EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 7
297-304
Year: 2019

# FORMULATION AND EVALUATION OF DELAYED RELEASE TABLETS OF LANSOPRAZOLE

**[1]*B. Premkumar, [1]K. P. Chandralekha, [1]Makam Sirisha, [1]K. Bindhumadhavi and [2]A. Srinivasa Rao**

[1]Department of Pharmaceutics, Bhaskar Pharmacy College, Yenkapally, Moinabad (M), Ranga Reddy (Dt), Hyderabad – 500 075, Telangana, India.
[2]Department of Pharmacy Practice, Bhaskar Pharmacy College, Yenkapally, Moinabad (M), Ranga Reddy (Dt), Hyderabad – 500 075, Telangana, India.

***Corresponding Author: B. Premkumar**
Department of Pharmaceutics, Bhaskar Pharmacy College, Yenkapally, Moinabad (M), Ranga Reddy (Dt), Hyderabad – 500 075, Telangana, India.

**Article Received on 13/05/2019** **Article Revised on 03/06/2019** **Article Accepted on 24/06/2019**

**ABSTARCT**
The objective of the study was an attempt to formulate and evaluate delayed release tablets of lansoprazole which is a benzimidazole anti ulcer agent and is one of the most widely used drugs for treating mild and severe ulcers. The stability of lansoprazole a proton pump inhibitor is a function of pH and it rapidly degrades in acidic medium of the stomach, but has acceptable stability in alkaline conditions. The present study demonstrates that the lansoprazole tablets could be successfully intestine targeted by using pH dependent polymers in different concentrations. The drug and excipient compatibility study was performed by FT-IR and study revealed that there was no interaction between drug & excipient. The tablets were evaluated for various parameters like hardness, friability, weight variation, percentage drug content and *in-vitro* disintegration time, *in-vitro* dissolution study, drug release kinetic study and stability study. By observing the dissolution profile for all the formulations, F1 was the better formulation. From the result of this study it may be concluded that the colon targeted drug delivery tablets using a combination of two polymers in optimized concentrations can be used to increase the delayed action of drug release to deliver the drug in a delayed manner.

**KEYWORDS:** Lansoprazole, polymers, direct compression technique, FTIR & *in-vitro* studies.

## INTRODUCTION

The term "drug delivery" can be defined as "the techniques that are used to get the therapeutic agents inside the body". The Oral Solid Dosage forms are the preferred route of administration for many drugs and most widely used formulations for new and existing modified release products. Indeed, for controlled release systems, the oral route of administration has by far received the most attention with respect to research on physiological and drug constraints as well as design and testing of products. This is because there is more flexibility in dosage form design for the oral route than there is for the parental route.[1-4] Delayed Release Drug Delivery System involves release of drugs only at a specific site in the gastrointestinal tract. The drugs contained in such a system are those that are.[5-6]

i) Destroyed in the stomach or by intestinal enzymes
ii) Known to cause gastric distress
iii) Absorbed from a specific intestinal site or
iv)Meant to exert local effect at a specific gastrointestinal site

The two types of delayed release systems are:
1. Intestinal release systems
2. Colonic release systems

## MATERIAL AND METHODS

### Materials

Lansoprazole was obtained from Chandra labs, Hyderabad. Microcrystalline cellulose, Cross povidone and Magnesium stearate were purchased from S. D. Fine Chemicals, Mumbai. Cross caramellose sodium and Sodium starch glycolate were procured from Mylan Chem. Ltd, Mumbai and Talc was obtained from ESSEL fine chem, Mumbai, India.

### Methods

### Preformulation studies

Pre formulation studies are performed to investigate the physical and chemical properties of a drug substance alone and also when combined with other substances such as excipient. It is the first step in the rational development of dosage forms.

**Preparation of Standard Calibration Curve of Lansoprazole in 0.1 HCl**

**Preparation of standard solution**

Standard stock solution of Lansoprazole was prepared in 0.1N HCl. 100mg of lansoprazole was accurately weighed into 100ml volumetric flask and dissolved in small quantity of 0.1N HCl. The volume was made up with 0.1N HCl to get a concentration of 1000µg/ml (SS-I). From this 10ml solution was withdrawn and diluted to 100ml of 0.1N HCL to get a concentration of 100µg/ml (SS-II).

**Preparation of working standard solutions**

Further, from (SS-II) aliquots of 0.2ml, 0.4ml, 0.6ml, 0.8ml and 1ml were pipette into 10ml volumetric flasks. The volume was made up with 0.1N HCl to get the final concentrations of 2, 4 6, 8 and 10µg/ml respectively. The absorbance of each concentration was measured at 207nm. The data are compiled in table 1 and in fig 1.

**Preparation of Standard Calibration Curve of Lansoprazole in pH 6.8 Phosphate buffer**

**Preparation of standard solution**

Standard stock solution of lansoprazole was prepared in phosphate buffer pH6.8. 100mg of lansoprazole was accurately weighed into 100ml volumetric flask and dissolved in small quantity of buffer. The volume was made up with water to get a concentration of 1000µg/ml (SS-I). From this 10ml solution was withdrawn and diluted to 100ml of phosphate buffer pH6.8 to get a concentration of 100µg/ml (SS-II).

**Preparation of working standard solutions**

Further, from (SS-II) aliquots of 0.2ml, 0.4ml, 0.6ml, 0.8ml and 1ml were pipette into 10ml volumetric flasks. The volume was made up with phosphate buffer pH6.8 to get the final concentrations of 2, 4, 6, 8 and 10µg/ml respectively. The absorbance of each concentration was measured at 207nm. The data are compiled in table 2 and in fig 2.

**Drug – Excipient Compatibility Study**

The physical properties of the physical mixture were compared with those of plain drug. Samples were mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in FTIR spectrophotometer and the IR spectrum was recorded from 4000 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

**Formulation of core tablets by direct compression:**

The inner core tablets were prepared by using direct compression method. As shown in table 3 powder mixtures of Lansoprazole, microcrystalline cellulose (MCC, Avicel PH-102), cross-carmellose sodium (Ac-Di-Sol), SSG, cross povidone, ingredients were dry blended for 20mins, followed by addition of Magnesium Stearate. The mixtures were then further blended for 10mins. 150mg of resultant powder blend was manually compressed using KBr hydraulic press at a pressure of 1 ton, with an 8mm round punch and die to obtain the core tablet.

**Table 3: Formulation for core tablet.**

| S. No | Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Lansoprazole | 30mg | 30mg | 30mg | 30mg | 30Mg | 30mg | 30mg | 30mg | 30Mg |
| 2 | Microcrystalline Cellulose | qs | qs | qs | qs | qs | qs | qs | qs | qs |
| 3 | Cross Povidone | 5% | 7.5% | 10% | | | | | | |
| 4 | Cross caramallose sodium | | | | 5% | 7.5% | 10% | | | |
| 5 | Sodium starch glycolate | | | | | | | 5% | 7.5% | 10% |
| 6 | Magnesium stearate | 2% | 2% | 2% | 2% | 2% | 2% | 2% | 2% | 2% |
| 7 | Talc | 2% | 2% | 2% | 2% | 2% | 2% | 2% | 2% | 2% |
| | **Total Weight** | 150mg | 150mg | 150mg | 150mg | 150Mg | 150mg | 150mg | 150mg | 150Mg |

**Formulation of mixed blend for barrier layer**

The various formulations containing Ethyl cellulose and HPMC in different compositions were weighed; dry blended at about 10 min and used as press-coating material to prepare press-coated tablets respectively by direct compression method.

**Preparation of press-coated tablets**

The core tablets were press-coated with 350mg of mixed blend/granules as given in table 4. 200mg of barrier layer material was weighed and transferred into a 12mm die then the core tablet was placed manually at the center. The remaining 1500mg of the barrier layer materiel was added into the dye and compressed at a pressure of 5 tons for 3min using KBr hydraulic press.

**Table 4: Formulation for press coat.**

| Press coat | P1F1 | P2F1 | P3F1 | P4F1 | P5F1 |
|---|---|---|---|---|---|
| HPMC | 150 | 200 | 175 | 100 | 250 |
| E.C | 200 | 150 | 175 | 250 | 100 |
| **Total wt** | 350mg | 350mg | 350mg | 350mg | 350mg |

**Preparation of enteric coating solution**
Polymer solution was prepared with HPMC phthalate, myvacet and colour in ethanol as solvent.

**Table 5: Enteric coated formula.**

| | |
|---|---|
| HPMC phthalate 55 | 17.17mg |
| Myvacet | 1.72mg |
| Ferric oxide (red) | 2.58mg |
| Ethanol | q.s |

**Pre Formulation Parameters**
**Angle of Repose**
The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured.[7] The angle of repose was calculated using the following formula:

$\tan \theta = h / r$
$\tan \theta$ = Angle of repose, h = Height of the cone, r = Radius of the cone base.

**Bulk density**
Bulk density is ratio of the given mass of powder and its bulk volume. Bulk density was determined by measuring the volume of known mass of powder sample that has been passed through the screen in to graduated cylinder or through volume measuring apparatus in to cup.[8]

$\text{Bulk density} = M / V_0$

M= mass of the powder; $V_0$=bulk volume of the powder.

**Tapped density**
A known quantity of powder was transferred to a graduated cylinder and volume $V_0$ was noted. The cylinder fixed to a density determination apparatus, tapped for 500 times then reading was observed. The density was achieved by mechanically tapped by a measuring cylinder containing the powder sample. After observing the initial volume, the cylinder was mechanically tapped and volume readings were taken until little further volume changes were observed.

$\text{Tap density} = M / Vr$

M = mass of the powder, Vr = final tapping volume of the powder.

**Compressibility index and Hausner ratio**
The compressibility index and Hausner ratio may be calculated using measured values of bulk density and tapped density as follows:
Compressibility index = 100 × tapped density / bulk density
Hausner ratio = tapped density / bulk density

**Evaluation of rapid release core (RRCT) and press-coated tablets of lansoprazole**
**Evaluation of Tablets**
**Weight variation test**
Twenty tablets were weighed individually and the average weight was calculated. The individual tablet weights are then compared to the average weight. Not more than two tablets should differ in their average weight by more than percentages stated in USP. No tablet must differ by more than double the relevant percentage.

**Hardness**
Hardness, which is now more appropriately called crushing strength determinations are made during tablet production and are used to determine the need for pressure adjustment on tablet machine. If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specifications; if it is too soft, it may not be able to withstand the handling during subsequent processing such as coating or packaging and shipping operations. The force required to break the tablet is measured in kilograms. The small and portable hardness tester measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet.

**Thickness and diameter**
The thickness and diameter of 10 tablets were recorded during the process of compression using vernier calipers.

**Friability**
A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked.

The percentage friability was determined by the formula:

$\% \text{ Friability} = (W1-W2) / W1 \times 100$

W1 = Weight of tablets before test, W2 = Weight of tablets after test.

**Disintegration test (RRCT)**

The U.S.P. device to test disintegration uses 6 glass tubes that are open at the top and 10 mesh screen at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2°C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. If one or two tablets fail to disintegrate, the test is repeated using 12 tablets.

Disintegration time: Uncoated tablet: 5-30 minutes.
Coated tablet: 1-2 hours

***In-vitro* release studies for RRCTs**

Tablet was introduced into the basket of the LABINDIA TS 8000 USP dissolution test apparatus and the apparatus was set in motion at 50 rpm for time period of 1 hr at 37+ 0.5°C. 5 ml of sample was withdrawn for every 5min intervals until 60mins and replaced by 0.1 N HCl solutions. Samples withdrawn were analyzed by UV spectrophotometer for presence of drug using 0.1N HCl solution as blank.[6,9]

***In-vitro* Dissolution methods for enteric press-coated tablets**

*In –vitro* dissolution studies of colon targeted drug delivery systems was done with the conventional paddle method of press coated tablets were performed at 37 ± 0.5 °C using 0.1N HCl in USP II paddle method at 50 rpm for first two hours and replaced with pH6.8 phosphate buffer. 5 ml of filtered aliquot was manually withdrawn at pre-determined time intervals and replaced with 5 ml of fresh buffer solution maintained at the same temperature. The samples were analyzed at 207nm using a UV spectrophotometer. The lag time and percentage release was determined for each formulation.

## RESULTS AND DISCUSSION

**Preparation of standard calibration curve of Lansoprazole**

**Table 1: Concentration and absorbance of Lansoprazole in 0.1N HCl.**

| S. No | Concentration | Absorbance |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 2 | 0.26 |
| 3 | 4 | 0.458 |
| 4 | 6 | 0.63 |
| 5 | 8 | 0.825 |
| 6 | 10 | 0.982 |

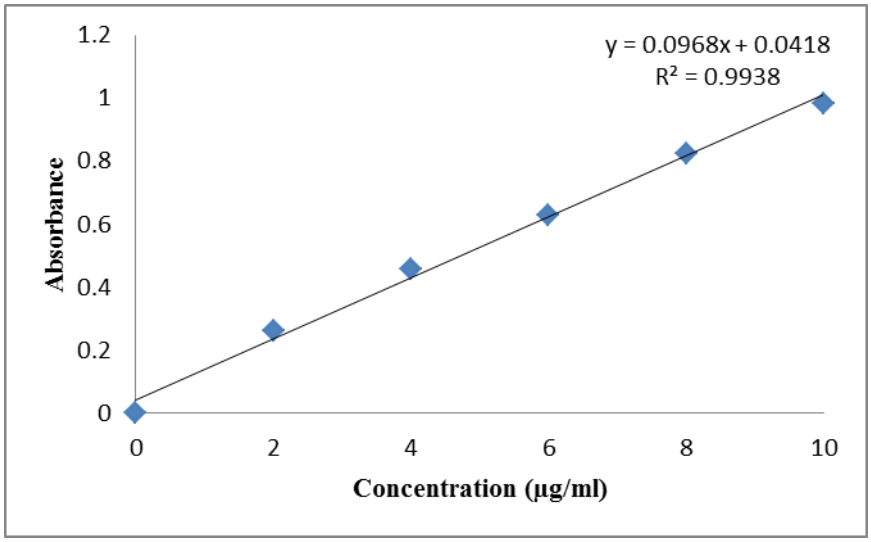


**Fig. 1: Calibration curve of Lansoprazole in 0.1N HCl.**

**Table 2: Concentration and absorbance of Lansoprazole in 6.8 pH Phosphate buffer.**

| S. No | Concentration | Absorbance |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 2 | 0.262 |
| 3 | 4 | 0.46 |
| 4 | 6 | 0.634 |
| 5 | 8 | 0.83 |
| 6 | 10 | 0.99 |

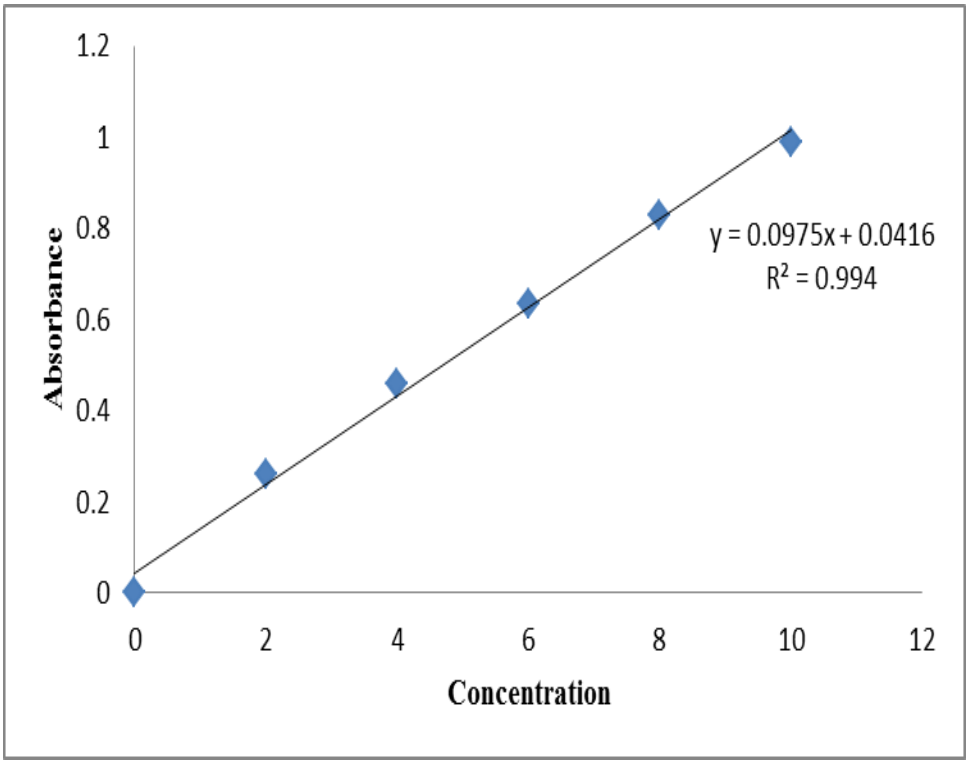


**Fig. 2: Calibration curve of Lansoprazole in 6.8 pH Phosphate buffer.**

**Drug Excipient Compatibility Studies**

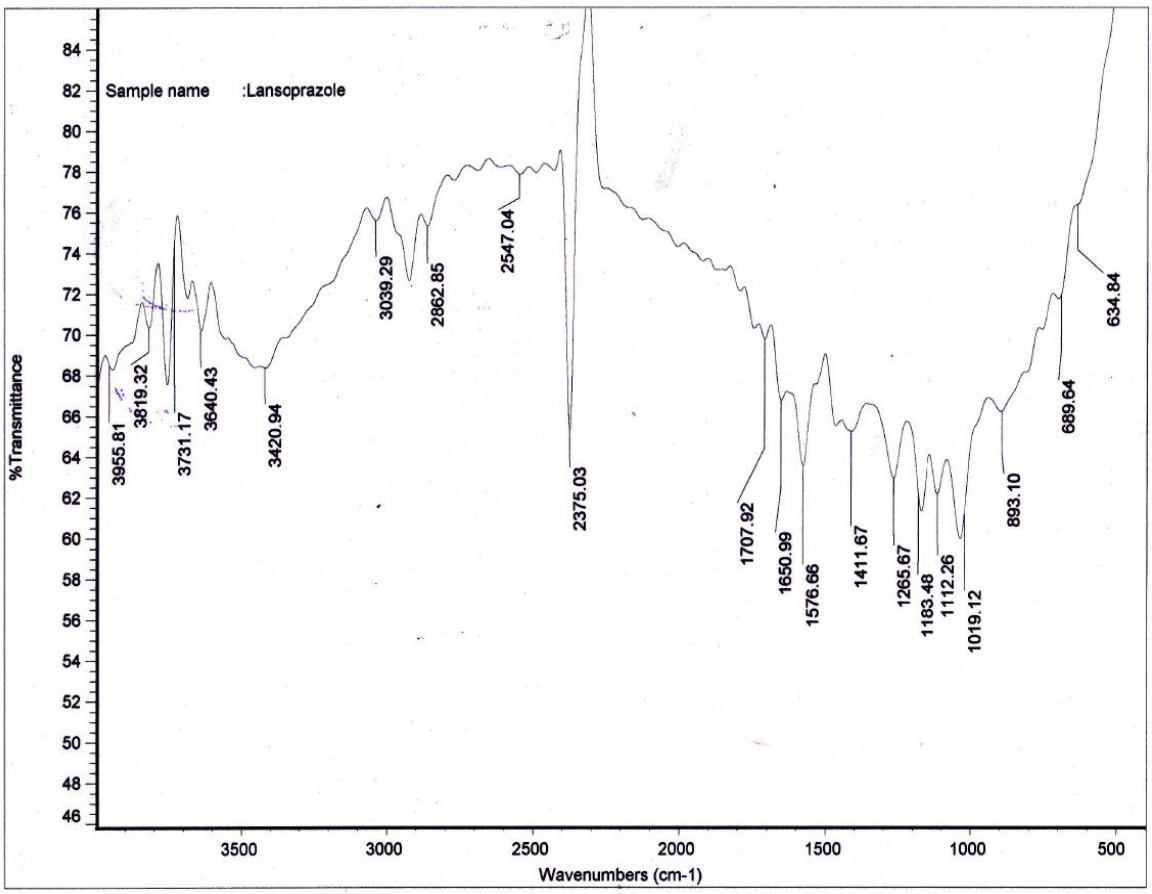


**Fig. 3: FTIR Spectra of Lansoprazole.**

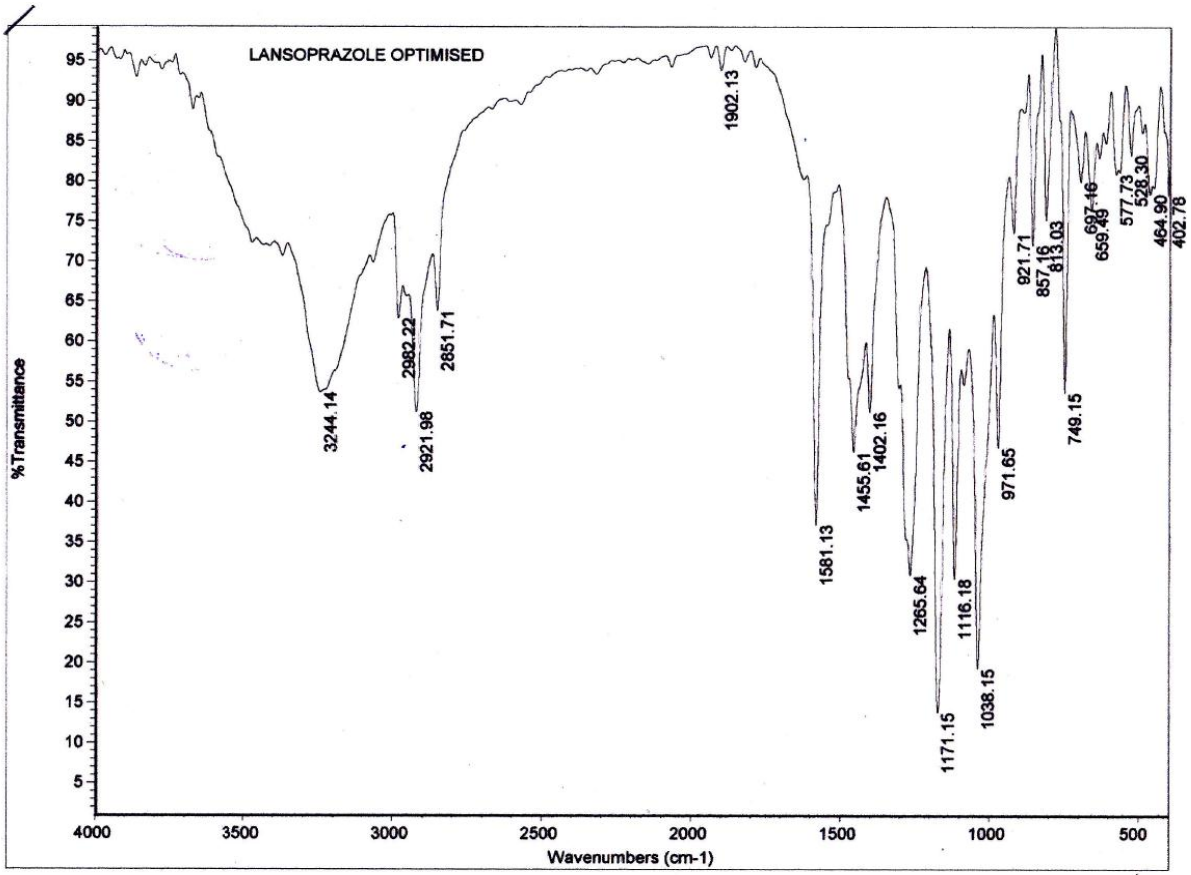


**Fig. 4: FTIR Spectra of Lansoprazole optimized formulation.**

**Pre Compression Parameters**

**Table 6: Pre compression parameters.**

| Formulations | Angle of Repose (θ) | Loose Bulk Density (g/ml) | Tapped Bulk Density (g/ml) | %Compressibility | Hausner's ratio |
|---|---|---|---|---|---|
| **F1** | $21^0 55'$ | 0.510 | 0.583 | 12.52 | 1.14 |
| **F2** | $22^0 43'$ | 0.416 | 0.482 | 13.69 | 1.15 |
| **F3** | $25^0 02'$ | 0.423 | 0.495 | 14.54 | 1.17 |
| **F4** | $24^0 18'$ | 0.309 | 0.353 | 12.46 | 1.14 |
| **F5** | $26^0 89'$ | 0.306 | 0.355 | 13.80 | 1.16 |
| **F6** | $22^0 57'$ | 0.322 | 0.376 | 14.36 | 1.16 |
| **F7** | $25^0 98'$ | 0.404 | 0.472 | 14.40 | 1.16 |
| **F8** | $26^0 42'$ | 0.511 | 0.576 | 11.28 | 1.12 |
| **F9** | $24^0 62'$ | 0.506 | 0.577 | 12.30 | 1.14 |

From the above pre-compression parameters it was clear evidence that drug and excipient has good flow properties and suitable for direct compression.

**Post Compression Parameters**

**Evaluation of rapid release core (RRCT) and press-coated tablets of lansoprazole**

**Table 7: Evaluation for rapid release core.**

| S. No. | Physical parameter | F 1 | F 2 | F 3 | F 4 | F 5 | F 6 | F 7 | F 8 | F 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **Avg Weight (mg)** | 151 | 150 | 148 | 149 | 152 | 150 | 150 | 149 | 148 |
| 2 | **Hardness ($Kg/cm^2$)** | 5.1 | 5.3 | 5.6 | 5.1 | 5.2 | 5.3 | 5.4 | 5.7 | 5.8 |
| 3 | **Thickness (mm)** | 3.51 | 3.48 | 3.51 | 3.5 | 3.5 | 3.47 | 3.49 | 3.52 | 3.61 |
| 4 | **Friability %** | 0.33 | 0.46 | 0.41 | 0.50 | 0.54 | 0.45 | 0.35 | 0.39 | 0.37 |
| 5 | **Disintegration time** | 3min 42sec | 3min 52sec | 3min 04sec | 3min 21sec | 2min 16sec | 2min 8sec | 4min 34sec | 3min 48sec | 3min 26sec |

***In vitro* dissolution studies for core and press coated tablets**

**Dissolution Study**

**Acidic Stage**

Medium : 0.1N HCl
Type of apparatus: USP - II (paddle type)
RPM : 50
Volume : 900ml
Temperature : 37ºC± 0.5
Time : 2hrs

**Buffer Stage**

Medium : 6.8pH phosphate buffer
Type of apparatus: USP - II (paddle type)
RPM : 50
Volume : 900ml

*In vitro* dissolution for core tablets were done in 0.1N HCl and enteric press coated tablets were initially placed in acidic stage and next was changed with phosphate buffer.

**Core tablets**

**Table 8: Dissolution for core tablet.**

| Dissolution time(Min) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **5** | 19.1 | 16.2 | 16.1 | 10.4 | 12.1 | 14.2 | 15.0 | 16.4 | 20.4 |
| **10** | 35.4 | 30.5 | 10.8 | 18.4 | 22.1 | 22.23 | 24.1 | 28.9 | 27.8 |
| **20** | 65.4 | 40.1 | 46.8 | 35.4 | 51.7 | 40.34 | 45.6 | 48.6 | 33.5 |
| **30** | 76.1 | 73.9 | 73.4 | 60.4 | 66.3 | 65.76 | 66.6 | 61.4 | 41.6 |
| **45** | 82.0 | 79.4 | 80.3 | 72.6 | 75.4 | 74.8 | 75.4 | 72.4 | 60.4 |
| **60** | 97.6 | 82.2 | 85.4 | 81.5 | 88.7 | 82.13 | 80.4 | 79.6 | 77.6 |

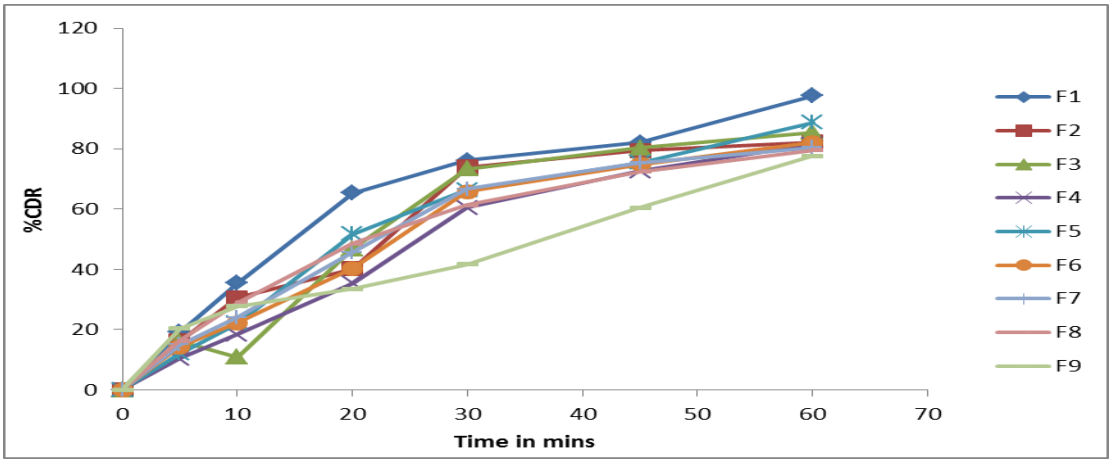


**Figure 5: Dissolution graph for formulations F1-F9.**

**Table 9: Evaluation for Press coated tablets.**

| S. No. | Physical parameter | P1F1 | P2F1 | P3F1 | P4F1 | P5F1 |
|---|---|---|---|---|---|---|
| 1 | **Avg Weight (mg)** | 551 | 550 | 549 | 549 | 550 |
| 2 | **Hardness (Kg/cm$^2$)** | 7.4 | 7.0 | 7.7 | 7.4 | 7.5 |
| 3 | **Thickness (mm)** | 2.45 | 2.49 | 2.5 | 2.51 | 2.5 |
| 4 | **Friability %** | 0.5 | 0.45 | 0.46 | 0.36 | 0.24 |

**Table 10: Dissolution for Enteric press coat.**

| Time(hrs) | P1F1 | P2F1 | P3 F1 | P4 F1 | P5 F1 |
|---|---|---|---|---|---|
| | **0.1N HCl** | | | | |
| 1 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 0 | 0 | 0 | 0 |
| | **6.8 pH Phosphate buffer** | | | | |
| 3 | 5.94 | 0.297 | 2.97 | 4.11 | 7.38 |
| 4 | 99.43 | 86.70 | 60.58 | 64.55 | 73.10 |
| 5 | 98.01 | 99.40 | 75.73 | 77.42 | 85.54 |
| 6 | 98.01 | 99.10 | 87.31 | 86.56 | 92.84 |
| 7 | 98.01 | 99.10 | 99.14 | 87.55 | 93.52 |
| 8 | 99.40 | 99.10 | 100.98 | 86.85 | 92.34 |

**Graph for Enteric Press Coat Formulation**

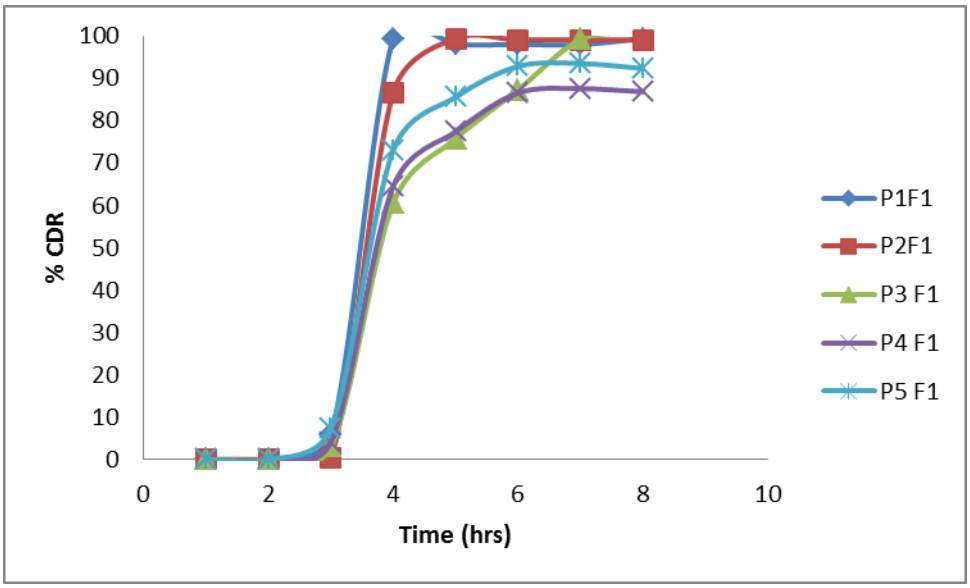


**Figure 6: Graph showing % CDR verses time in hrs for formulations P1F1 to P5F1.**

## CONCLUSION

Lansaprazole, a proton pump inhibitor used in the treatment of Ulcers. The tablets were formulated using polymers HMPC and EC. All the formulations were prepared by direct compression method. The pre-compression parameters of all formulations showed good flow properties and these can be used for tablet manufacture. The post-compression parameters of all formulations were determined and the values were found to be satisfactory. From the *in-vitro* dissolution studies of the rapid release core formulations, it was concluded that the formulation F1 was the best formulation. So finally based on all parameters P1F1 showed delayed release pattern in a much customized manner. As a result of this study it may be concluded that the colon targeted drug delivery tablets using a combination of two polymers in optimized concentrations can be used to increase the delayed action of drug release to deliver the drug in a delayed manner. The concept of formulating colon specific drug delivery of lansaprazole offers a suitable and practical approach in serving desired objectives of colon specific tablets.

## REFERENCES

1. Agarwal SP, Vasudha S, Anitha P. Spectrophotometric determination of atenolol and timolol dosage forms via charge-transfer complexation, Ind. J. Pharm. Sci., 1998; 53-55.
2. Ali J, Saigal N, Qureshi M.J, Baboota S, Ahuja A, Chronopharmaceutics: a promising drug delivery finding of the last two decades, Recent Pat. Drug Deliv. Formul, 2010; 4: 129–144.
3. Anna Viridén, BengtWittgren, Anette Larsson, Investigation of critical polymer properties for polymer release and swelling of HPMC matrix tablets, Eur. J. Pharm, Sci., 2009; 36: 297–309.
4. Aschoff J. Circadian parameters as individual characteristics, J. Biol. Rhythms, 1998; 13: 123–131.
5. Aulton M.E, Kevin Taylor. Aulton's Pharmaceutics: The Design and Manufacture of Medicines, 3rd ed. Chuchill, Livingstone, 2007.
6. BASF. Technical information for Kollidon® SR, BASF AG, Ludwigshafen/Rh., Germany, 1999.
7. Shah RB, Tawakkul MA, Khan MS. Comparative evaluation of flow for pharmaceutical powders and granules. AAPS Pharm Sci. Tech, 2008; 9: 251-60.
8. Arunachalam A, Mazumde A. The outcome of formulation and in vitro release studies of levothyroxine sodium tablets. Asian J Pharm Sci Tech, 2011; 1: 33-9.
9. Salunkhe, K. S., Raosaheb, S. S., and Kulkarni, M. V., "Formulation and in-vitroEvaluation of Dextrin Matrix Tablet of Albendazole for Colon Specific Drug Delivery," *Journal of Pharmacy Research*, 2009; 2(3): 429-431.
10. Mei-Juan, Z., Gang, C., Hirokazu, Okamoto., Xiu-Hua, H., Feng, A., Fu-De, C., Kazumi, D., "Colon-Specific Drug Delivery Systems based on Cyclodextrinprodrugs, in vivo Evaluation of 5-Aminosalicylic Acid from its Cyclodextrin Conjugates," *World Journal of Gastroenterology*, 2005; 11(47): 7457-7460.