35	92.2±1.21	90.32±0.32
50	98.76±0.59	97.55±0.51	95.67±0.32	94.53±1.1
60	99.89±0.1	99.13 ±0.69	98.76±0.59	97.32 ±0.71

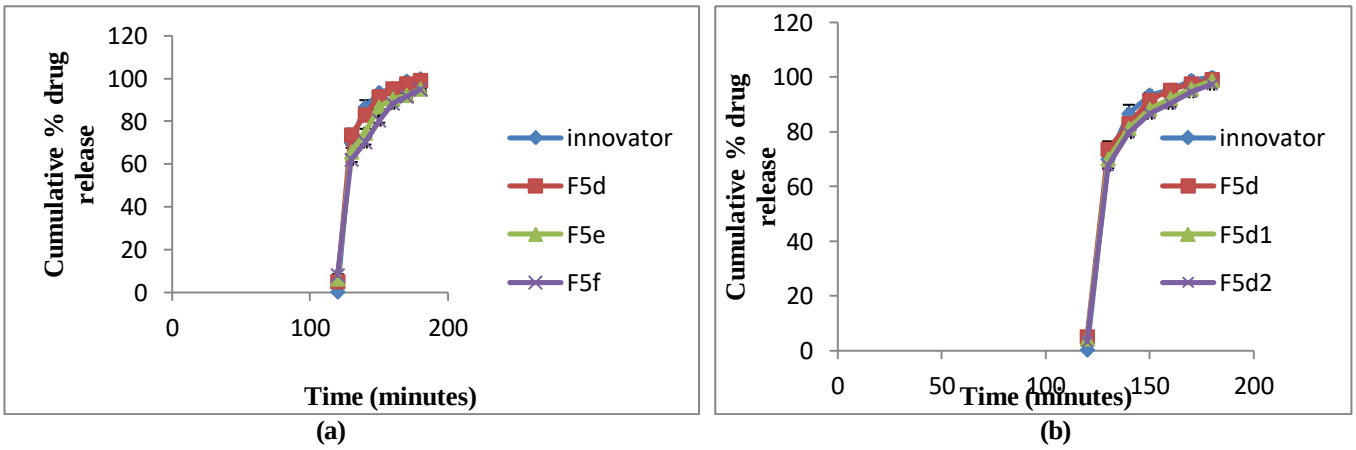

Figure 3: *In vitro* release patterns of formulations (a) F5d, F5e & F5f (b) F5d, F5d1 & F5d2

In vitro dissolution revisions were executed for all the formulations using USP apparatus 6 tablet dissolution tester retaining paddle type at 75 rpm using 500 ml of 1.2 pH 0.1N HCl and 6.8 pH phosphate buffer as dissolution medium. The drug release was assessed using UV spectroscopy. The dissolution study for formulation (F5a-F5c) with 5% weight buildup was not executed, since they could not conceded disintegration test. The drug release data for formulation F5d - F5f, is assumed in the table 6. All the formulations (F5d-F5f) have revealed exceptional physical resistance to the acid medium after 2 hour and the drug release was found to be within quantified limits. In case of formulations F5d, F5e, F5f, (8% weight buildup), drug release in the phosphate buffer (pH 6.8) at 15mins was found to be 21.07, 13.76, 10.93% correspondingly and at the end of 60mins drug release was found to be 99.13 ± 0.69, 95.13 ± 0.7, 94.85 ± 0.81%

correspondingly. It was found that percentage drug release was more in formulation F5d at the end of 60mins.

Amid all formulations (F5d-F5f), the formulation F5d was reflected optimum because in acid medium drug release was less than 10% and drug release in the phosphate buffer (pH 6.8) was found to be practically complete. For the optimized above formulation F5d, the effect of plasticizer was also premeditated which exhibited that proliferation in concentration dwindled drug release in both 0.1 N HCl and phosphate buffer of pH 6.8.

Similarity Factor (f_2): Similarity factor (f2) amongst the marketed and optimized formulation was institute to be 80.027

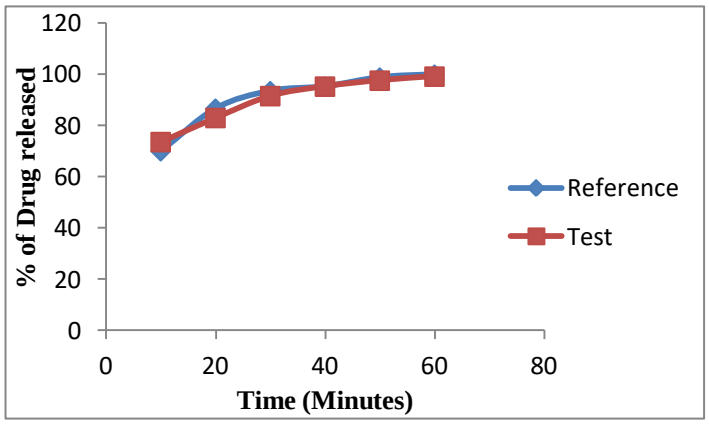

Figure 4: Similarity factor between the optimized and marketed formulation

Release Kinetics: The formulation F5d follows first order and Korsemeyer- peppas order release kinetics overseen by Fickian diffusion mechanism. Consequently, the release of drug from the prepared tablets is controlled by the initial swelling of the polymer, monitored by drug solution diffusion through the channels of the swollen polymer.

Table 7: Correlation Coefficient (R^2) of different kinetic models for optimized formulation

Formulation	% Drug release	Time (hrs)	R^2 Value				n value
			Zero order	First order	Higuchi	Korsemeyer- peppas	
F5d	99.13	1	0.6142	0.9829	0.8669	0.9845	0.1722
***Each value represents the mean ± SD (n=3)							

Stability Studies: Stability studies were conceded out at refrigerator & work bench for the designated formulation (F5d) for 3 months.

Physical appearance

The physical appearance of the illustrations kept for stability studies were patterned each month and found that there was no alteration in the appearance.

Table 8: Stability Studies for formulation F5d kept for stability studies at refrigerator & work bench

Time in months	Refrigerator		Work bench	
	Disintegration (0.1 N HCl)	Disintegration (6.8 buffer)	Disintegration (0.1 N HCl)	Disintegration (6.8 buffer)

0	Passed	10.37 ± 0.41	Passed	10.41 ± 0.23
1	Passed	10.47 ± 0.34	Passed	10.5 ± 0.34
2	Passed	10.6 ± 0.22	Passed	10.54 ± 0.52
3	Passed	10.42 ± 0.43	Passed	10.47 ± 0.45
Time in months	**Dissolution (0.1 N HCl)**	**Dissolution (6.8 buffer)**	**Dissolution (0.1 N HCl)**	**Dissolution (6.8 buffer)**
0	1.56 ± 0.78	99.13 ± 0.06	1.54 ± 0.07	99.12 ± 0.03
1	1.55 ± 0.025	99.89 ± 0.026	1.563 ± 0.07	99.1 ± 0.02
2	1.6 ± 0.015	99.05 ± 0.025	1.61 ± 0.03	99.07 ± 0.06
3	1.68 ± 0.02	98.99 ± 0.036	1.68 ± 0.015	98.87 ± 0.045
***** Each value is the mean ± SD (n=3)				

Table 9: Assay for selected formulation stored at refrigerator & work bench

Time in months	Refrigerator	Work bench
0	99.55	99.53
1	99.32	99.38
2	99.1	99.04
3	98.87	98.52

The stability studies were achieved on designated formulation where the drug release was low in 0.1N HCl (i.e. F5d) at refrigerator & work bench. The samples were examined for disintegration time, drug content and dissolution studies in 0.1N HCl and in phosphate buffer pH 6.8. The physical appearance of the samples kept for stability studies were patterned and found that there was no variance in the appearance. The drug content exploration also revealed that the products were stable (Table 8). Auxiliary the formulations did not illustration any substantial variance in dissolution rate after a study period of 3 months.

CONCLUSION

In the present study, an endeavor was made to distribute an antiulcer drug Lansoprazole through the oral route in the form of enteric coated tablets. Lansoprazole enteric coated with Eudragit L30 D55 exhibited admirable physical resistance in gastric fluids and better drug release characteristics in intestinal fluids. All the formulations were assessed for their physicochemical parameters like thickness, disintegration time, drug content and dissolution studies. Further, the plasticizer effect on Eudragit L30 D55 was also premeditated and institute, with proliferation in concentration of plasticizer there is dwindled drug release in both 0.1 N HCL and 6.8 pH phosphate buffer. The designated formulation was imperiled for stability studies at refrigerator & work bench. Formulation imperiled for stability studies were patterned for physical appearance, disintegration test, drug content, related substances, and dissolution for 3months. The formulation was institute to be stable as no substantial change was perceived in the various evaluated constraints of the formulation.

REFERENCES

[1]. Liu, F., Moreno, P., Basit, AW. A novel double-coating approach for improved pH-triggered delivery to the ileocolonic region of the gastrointestinal tract. *Eur J Pharm Biopharm.* **2010**. 74: 311-315.

[2]. Bown, RL. An overview of the pharmacology, efficacy, safety and cost-effectiveness of lansoprazole. *Int J Clin Pract.* **2002.** 56:132-139.

[3]. Robinson, M. Proton pump inhibitors: Update on their role in acid-related gastrointestinal diseases. *Int J Clinical Practice.* **2005**. 59(6): 709-715.

[4]. Richardson, P., Hawkey, CJ., Stack, W. A proton pump inhibitor; Pharmacology and rationale for use in gastrointestinal disorder. *Drugs*. **1998**.56: 307-335.

[5]. Pilotto, A., et al. Comparison of four proton pump inhibitors for the short-term treatment of esophagitis in elderly patients. *W J gastroenterol.* **2007**. 13(33): 4467-4472.

[6]. Ashford, M. et al. An *in vitro* investigation into the suitability of pH-dependent polymers for colonic targeting. *Int J Pharm.* **1993**. 91: 241-245.

[7]. Marvola, M., et al. Enteric polymers as binders and coating materials in multiple-unit site-specific drug delivery systems. *Eur J Pharm Sci*. **1999**. 7: 259-267.

[8]. Liu, F., et al. A novel concept in enteric coating: a double-coating system providing rapid drug release in the proximal small intestine. *J Control Release.* **2009**. 133: 119-124.

[9].Olzaltin, N. Determination of lansoprazole in pharmaceutical dosage forms by two different spectroscopic methods. *J Pharm and Biomed Anal*. **1999**. 20: 599-606.

[10]. Stellaard, F., et al. Pulsatile drug delivery to ileo-colonic segments by structured in-corporation of disintegrants in pH-responsive polymer coatings. *J Control Release.* **2008**.132: 91-98.

[11]. Shimizu, T., et al. Formulation study for lansoprazole fast-disintegrating tablet. III. Design of rapidly disintegrating tablets. *Chem Pharm Bull.* **2003**. 51: 1121-1127.

[12]. Hogan, D., et al. Oral pantoprazole in the form of granules or tablets are pharmacodynamically equivalent in suppressing acid output in patients with gastro-oesophageal reflux disease and a history of erosive oesophagitis. *Aliment Pharmacol Ther.* **2007**. 26(2):249-256.

[13]. Rehner, M., et al. Comparison of pantoprazole verses omeprazole in the treatment of acute duodenal ulceration. *Aliment Pharmacol Ther.* **1995**. 9(4):411-416.

[14]. Tatiane, P., et al. Eudragit E as excipient for production of granules and tablets from Phyllanthusniruri L spray-dried extract. *AAPS Pharm Sci Tech*. **2007**. 8(2): E54-E60.

[15]. Deepti, J., et al. Eudragit S100 Entrapped Insulin micro spheres for oral delivery. *AAPS Pharm Sci Tech*. **2005**. 6(1): E100-E107.

[16]. Castell, D., et al. Comparison of the effects of immediate release omeprazole powder for oral suspension and pantoprazole delayed release tablet for nocturnal acid breakthrough in patients with symptomatic gastro esophageal reflux disease. *Alient pharmacol Ther*. **2005**. 21(12):1467-1474.

[17]. Sinha, V.,R., et al. Coating polymers for colon specifi c drug delivery: A comparative *in vitro* evaluation. *Acta pharm*. **2003**. 53: 41-47.

[18]. Marvola, M., et al. Enteric polymers as binders and coating materials in multiple-unit site-specific drug delivery systems. *Eur J Pharm Sci*. **1999**. 7: 259-267.

[19]. Wei, G., et al. Simple coacervation of hydroxyl propyl methyl cellulose phthalate (HPMCP) II. Microencapsulation of ibuprofen. *Int J Pharm*. **1995**. 124: 97-105.

[20]. Bladh, N., et al. A new esomeprazole packet (sachet) formulation for suspension: *in vitro* characteristics and comparative pharmacokinetics versus intact capsules/tablets in healthy volunteers. *Clin Ther*. **2007**. 4: 640-649.

[21]. Stability testing of new drug substances and products. ICH Harmonised Tripartite Guidelines. **2003**.