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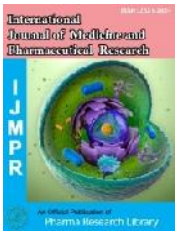

Research Article **Open Access**

Fabrication of Lansoprazole sustained *Release Matrix Tablets: In vitro evaluation*

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A B S T R A C T

The main objective of the present study was to develop matrix tablets of Lansoprazole and to study its sustained release for prolonged time in tablet formulations. Compatibility of Lansoprazole with excipients used was verified by DSC and FTIR studies. The prepared tablets were found to have better uniformity of weight and drug content with low SD values. The swelling behavior and release rate characteristics were studied and found good. The dissolution study proved that the Lansoprazole released from the dosage form in sustained manner for prolonged time.

Keywords: Lansoprazole, matrix, tablets, sustained release.

A R T I C L E I N F O

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1. Introduction

Lansoprazole is a proton pump inhibitor used in treating gastric ulcers and gastro esophageal reflux disease (GERD) and also maintaining of all grades of erosive esophagitis (EE) [1]. Thus sustained release drug delivery system has gained its importance to reduce multiple dosing. Drug administration by conventional dosage form causes poor compliance among the patients and also causes fluctuations in plasma level[2].

2. Materials and Methods

Materials

Lansoprazole was obtained as a gift sample from Waksman Selman Pharmaceuticals Pvt. Ltd., Anantapur, India. Sodium Carboxy Methyl Cellulose, Hydroxy Propyl Methyl Cellulose K15 M, Sodium Alginate, Gelatin, Aerosil, Starch, Talc, Magnesium stearate used were of AR grade and double distilled water was used throughout the experiments.

Methods

Drug-excipient compatibility studies

Differential Scanning Calorimetry (DSC)

DSC analysis was performed using Shimadzu DSC-60, Shimadzu Limited Japan. A 1:1 ratio of drug and excipient was weighed into aluminum crucible. And sample was analyzed by heating at a scanning rate of 20^0C over a temperature range 20^0-300^0 under nitrogen environment.

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks using a Shimadzu Corporation, (Tokyo, Japan) Model-1601 PC. Samples were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was from 400 to 4000 cm^{-1}.

Preparation of matrix tablets

Sustained release matrix tablets of Lansoprazole with various excipients were prepared[3] by using different drug: polymer ratios as shown in Table 1. Sodium Carboxy Methyl Cellulose, Hydroxy Propyl Methyl Cellulose K15 M, Sodium Alginate, Gelatin were used as matrix forming materials while starch as a diluent and Aerosil, Talc and Magnesium stearate as lubricants. All ingredients used were passed through a sieve 100, weighed and blended.

Evaluation for pre compression parameters

Angle of repose (Θ)

Angle of repose was determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height, h, was obtained. Diameter of heap, D, was measured. The angle of repose, Θ, was calculated by the following equation[4].

$$\Theta = \tan^{-1} (h / r)$$

Where, Θ is the angle of repose, h is the height in cm and r is the radius.

Bulk Density (D_b)

Bulk density was determined by pouring pre sieved drug excipient granules into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/ml and is given by the following equation[4].

$$D_b = M / V_0$$

Where, M is the mass of powder and V_0 is the Bulk volume of the powder

Tapped Density (D_t)

It was determined by placing a graduated cylinder, containing a known mass of granules on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml and is given by the following equation[4].

$$D_t = M / V_t$$

Where, M is the mass of powder and V_t is the tapped volume of the powder.

Carr's Index (I)

It is expressed in percentage and is expressed by the following equation[4].

$$I = D_t - D_b / D_t$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Hausner ratio: It is expressed in percentage and is expressed by the following equation[4].

$$H = D_t / D_b$$

Post compression parameters

Thickness: The thickness of the prepared tablets was measured by Vernier Calipers[5]. It is expressed in mm.

Weight Variation

20 tablets were selected at random and average weights were determined. Then individual tablets weighed and the individual weight was compared with the average[6].

Hardness: The hardness of the tablet was determined using a Pfizer hardness tester[6]. It is expressed in kg / cm^2.

Friability (F)

The friability of the tablet was determined using Roche Friabilator. It is expressed in percentage (%). 20 tablets were initially weighed ($W_{initial}$) and transferred into the friabilator. The friabilator was operated at 25 rpm per min for 4 min (100 revolutions). The tablets were weighed again (W_{final}). The % friability was then calculated by the following equation[7].

$$F = W_{initial} - W_{final} / W_{initial} \times 100$$

Content uniformity

20 tablets were weighed and powdered; a quantity of powder equivalent to 30 mg of Lansoprzole was dissolved in 100ml of methanol (1000µg/ml). From this solution 0.9 ml solutions were pipetted and volume was made up to 10 ml using methanol to get the concentration of 9 µg/ml. The drug content was determined by measuring the absorbance at 294nm using UV spectrophotometer. Drug content was calculated using the standard calibration curve[8].

Preparation of standard calibration curve of Lansoprazole in 0.1 N HCl

Preparation of standard solution:

Standard stock solution of Lansoprazole was prepared in 0.1N HCl. 100 mg 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 10 ml solution was withdrawn and diluted to 100ml of 0.1N HCl to get a concentration of 100µg/ml (SSII).

Preparation of working standard solutions:

Further, from (SS-II) aliquots of solutions were pipetted into 10ml volumetric flasks. The volume was made up with 0.1N HCl to get the final concentrations of 1, 2, 3, 4, 5 and 6µg/ml respectively. The absorbance of each concentration was measured at 294nm.The data are compiled in Table and plotted a graph. [λ max of 294nm. Beer's range: 3-18 µg /ml][9] (Fig.4).

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. 100 mg 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 10 ml solution was withdrawn and diluted to 100ml of phosphate buffer pH6.8 to get a concentration of 100µg/ml (SS-II) (Fig.5).

Preparation of working standard solutions:

Further, from (SS-II) aliquots of samples were pipetted into 10ml volumetric flasks. The volume was made up with phosphate buffer pH6.8 to get the final concentrations of 1,

2,3,4,5 and 6µg/ml respectively. The absorbance of each concentration was measured at 294nm.The data are compiled in Table and plotted a graph. [λ Max :294nm. Beer's range: 3-18 µg /ml].

Swelling behavior of matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation F-1, F-2, F-3, F-4 and F-5 were studied. One tablet from each formulation was kept in a Petri dish containing phosphate pH 6.8. At the end of 2 h, the tablet was withdrawn, kept on tissue paper and weighed, repeated for every 2 h till the end of 12 h. The % weight gain by the tablet was calculated by following equation[10].

$$S.I = \{(M_t-M_0) / M_0\} X 100$$

Where, S.I = Swelling Index, M_t = Weight of tablet at time 't' and

M_o = Weight of tablet at time 0. Swelling behavior of Controlled release matrix tablets were represented in Fig.6.

In vitro drug release studies

Release of Lansoprazole from the matrix tablets was studied using United States Pharmacopoeia (USP) 6-station Dissolution Rate Test Apparatus (Model Electro lab, TDT-06T, Mumbai, India) with a rotating paddle stirrer at 100 rpm and 37±0.5^{0}C. First 2 h in 0.1N HCl (900 ml) and in phosphate buffer of pH 6.8 (900 ml) for next 10h. A sample of Lansoprazole matrix tablets was used in each test. Samples of dissolution fluid were withdrawn through a filter (0.45 µm) at different time intervals and were assayed at 294 nm for Lansoprazole[11] content using a UV/ visible double beam spectrophotometer (Systronics Corporation, Mumbai, India). The drug release experiments were conducted in triplicate (n = 3) (Fig.7).

Accelerated stability studies

The best formulation among the prepared matrix tablets (F-2) was tested for its physical nature at stressed storage conditions as per ICH guidelines[12].

3. Results and Discussion

The DSC thermogram of Lansoprazole and the formulated matrix tablet blend was shown in Fig.1. The DSC scan of Lansoprazole showed a short endothermic peak at 179.62^{0}C. The thermo gram of formulated matrix tablets showed an endothermic peak of drug at 176.14^{0}C indicating a slight change in terms of shifting towards the lower temperature. It has been reported that the quantity of material used effects the peak shape and enthalpy. Thus these minor changes in the melting endotherm in the drug could be due to the mixing of the drug and excipients which lower the purity of each component in the mixture and may not necessarily indicate potential incompatibility.

The IR spectrum of Lansoprazole and the matrix tablets of Lansoprazole were showed in Fig. 2 and 3. The characteristic bands of lansoprazole were observed in drug excipient blend. This indicates that that there is no chemical incompatibility between Lansoprazole with the excipients used. The Angle of repose of granules was found to be in the range of 28.35^o±0.01 to 31.90^o±0.02 indicated the granules had excellent flow properties. The Carr's index was in the range of 12.82±0.02 to 17.15±0.02 and Hausner ratio in the range of 1.147±0.02 to 1.207±0.05. All these values were tabulated in table 2. The thickness of prepared tablets were in the range of 5.8±0.02 to 6.2±0.01 mm. The hardness was more than 4 kg/cm^2. The loss on friability was ranged from 0.14±0.03 to 0.23±0.01%, which is less than 1% indicates the firmness of the formulated tablets. The drug content in the formulated tablets was ranged from 99.52±2.11 to 101.54±5.25%. All these values were tabulated in table 3. The prepared tablets were found to have good swelling properties (Fig.6). The release of Lansoprazole form the formulation showed zero order release (Fig.7). The accelerated stability studies further proved the formulation is stable even at accelerated environmental conditions (Table 4).

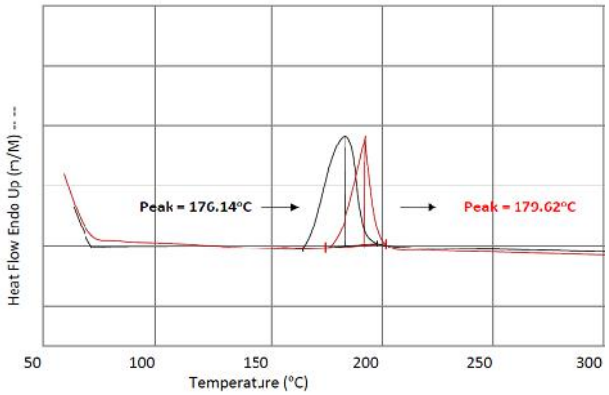

Figure 1: DSC thermo gram of Lansoprazole and its blend with excipients

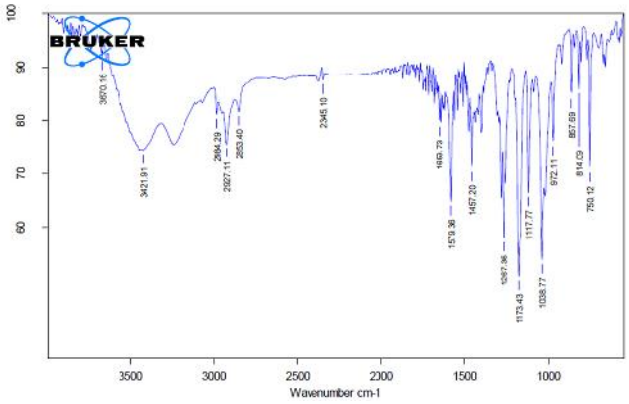

Figure 2: Infrared Spectrum of Lansoprazole Pure drug

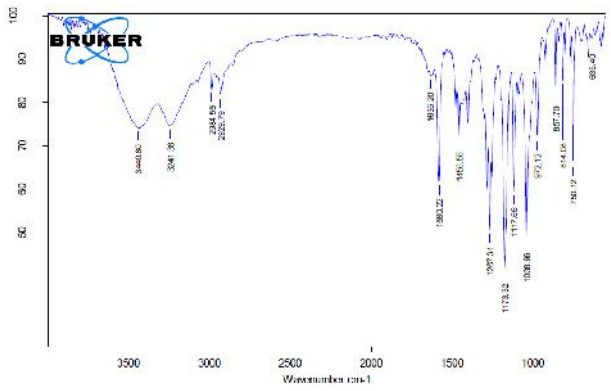

Figure 3: Infrared Spectrum of formulation blend

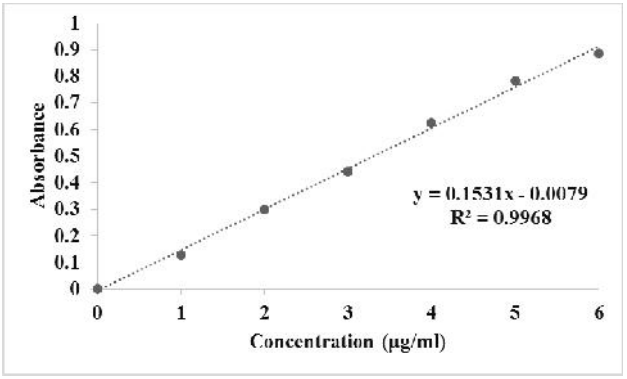

Figure 4: Standard calibration curve of Lansoprazole (0.1N HCl)

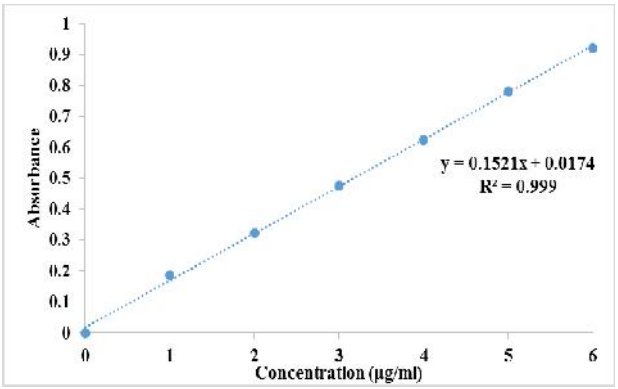

Figure 5: Standard calibration curve of Lansoprazole (pH 6.8 PBS)

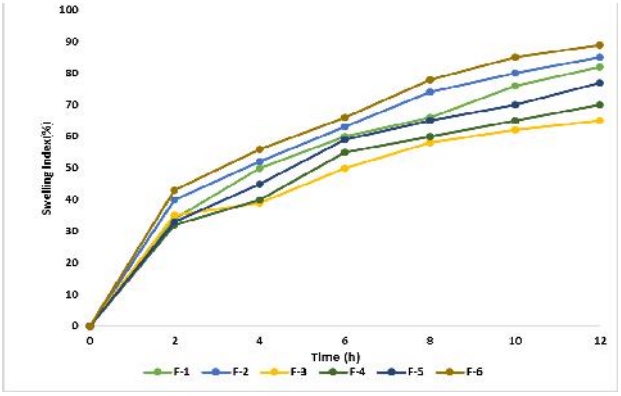

Figure 6: Swelling Index of formulated matrix tablets

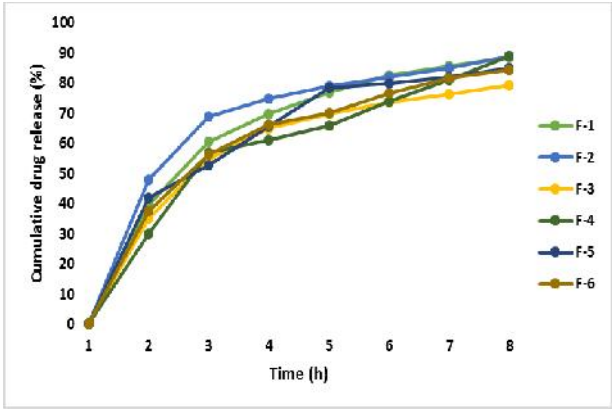

Figure 7: Zero order release Plots of formulations

Table 1: Formulae of matrix tablets

Ingredients (mg)	Formulations					
	F-1	F-2	F-3	F-4	F-5	F-6
Lansoprazole	30	30	30	30	30	30
Sod. CMC	5.5	5.5	5.5	5.5	5.5	5.5
HPMC K15 M	5.5	8.25	5.5	-	-	-
Sodium Alginate	-	-	-	5.5	8.25	5.5
Gelatin	0.25	0.25	0.25	0.25	0.25	0.25
Starch	107.25	104.5	107.25	107.25	104.5	107.25
Aerosil	0.5	0.5	0.5	0.5	0.5	0.5
Talc	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium stearate	0.5	0.5	0.5	0.5	0.5	0.5
Total weight of tablet	150	150	150	150	150	150

Table 2: Flow properties of granules

Formulation	Angle of repose (º)	Loose Bulk density	Tapped bulk density	Carr's Index (%)	Hausner ratio
F1	31.90±0.02	0.34±0.01	0.39±0.02	12.82±0.02	1.147±0.02
F2	29.67±0.01	0.29±0.02	0.35±0.01	17.14±0.01	1.206±0.05
F3	28.35±0.01	0.35±0.01	0.41±0.02	14.63±0.02	1.171±0.01
F4	29.53±0.01	0.32±0.02	0.38±0.01	15.78±0.01	1.187±0.05
F5	28.65±0.02	0.34±0.01	0.41±0.02	17.07±0.01	1.205±0.03
F6	29.59±0.01	0.29±0.02	0.35±0.01	17.15±0.02	1.207±0.05
All values mentioned as Mean± SD: N=3					

Table 3: Physical properties of formulated matrix tablets

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F-1	6.1±0.01	5.50±0.05	0.20±0.02	100.13±1.95
F-2	5.9±0.02	5.10±0.01	0.15±0.01	101.54±5.25

F-3	5.8±0.02	5.80±0.05	0.14±0.03	99.52±2.11
F-4	6.2±0.01	5.50±0.02	0.22±0.01	99.99±2.18
F-5	6.0±0.02	5.40±0.01	0.23±0.01	100.1±2.66
All values mentioned as mean ± SD; Number of trials (n) = 5				

4. Conclusion

The present study revealed that combination of HPMC K15 M is a good polymer for prolonging the drug release compared to sodium alginate for sustained release of Lansoprazole from the matrix tablets.

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