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FORMULATION AND EVALUTION OF LANSOPRAZOLE DELAYED RELEASE TABLETS BY USING PRESS COATING TECHNIQUE

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ABSTRACT

The aim of this study was to formulate and investigate the in vitro performance of Lansoprazole press-coated tablets for delayed release. To develop pharmaceutically stable, cost effective and quality improved formulation of Lansoprazole delayed release tablets. To study the effect of various concentrations of different dry polymers for the formulation of press -coated delayed release Lansoprazole tablets. The formulation of Delayed release Lansoprazolepress coated tablets Press coated tablets was done by using polymer with , Eudragit RL 100 , Ethyl cellulose ,HPMC K 100 M. Hydrophilic Press coated tablets of an optimized formulation F5 Eudragit was prepared by using polymer of by direct compression technique.The Delayed release Lansoprazolesodium press coated tablets using prepared by direct compression technique. In-vitro drug release rate of F5formulation shows controlled release with in specification limits. The F5 follows zero order kinetics with release mechanism according to peppa's model of kinetics.

Key Words: *Delayed Release Tablets, Dissolution Studies, Lansoprazole Sodium, Press Coating.*

INTRODUCTION

Oral ingestion has the most convenient and commonly employed route of drug delivery. 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].

1. Delayed Release Drug Delivery System:

The design of such 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 [4-6]:

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

MATEIALS AND METHODS

1. Materials used:

Lansoprazole, HPMC K 100, MCC (Micro Crystaline Cellulose), Lactose, Cross Povidone, Ethyl Cellulose, Eudragit, Magnesium Sterate, Talc.

2. Methods used:

2.1. Physical Characterization of the drug:

A. Colour: A small quantity of pure Lansoprazole powder was taken in a butter paper and viewed in well illuminated place.

B. Taste and odour: Very less quantity of Lansoprazole was used to get taste with the help of tongue as well as smelled to get the odour.

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C. Determination of Melting point: Capillary melting point or a melting–point apparatus are most often used for the determination of the melting point of a solid. A few crystals of the drug was placed in a thin walled capillary tube 10-15cm long about 1mm inside diameter and closed at end. The capillary, which contains the sample, and a thermometer were then suspended so they can be heated slowly and evenly. The temperature range over which the sample was observed to melt was taken as the melting point [7, 8].

D. Solubility studies: Solubility studies were conducted in various solvents and different pH solution the solubility of API was determined by dissolving the drug in 250 ml of buffer for this purpose purified water, organic solvents, 6.8 buffers and pH .4 phosphate buffer used. Maximum amount of drug was dissolved in 250 ml of medium and was kept untouched for 12 hrs later on the insoluble drug was filtered off and the solution was analyzed to find out the solubility [9, 10].

2.2. Evaluation of pre compression blend:

a) Angle of Repose:

The angle of repose of granules was determined by the funnel-method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone measured and angle of repose was calculated using the following equation [11-14].

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

Where h and r are the height and radius of the powder cone, θ is the angle of repose.

Table No. 1: Angle of Repose

Angle of repose(θ)	Flow property
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor
56-65	Very poor
>66	Very very poor

b) Determination of Bulk Density and Tapped Density:

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and volume (V_0) was measured. Then the graduated cylinder was closed with lid and set into the tap density tester (USP). The density apparatus was set for 100 tabs and after that the volume (V_f) was measured and continued operation till the two consecutive readings were equal .The bulk density and the tapped density were calculated using the following formulae [15, 16].

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

$$\text{Tapped density} = W/V_f$$

Where, W= Weight of the powder; V_0 = Initial volume; V_f = final volume

c) Compressibility Index (Carr's Index):

Carr's index (CI) is an important measure that can be obtained from the bulk and tapped densities.

$$CI = (TD\text{-}BD) \times 100/TD$$

Where, TD is the tapped density and BD is the bulk density.

d) Hausner's Ratio:

It is the ratio of tapped density and bulk density. Hausner found that this ratio was related to interparticle friction and, as such, could be used to predict powder flow properties. Generally a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index [17, 18].

Hausner's ratio= TD/BD.

2.3. By UV Spectroscopy (Determination of λ max):

Stock solution of (10 µg/ml) Lansoprazolewas prepared in 6.8 buffer solution. The solution was kept in a fused silica cuvette 10 mm. The UV spectrum was recorded in the range of 200-400 nm on UV-visible spectrophotometer at 1 cm, slit width. It showed a λ max at absorption maxima 274 nm.

2.4. Preparation of standard stock solution:

100mg pure drug was taken in 100ml volumetric flask and the volume is made up with buffer solution. From this 1ml is taken and diluted to 10ml in a 10ml volumetric flask. From this 1ml is taken and diluted to 10ml in a 10ml volumetric flask to get10µg/ml concentration of solution. From the standard stock solution 0.5ml was pipetted into 100ml volumetric flask. The volume was diluted to 100ml with buffer solution (0.1N HCl) to obtain a solution of strength 5 µg/ml was scanned between 200 to 400 nm. Appearance, Assay and the solid state property of the drug in the blended mixture ratios.

Table No. 2: Composition of Core Tablets

F.Code	S1
API Lansoprazole (mg)	20
Lactose	63
HPMC (low viscosity grade) (mg)	10
Cross Povidone (mg)	5
Talc	1
Mg sterate (mg)	1
Total(mg)	100

Table No. 3: Composition of Press coated Tablets

F. Code	F1	F2	F3	F4	F5	F6	F7	F8
Ethyl cellulose	100mg	150mg	-	-	-	-	-	-
HPMC K100M	-	-	100mg	150mg	-	-	-	-
Eudragit S 100 (mg)	-	-	-	-	100mg	150mg	-	-
M.C.C	98mg	48mg	98mg	48mg	98mg	48mg	98mg	48mg
Mg. Sterate	2mg	2mg	2mg	2mg	2mg	2mg	2mg	2mg
Total(mg)	**200mg**	**200mg**	**200mg**	**200mg**	**200mg**	**200mg**	**200mg**	**200mg**

RESULTS AND DISCUSSION

Table No. 4: Absorbance values of drug in pH 6.8 phosphate buffer

Sl. No.	Concentration (µg/ml)	Absorbance (284nm)
1	0	0
2	10	0.0614
3	20	0.1249
4	30	0.1945
5	40	0.2614
6	50	0.3257

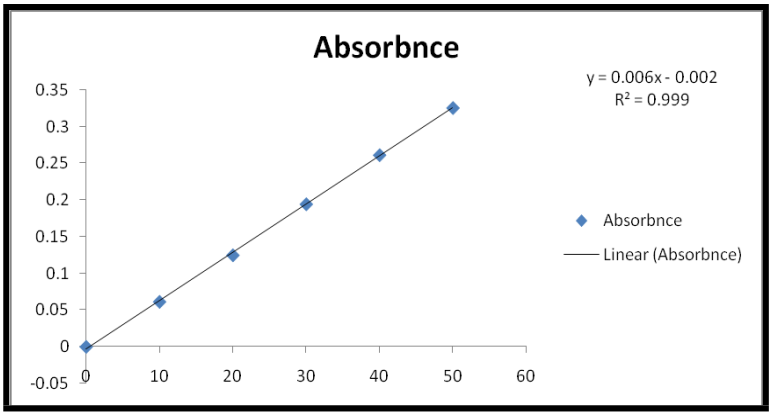

Fig. 1: Standard graph of drug in 6.8 pH phosphate buffer

Table No. 5: Physical Properties of Lansoprazole(API) Blend

Formula Code	Angle of repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's ratio
API	33±0.56	1.20000	1.3846	13.3333	1.1538

Table No. 6: Physical Properties of Core S1 Pre-compression Blend

Formula Code	Angle of repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's ratio
Core (S1)	27±2.0	1.2000	1.2857	6.6666	1.0714

Table No. 7: Physical Properties of Pre-compression Blend

Formula Code	Angle of repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's ratio
F1	23.2	0.607	0.647	6.18	1.066
F2	26.1	0.566	0.626	9.58	1.106
F3	30.3	0.556	0.612	9.15	1.10
F4	24.5	0.55	0.62	11.29	1.127
F5	31.15	0.611	0.639	4.38	1.046
F6	**33.3**	**0.614**	**0.646**	**4.95**	**1.052**

Table No. 8: Physical Evaluation of press coated tablets

Formula Code	Hardness (kg/cm²)	Thickness (mm)	Weight (mg)	Friability (%)	Drug content (%)
F1	4.15±0.12	4.21±0.02	301.1±2.11	0.16	98±1.14
F2	4.56±0.10	4.12±0.03	298.3±1.12	0.12	97±0.80
F3	4.32±0.02	4.0±0.04	297.2±2.45	0.25	99±2.47
F4	5.11±0.12	4.14±0.02	301.1±7.14	0.17	98±1.87
F5	4.32±0.13	4.22±0.08	303.4±3.13	0.15	98±1.22
F6	5.21±0.10	4.0±0.06	300.3±3.32	0.23	99±1.37

Table No. 9: Physical Evaluation of Core tablets

Core Formula Code	Hardness (kg/cm²)	Thickness (mm)	Weight (mg)	Friability (%)	Drug content (%)	Disintegration time (min)
C.F1	2.0±2.0	2.0±0.42	100±0.15	0.48	99±0.5	4.20±0.2

Table No. 10: Swelling Index of Delayed release Lansoprazolepress coated tablets

Time (hrs)	Swelling Index (%)					
	F_1	F_2	F_3	F_4	F_5	F_6
1	52.38	31.14	23.44	48.27	25.02	50.13
2	63.77	45.33	31.11	61.51	42.28	60.29
3	78.56	52.83	38.53	74.81	41.14	70.32
4	88.92	64.44	47.41	84.56	60.32	75.15

5	84.21	77.33	51.20	87.17	58.24	80.41
6	62.11	53.42	47.33	61.43	50.15	61.16
7	33.01	38.22	42.11	30.98	28.11	30.18
8	**15.12**	**26.93**	**38.57**	**18.26**	**15.21**	**12.45**

Table No. 11: In-vitro Drug release data of Delayed release Lansoprazole press coated tablets

Time in (Min)	C.F1
0	0
10	38
20	55
30	63
40	73
50	86
60	98

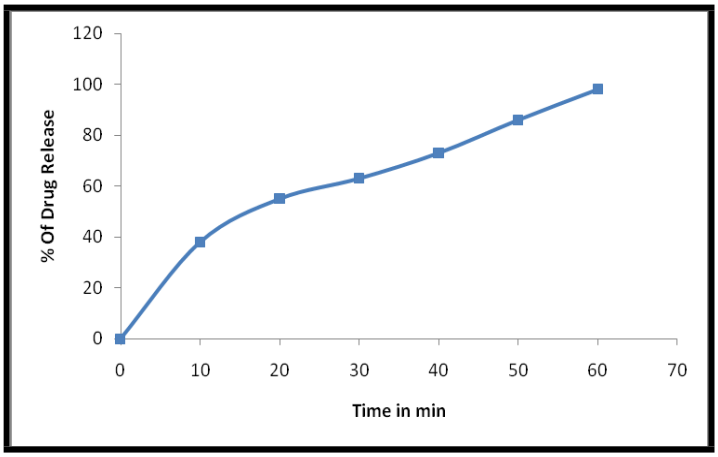

Fig. 2: In-Vitro Dissolution Profiles of Lansoprazole Sodium from core tablet

Table No. 12: In-vitro Release data of Delayed release Lansoprazoleusing press coated tablets

Time in (min)	F1	F2	F3	F4	F5	F6
0	**0**	**0**	**0**	**0**	**0**	**0**
60	3.5	4.9	3	4.5	2.9	4.2
120	12	9.5	7	8	7	8
130	22	29	34	32	25	28
140	38	46	41	51	34	35
150	66	68	66	71	65	64
160	74	79	80	82	75	70
170	85	80	88	92	97	82

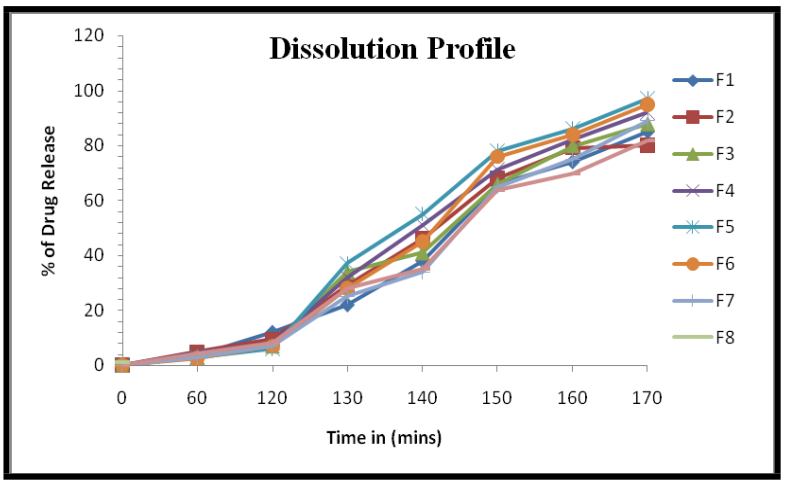

Fig. 3: In-Vitro Dissolution Profiles of Delayed release Lansoprazoleusing press coated tablets

Table No. 13: Drug Release Kinetics of Batch (F5) Delayed release Lansoprazoleusing press coated tablets

Time	Log Time	Square root of Time	Cumulative % Drug Released	Log Cumulative % Drug Released	Cumulative % Drug Remained	Log Cumulative % Drug Remained
0	0	0	-	-	100	2
60	7.745967	1.778151	2.9	0.462398	97.1	1.98721923
120	10.95445	2.079181	7	0.90309	92	1.963787827
130	11.40175	2.113943	25	1.69897	50	1.698970004
140	11.83216	2.146128	34	1.8129134	35	1.544068044
150	12.24745	2.176091	65	1.8573325	28	1.447158031
160	12.64911	2.20412	75	1.90309	20	1.301029996
170	**13.0384**	**2.230449**	**97**	**1.9867717**	**3**	**0.477121255**

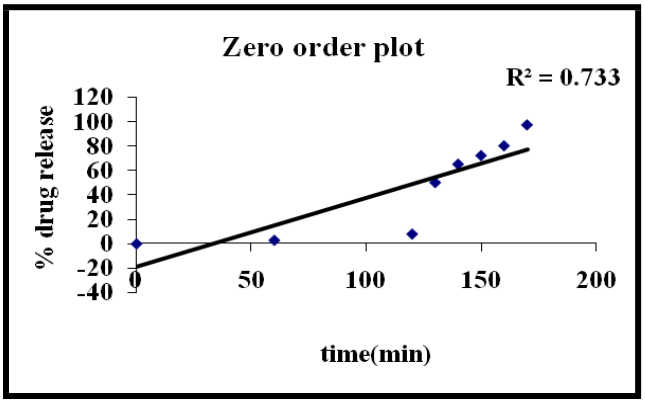

Fig. 4: Zero Order Graph of Optimized Formulation (F5)

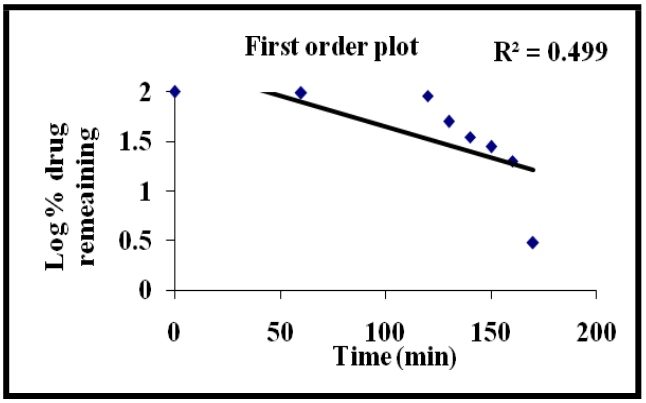

Fig. 5: First Order Graph of Optimized Formulation (F5)

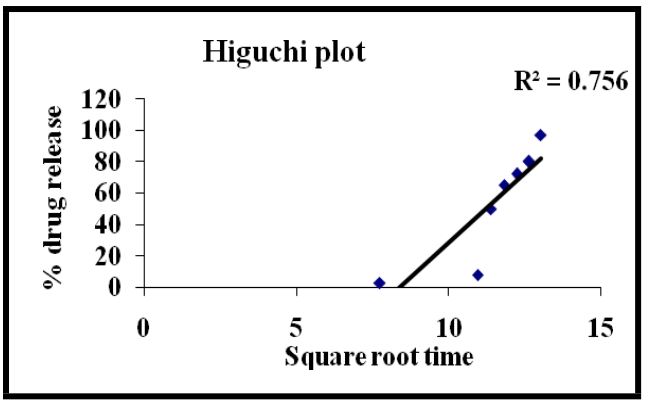

Fig. 6: Higuchi Plot of Optimized Formulation (F5)

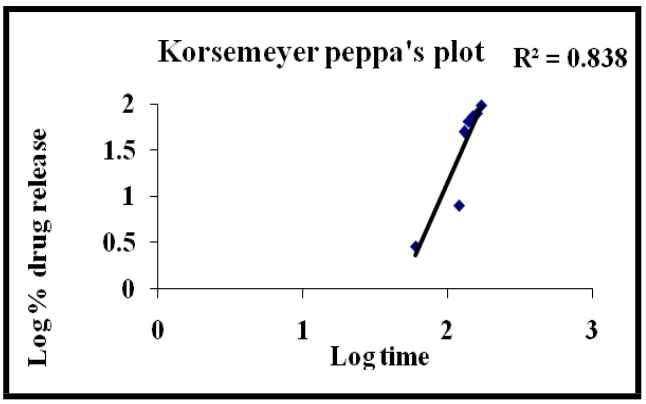

Fig. 7: Korsmeyer-Peppas plot for Optimized Formulation (F5)

SUMMARY

In the present work the physical compatibility studies show no incompatibility between the drug, polymer and other excipients. The FTIR & D.S.C spectral studies show no interaction of drug with polymer and excipients.The formulation of Delayed release Lansoprazole press coated tablets Press coated tablets was done by using polymer with , Eudragit RL 100 , Ethyl cellulose ,HPMC K 100 M, Hydrophilic Press coated tablets of an optimizedFormulation F5 Eudragit was prepared by using polymer of by direct compression technique.

The Lansoprazole sodium Drug and the Delayed release Lansoprazolepress coated tablets in direct compression blend was evaluated for angle of repose, bulk density, and tapped density. The angle of repose of granules shows good flow property than the Lansoprazole Drug. All the formulations are evaluated for the hardness, thickness, friability and weight variation. Loss on drying and melting point shows that the drug is pure and the assay of Lansoprazole sodium was carried out by U.V method.The Press coated tablets batch no F5 shows controlled drug release by using Eudragit Polymer The release kinetics of Delayed release Lansoprazole press coated tablets follows zero order kinetics and obtained by plotting % drug release Vs time.

CONCLUSION

In the present study the IR studies & D.S.C reveals that there is no interaction of drug and excipients. The further in vivo studies and long term stability studies of batch F5 trial are recommended.The attempts was made to formulated and evaluate Press coated tablets in pulsatile drug delivery system by Delayed release Lansoprazole press coated tablets .The use of permeable polymer such as Eudragit along with gellable polymers such as coat allows the production of 'timed-release' pharmaceutical dosage form. Press-coated tablets utilizing Eudragit in the outer shell displayed a timed-release function, i.e. a lag phase was observed in the dissolution profile and the drug was released rapidly after the complete erosion of shell when permeable polymer was used. The effect of amount of outer coating material (thickness of coating) was also investigated, increasing the amount of outer shell seemed to prolong lag time and the time required to complete the dissolution or erosion of the outer shell would be longer. Hydrophilic polymer used has less effect on lag time. As the viscosity grade and amount of polymer increases, the lag time also increases.

The Delayed release Lansoprazole press coated tablets using prepared by direct compression technique. In-vitro drug release rate of **F5** formulation shows controlled release with in specification limits. The F5 follows zero order kinetics with release mechanism according to poppa's model of kinetics.

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