ISSN No. 2456-4400
Int J Med Lab Res 2024, 9(1):1-20

IJMLR International Journal of Medical Laboratory Research

RESEARCH ARTICLE

DEVELOPMENT OF CONTROLLED RELEASE FORMULATIONS OF DEXLANSOPRAZOLE TO IMPROVE BIOAVAILABILITY

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Received: 27 Jan, 2024 /Revision: 13 Feb, 2024 /Accepted: 13 April, 2024

Abstract: The present work was aimed to development of controlled release formulations of Dexlansoprazole to improve bioavailability. Dexlansoprazole is the proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H+/K+-ATPase in the gastric parietal cell. By acting specifically on the proton pump, Dexlansoprazole blocks the final step in acid production, thus reducing gastric acidity. Construction of calibration curve of Dexlansoprazole and to investigate the drug and polymer interaction studies by FTIR and DSC. To prepare the different controlled release formulations of Dexlansoprazole tablets with different polymers such as acrylic acid polymer such as Carbopol-974P, HPMC grades for prevalence HPMC-K4M, HPMC-K15M, HPMC-K100M, Natural Polymers akin to Xanthan gum, Guar gum, Sodium Carboxy Methyl Cellulose, and Pectin by Direct Compression method. Evaluation of Dexlansoprazole pre compression parameters such as Bulk density, Tapped density, Hausner's ratio, Carr's index, Angle of repose. Evaluation of post-compression parameters of Dexlansoprazole controlled release tablets such as Weight variation, Hardness, Friability test, Thickness, Drug Content and *In-vitro* dissolution studies. Evaluation of *in-vitro* dissolution uniqueness of all the formulations of Dexlansoprazole by using USP dissolution apparatus type-II (paddle). To study the mechanism of drug dissolution by applying kinetic parameters. To perform the stability studies of optimized formulations of Dexlansoprazole as per ICH guidelines.

Key words: Dexlansoprazole, Carbopol-974P, HPMC-K4M, HPMC-K15M, HPMC-K100M, Xanthan gum, Guar gum, Sodium Carboxy Methyl Cellulose, and Pectin.

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INTRODUCTION:

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to acquire quick and entire systemic drug absorption. Such immediate release products result in comparatively rapid drug absorption and onset of associated pharmacodynamic effects. Although, after absorption of the drug from the dosage form is whole, plasma drug concentrations refuse according to the drugs PK profile. Ultimately plasma drug concentrations reduce below the minimum effective plasma concentration (MEC), ensuing in loss of therapeutic activity. Before this point is reached, another dose is frequently given if a sustained therapeutic effect is required. A substitute to administer an additional dose is to use a dosage form that will afford sustained drug release, and hence maintain plasma drug concentrations, ahead of what is typically seen using immediate release dosage forms.

MATERIALS AND METHODS

Dexlansoprazole is highly effective inhibitor of gastric acid secretion used in the therapy of stomach ulcers and zollinger-ellison syndrome. The drug inhibits the H(+)-K(+)-ATPase (H(+)-K(+)- exchanging ATPase) in the proton pump of gastric parietal cells.

Description: White or almost white crystalline powder.

Chemical Structure:

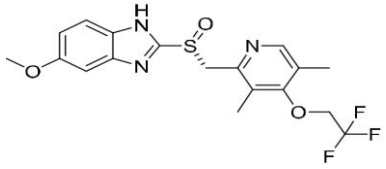

Figure No: 1 Structure of Dexlansoprazole

***Chemical Formula*:** $C_{16}H_{14}F3N_3O_2S$

Molecular weight: 369.363 g/mol

IUPAC Name: Sodium-[5-(difluoromethoxy)- 2-[(3,4-dimethoxypyridin-2-yl) methylsulfinyl]-*1H*-benzoimidazole sesquihydrate

Solubility: Freely soluble in water, very slightly soluble in phosphate buffer at pH 7.4 and practically insoluble in n-hexane.

Categories: In the treatment of peptic ulcer mainly for gastro-esophageal reflux diseases.

Pharmacokinetic data:

Bio-Availability: ~60%
Protein Binding: 96 to 99 %
Metabolism: Rapidly metabolized in liver
Excretion: 50% Renal and 47% in the Feces
Half Life: 1 to 2 hours

Mechanism of Action: Dexlansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H, K)-ATPase at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (-proton) pump within the parietal cell, Dexlansoprazole has been characterized as a gastric proton-pump inhibitor, in that it blocks the final step of acid production.

List of chemicals used in study and their manufacturers is shown in **Table 1** and List of equipments used in study and their manufacturers is shown in **Table 2**.

Table 1: List of chemicals used in study and their manufacturers

S. No	CHEMICALS	MANUFACTURER	PURPOSE
1.	Dexlansoprazole	Zydus Takeda Pharma Ltd, Mumbai	API
2.	Carbopol-974 P	Yarrow Chem. Products, Mumbai	Polymer
3.	HPMC-K 100M	Otto Chemie Pvt.Ltd, Mumbai	Polymer
4.	HPMC-K 15M	Trexchem Pvt.Ltd, Ahmedabad	Polymer
5.	HPMC-K 100M	Otto Chemie Pvt.Ltd, Mumbai	Polymer
6.	Xanthum gum	Akhil Health care Pvt. Ltd, Gujarat	Polymer
7.	Guargum	Akhil Health care Pvt. Ltd, Gujarat	Polymer
8.	Pectin	Yarrow Chem. Products, Mumbai	Polymer

9.	Sodium C MC	Akhil Health care Pvt. Ltd, Gujarat	Polymer
10.	Aerosil	Yarrow Chem. Products, Mumbai	Glidant
11.	Magnesium Stearate	Yarrow Chem. Products, Mumbai	Lubrica nt
12.	Micro Crys talline Cell ulose	Yarrow Chem. Products, Mumbai	Diluent

Table 2: List of equipment's used in study and their manufacturers

S. No	INSTRUMENTS	MAKE	MODEL
1	Tablet Compression Machine	Karnavathi	Rimek mini pre ss I
2	FT-IR spectrophotometer	Bruker	Alpha-T-1020
3	Differential Scanning C alorimetry	Hitachi	6300
4	HPLC	Agilent Techno logies	1200
5	UV-Visible spectrophotomet er	Lab india	UV 3200+
6	Dissolution test apparat us	Lab india	DS-8000
8	Electronic Weighing bal ance	Shimadzu	ATX224
9	Friabilator	Lab india	FT 1020
10	Hardness tester	Monsanto	SISCO
11	Tapped density apparatu s	Lab india	TD 1025
12	Bulk density apparatus	Thermonik	PD-100
13	Sonicator	Ultrasonic's,	1.5L (H)
14	Centrifuge	Remi	C-854/6
15	Hot air oven	Universal	D-5247
16	Seive no's 16,40 and 60	Jayant Scientifi c	J-82
17	Stability chamber	Cintex IC	CIC-64 AA
18	PH meter	Lab india	SAB 5000

PREFORMULATION STUDIES:

The goals of the preformulation study are:

- ✓ To establish the necessary physicochemical characteristics of a new drug substance.
- ✓ To determine its kinetic release rate profile.
- ✓ To establish its compatibility with different excipients.

Hence, preformulation studies on the obtained sample of drug include colour, taste, solubility analysis, melting point determination and compatibility studies and flow properties.[38, 39]

Preparation of standard solutions of Dexlansoprazole

Accurately weighted 10mg Dexlansoprazole (working standard) was transferred into a 10 ml volumetric flask.7ml of diluent was added and sonicated to dissolve the powder drug completely and finally volume was made up to the mark with the same solvent (stock solution). Further 1.0 ml of the above stock solution was pipetted into a 10ml volumetric flask and diluted up to the mark with diluent. Finally, the preparation was filtered through 0.45µm filter. Different concentrations (1, 10, 20, 30 & 40 µg/ml) were prepared for Linearity test.

Drug and excipient compatibility studies:

Determined by using Fourier Transform Infrared Spectroscopy (FTIR) studies and Differential Scaning Caloriemetry (DSC)

Fourier Transform Infrared Spectroscopy (FTIR) studies

The drug- polymer and polymer-polymer interaction was studied by FTIR. Two percent (w/w) of the sample with respect to a potassium bromide disc was mixed with dry KBr. The mixture was ground into a fine powder using an agate mortar and then compressed into a KBr discs in a hydraulic press at a pressure of 10000 psi. Each KBr disc was scanned 16 times at 2 mm/sec at a resolution of 4 cm–1 using cosine apodization. The characteristic peaks were recorded. Ratio of Drug and Excipients taken for compatibility studies is shown in **Table 3**.

Table 3: Ratio of Drug and Excipients taken for compatibility studies

Ingredients	Ratio of Drug and Excipients
Dexlansoprazole	1:0
Dexlansoprazole + Carbopol-974 P+ HPMC K4M	1:1

Differential scanning calorimetry studies

DSC is a thermoanalyticaltechnique in which the difference in the amount of heat required to increase the temperature of a sample and reference is measured as a function of temperature. Both the sample and reference are maintained at nearly the same temperature throughout the experiment. Generally, the temperature program for a DSC analysis is designed such that the sample holder temperature increases linearly as a function of time. The reference sample should have a well-defined heat capacity over the range of temperatures to be scanned.

Flow properties: [41-44]

Angle of Repose:

It is performed to determine the flow rate of powder done by the funnel method. The powder was poured into a funnel which is fixed from height of 2cm of the plane surface. Circumference was drawn with a pencil on the graph paper and the radius of base of a pile was measured at 5 different points and average was taken for calculating Angle of repose using following formula:

$$\Theta = \tan^{-1} H/R$$

Θ=angle of repose, H=height of powder cone, and R=radius of powder cone

Angle of Repose less than 300 shows the free flowing property of the material.

Bulk density:

Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / Vo$$

Where, M = weight of sample and
Vo = apparent volume of powder

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

$$Tap = M / V$$

Where, Tap= Tapped Density,
M = Weight of sample and
V= Tapped volume of powder

Carr's consolidation index:

The Carr index is an indication of the compressibility of a powder.

A Carr index greater than 25 is considered to be an indication of poor flowability, and below 15 of good flowability.

Hausner's ratio:

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. Hausner's ratio greater than 1.25 is considered to be an indication of poor flowability.

FORMULATION DEVELOPMENT OF TABLETS:

Preparation of Tablets:

Direct Compression method:

Different tablets formulations were prepared by direct compression technique. All powders were passed

through 60mesh. Required quantities of drug and polymers were mixed thoroughly Magnesium stearate was added as lubricant. Aerosil was used as glidant. Micro crystalline cellulose was used as diluent. Finally, the powder mix was subjected to compression after mixing uniformly in a polybag. Prior to compression, the blends were evaluated for several tests. **Table. 4 and 5**

Table No: 4 Compositions of Dexlansoprazole CR tablets (F1-F12)

S.No	Ingredients(mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Dexlansoprazole	30	30	30	30	30	30	30	30	30	30	30	30
2	Carbopol-974P	150	75	50	100	75	50	100	20	-	-	-	-
3	HPMC K4M	-	75	100	50	-	-	-	150	-	-	-	-
4	HPMC K 15M	-	-	-	-	75	100	50	-	150	75	50	100
5	Sodium CMC	-	-	-	-	-	-	-	-	-	75	100	50
6	Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
7	Aerosil	5	5	5	5	5	5	5	5	5	5	5	5
8	MCC	60	60	60	60	60	60	60	60	60	60	60	60
	Total Weight	250	250	250	250	250	250	250	250	250	250	250	250

Table No: 5 Compositions of Dexlansoprazole CR tablets (F13-F22)

S.No	Ingredients(mg/tab)	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22
1	Dexlansoprazole	30	30	30	30	30	30	30	30	30	30
2	Xanthan gum	75	100	15	--	--	---	--	--	--	--
3	Guar gum	--	--	50	75	--	---	--	--	--	--
4	Pectin	--	--	--	--	75	100	--	--	--	35
5	HPMC K 100M	--	--	--	--	--	---	50	75	100	50
6	Magnesium stearate	5	5	5	5	5	5	5	5	5	5
7	Aerosil	5	5	5	5	5	5	5	5	5	5
8	MCC	60	60	60	60	60	60	60	60	60	60
	Total Weight	250	250	250	250	250	250	250	250	250	250

Evaluation of post compression parameters for prepared Tablets:

The designed formulation compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.[49-54]

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula. **Table. 6**

Deviation = (Individual weight – Average weight / Average weight) × 100

Table No: 6 Pharmacopoeia specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability test:

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche friabilator (Lab India, FT 1020). It is expressed in percentage (%). Ten tablets were initially weighed [W (initial)] and transferred into friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions.

Determination of drug content:

The compression tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Esomeprazole were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In-vitro* dissolution studies:**

The *in-vitro* dissolution was carried out using USP type II dissolution apparatus was determined using USP Dissolution testing apparatus type-II (Paddle method; Lab India DS 8000+), Temperature is 37±0.5ºC and RPM is 50. Dissolution medium was maintained at acid buffer (pH-1.2) for 2 hrs, 4.5 pH acetate buffer for 2 hrs, 6.8 pH phosphate buffer for 8 hrs and 7.4 pH phosphate buffer for 12 hrs % Drug release was calculated at various time intervals.[58-65]

The tablets were placed in the dissolution medium and the apparatus was run. At intervals of 1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24 hours 5 ml aliquots were withdrawn and replacement was done each time with equal amounts of fresh dissolution medium maintained at same temperature. Each 5 ml aliquot was filtered through Whatman filter paper (No.41). 5 ml of sample was diluted to 10 ml acid buffer (pH-1.2) for 2 hrs, 4.5 pH acetate buffer for 2 hrs, 6.8 pH phosphate buffer for 8 hrs and 7.4 pH phosphate buffer for 12 hrs and absorbance of these solutions was measured by using a UV spectrophotometer. Drug concentrations in the sample were determined from standard calibration curve. The release data were calculated.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data are fitted to the following equation.

$$F = Ko\ t$$

Where, ‘F’ is the drug release at time‘t’, and ‘Ko’ is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$\text{Log } (100\text{-}F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs.time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k\ t1/2$$

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer-Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$Mt/ M\infty = K\ t^n$$

Where, Mt/ M∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n=0.5; for zero-order release (case-II transport), n=1; and for super case-II transport, n > 1.In this model, a plot of log (Mt/ M∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100\text{-}Qt)^{1/3} = 100^{1/3} - KHC.t$$

Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets)

Stability Studies:

The goal of formulation development is to determine a composition for the final dosage form that results in a safe, efficacious product which remains stable over the course of its intended use.

Under the influence of a variety of environmental factors such as temperature, humidity and light enabling recommended storage conditions, re-test periods and shelf lives.

RESULTS AND DISCUSSION:

The present study was aimed to developing Controlled release tablets of Dexlansoprazole using various polymers. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

Analytical Method: Graphs of Dexlansoprazole were taken in Simulated Gastric fluid (pH 1.2) and in pH 6.8 phosphate buffer at 232 nm and 234 nm respectively. **Table.7 and 8**

Table 7: Observations for graph of Dexlansoprazole in 0.1N HCl (232nm)

Concentration (µg/ml)	Absorbance (nm)
0	0
5	0.105
10	0.202
15	0.298
20	0.397
25	0.487
30	0.588
35	0.676

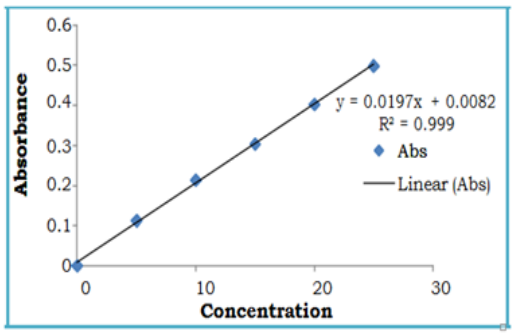

Fig. 2: Standard graph of Dexlansoprazole in 0.1N HCL

Discussion: Based on above results, it has been inferred that API shows linearity in concentration range of 5-40µg/ml by using Simulated Gastric fluid (pH 1.2). The regression coefficient of calibration curve was found to be 0.999

Table 8: Observations for graph of Dexlansoprazole in pH 6.8 phosphate buffer (234nm)

Concentration (µg/ml)	Absorbance (nm)
0	0
5	0.112
10	0.213
15	0.303
20	0.402
25	0.498

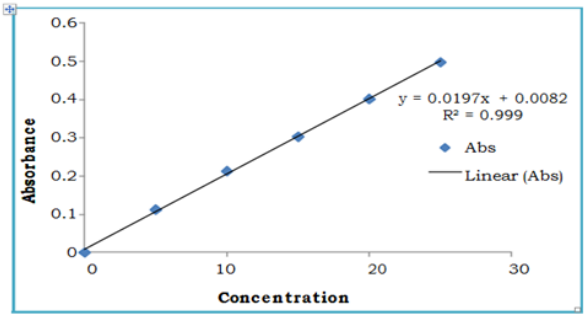

Fig. 3: Standard graph of Dexlansoprazole in pH 6.8 phosphate buffer

Discussion: Based on above results, it has been inferred that API shows linearity in concentration range of 5-40µg/ml by using pH 6.8 phosphate buffer. The regression coefficient of calibration curve was found to be 0.999.

Drug - Excipient Compatibility Studies:

FTIR STUDIES

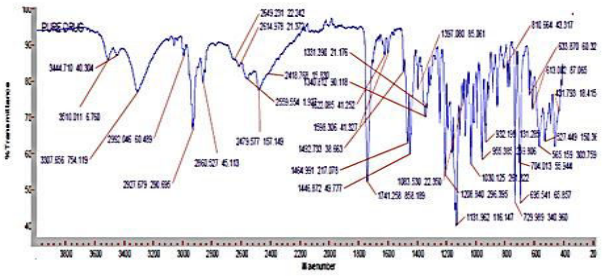

Fig. 4: FTIR Spectrum of Dexlansaprazole pure drug

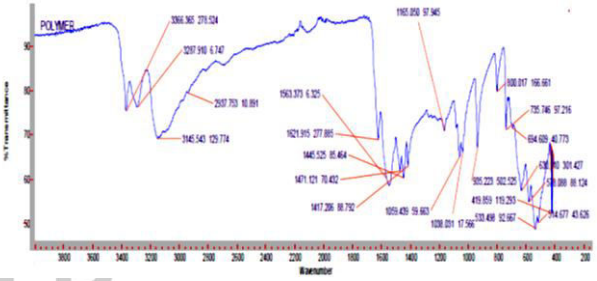

Fig. 5: FTIR Spectrum of Dexlansaprazole Pure Drug+Carbopol 974P+HPMC K4M

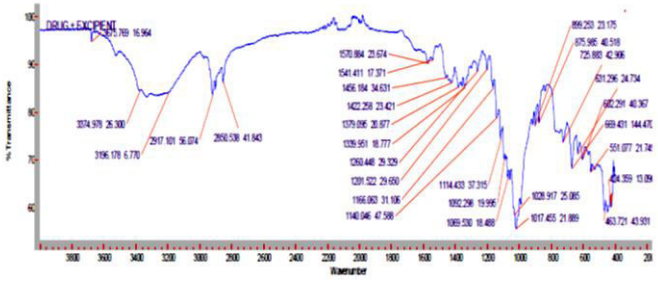

Fig. 6: FTIR Spectrum of Dexlansaprazole optimized formulation

Table 9: FT-IR Data Interpretation for Dexlansoprazole

S. No	Wave number in formulation (cm-1)			Characteristic	Bond
				Wave number range (cm-1)	nature and bond
	Dexlansoprazole	Wave number range (cm-1)	Optimized formulation		attributed
1	2928	3146	2917	3400-2400	O-H stretching Carboxylic acid.
2	2992	2938	2851	3000-2850	C-H stretching Alkanes.
3	1598	1563	1571	1600-1475	-C=C- stretching Aromatic.
4	1465	1471	1456	1500-1400	C-C stretch in ring Aromatics.
5	1132	1165	1166	1350-1000	C-Nstretcha mines.
6	811	800	876	910-665	N-H 10,20 amines.
7	704	736	726	900-690	C-H out-of-plane bend aromatics.

Discussion: The progress of a successful formulation depends only on suitable selection of excipients. Hence the physical state of the drug, Dexlansoprazole Pure drug, Dexlansoprazole+Carbopol-974P+ HPMC-K 4M, Dexlansoprazole and altered polymers for occurrence Carbopol-974P, HPMC-K 4M, Mg.Stearate, Aerosil, Micro crystalline cellulose individually and the admixture of Dexlansoprazole and polymers used were studied by FTIR to know the drug - polymer compatibility after interpretation and the results were shown in IR spectra in **Fig.; 4-6 and Table.9.**

The physicochemical compatibility of the drug and the polymer was established through FTIR studies. IR spectral analysis of Dexlansoprazole pure drug showed the peaks at wave numbers of 2927.679 (O-H stretching Carboxylic acid), 2992.046 (C-H stretching Alkanes), 1598.306 (-C=C- stretching aromatic), 1464.991(C-C stretch in ring aromatics), 1131.962 (C-N stretch amines), 810.664 (N-H 10, 20 amines), 704.013 (C-H out-of-plane bend aromatics) Confirming the purity of drug with standard respectively.

IR spectral analysis of Dexlansoprazole+Carbopol-974P+ HPMC-K 4M showed the peaks at wave numbers of 3145.543 (O-H stretching Carboxylic acid), 2937.753 (C-H stretching Alkanes), 1563.373 (-C=C-stretching aromatic), 1471.121(C-C stretch in ring aromatics), 1165.050 (C-N stretch amines), 800.017 (N-H 10, 20 amines), 735.746 (C-H out-of-plane bend aromatics) Confirming the purity of drug with standard respectively. **Fig 2-3**

In the physical mixture of Dexlansoprazole with various excipients such as Carbopol-974P, HPMC-K 4M, Mg.Stearate, Aerosil, Micro crystalline cellulose the major peaks at wave numbers of 2917.101 (O-H stretching Carboxylic acid), 2850.538 (C-H stretching Alkanes), 1570.884 (-C=C- stretching aromatic), 1456.184(C-C stretch in ring aromatics), 1166.063 (C-N stretch amines), 875.985 (N-H 10,20 amines), 725.883 (C-H out-of-plane bend aromatics). However, extra peaks were absorbed in considerable mixtures which can be due to occurrence of polymers and indicated that there was no chemical interaction between Dexlansoprazole with various other polymers.

Differential Scanning Calorimetry (DSC):

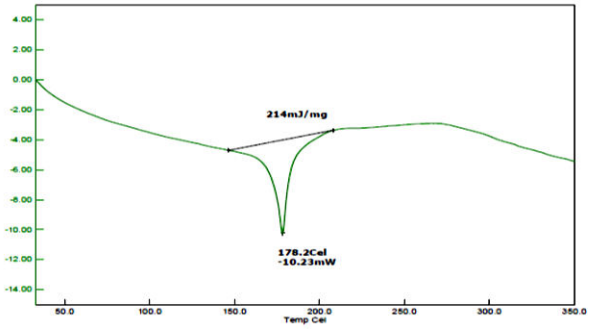

Fig. 7: DSC of Dexlansaprazole pure drug

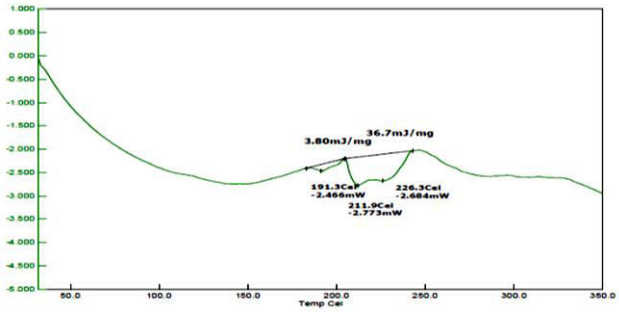

Fig. 8: DSC of Dexlansaprazole pure drug+Carbopol 974P+HPMC K4M

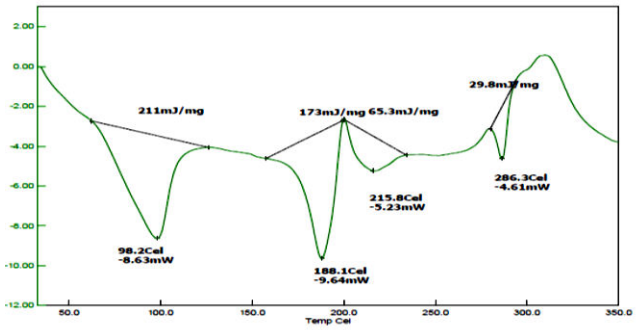

Fig. 9: DSC of Dexlansaprazole optimized formulation

Table 10: Data of DSC thermogram parameters for Dexlansoprazole

S. No	Name of ingredients and physical mixtures used in formulation	Temperature at which peak obtained
1	Dexlansoprazole	178.2°C
2	Dexlansoprazole+Carbopol-974P+ HPMC-K 4M	191.3°C
3	Dexlansoprazole + Carbopol-974P+ HPMC-K 4M +Mg.Stearate +Aerosil+ MCC	188.1°C

Discussion: The compatibility and interactions between drugs and polymer were checked using DSC results obtained were shown in **Fig.7-9 and Table. 10**. The DSC thermograph for Dexlansoprazole showed melting peak at 178.2°C and the mixer of the Dexlansoprazole +Carbopol-974P + HPMC-K 4M showed melting points starting at 191.3°C ending at 226.3°C and Dexlansoprazole + Carbopol-974P + HPMC-K 4M +Mg.Stearate +Aerosil+ Micro Crystaline cellulose showed melting points starting at 98.2°C ending at 286.8°C respectively. The endothermic energy of Dexlansoprazole was -10.23 mW and the mixer of the Dexlansoprazole + Carbopol-974P + HPMC-K 4M and Dexlansoprazole + Carbopol-974P+ HPMC-K 4M + Mg.Stearate + Aerosil + Micro Crystaline cellulose were -2.466 mW and -9.64 mW respectively. DSC studies were carried out to conclude the compatibility among Dexlansoprazole and polymers in optimized formulation. From the studies it was manifest that there were no major change in the melting point of Dexlansoprazole unaccompanied and its melting point when it was combined with other polymers of optimized formulation.

FORMULATION STUDIES:

In-vitro **evaluation of Dexlansoprazole Controlled Release tablets for physico chemical characteristics: (Mean +SD) (n=3)**

Table 11: Flow properties of powder blend for Dexlansoprazole

Formulation Code	Bulk density (gm/cm3)	Tapped density (gm/cm3)	Hausner ratio (HR)	Carr's index (CI)	Angle of repose (θ)
F1	0.48±0.01	0.59±0.04	1.3±0.25	14.76±0.04	27°.7'±0.61
F2	0.35±0.09	0.61±0.07	1.1±0.26	13.63±0.86	25°.1'±0.30
F3	0.47±0.07	0.74±0.05	1.13±0.01	13.55±0.43	26°.2'±0.42
F4	0.36±0.09	0.69±0.06	1.2±0.09	12.18±0.97	25°.6'±0.18
F5	0.42±0.04	0.51±0.02	0.9±0.29	11.68±0.07	26°.9'±1.12
F6	0.49±0.05	0.64±0.09	0.97±0.17	16.36±0.34	29°.7'±0.79
F7	0.34±0.06	0.55±0.07	0.9±0.36	12.26±0.31	30°.3'±0.65
F8	0.42±0.03	0.62±0.04	1.13±0.42	14.68±0.88	26°.5'±0.69
F9	0.38±0.08	0.76±0.05	0.89±0.69	15.23±0.39	27°.5'±1.46
F10	0.39±0.06	0.52±0.05	0.7±0.76	14.87±0.53	28°.7'±1.20
F11	0.46±0.03	0.64±0.07	1.14±0.53	14.63±0.75	29°.9'±0.27
F12	0.38±0.02	0.63±0.04	0.9±0.66	12.55±0.59	26°.5'±0.24
F13	0.43±0.05	0.78±0.06	1.1±0.49	13.53±0.97	28°.3'±0.36
F14	0.39±0.01	0.74±0.06	1.14±0.65	14.87±0.76	29°.5'±0.71
F15	0.44±0.02	0.65±0.01	0.9±0.66	12.32±0.42	27°.3'±0.39
F16	0.48±0.09	0.69±0.05	1.15±0.53	11.89±0.87	24°.5'±0.65
F17	0.36±0.05	0.76±0.03	1.16±0.42	13.56±0.65	26°.9'±0.99
F18	0.39±0.04	0.69±0.06	1.12±0.87	12.72±0.43	29°.7'±0.43
F19	0.43±0.05	0.77±0.01	1.1±0.58	14.36±0.98	27°.2'±0.65
F20	0.40±0.07	0.60±0.09	1.11±0.32	12.75±0.46	25°.3'±0.98
F21	0.46±0.08	0.61±0.04	1.15±0.24	11.87±0.76	28°.6'±0.54
F22	0.48±0.05	0.68±0.09	0.9±0.34	13.42±0.54	29°.4'±0.76

Discussion: Tablet powder blend was subjected to various preformulation parameters. The bulk density of all the formulations was found to be in the range of 0.34±0.06 to 0.49±0.05 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.51±0.02 to 0.78±0.06 showing the powder has good flow properties. The hausner's ratio ranging between 0.9±0.29 to 1.3±0.25 indicating the powder has good flow properties. The Carr's index of all the formulations was found to be in the range of 11.68±0.07 to 16.36±0.34. The angle of repose of all the formulations was found to be in the range of 24°.5'±0.65 to 30°.3'±0.65. All these values indicates that the powder blend has good flow properties.

Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug Content and Dissolution studies in different media were performed as per Pharmacopoeia. **Table. 12**

***In-vitro* evaluation of Dexlansoprazole Controlled Release tablets for Post Compression characteristics:**

Table 12: Physico Chemical Characterization of Dexlansoprazole Controlled Release Tablets.

Formulation Code	Weight variation(mg)	Hardness (kg/cm2)	Friability (%)	Thickness (mm)	Drug content (%)
F1	249±0.74	4.2±0.32	0.58±0.25	3.62±0.53	99.81±0.08
F2	250±0.67	4.9±0.89	0.59±0.53	3.98±0.71	99.98±0.03
F3	251±0.75	3.9±0.46	0.62±0.61	3.69±0.23	101.2±0.07

F4	249±0.23	3.9±0.72	0.58±0.42	3.25±0.97	99.41±0.26
F5	249±0.05	4.3±0.18	0.79±0.15	4.1±0.07	99.24±0.75
F6	251±0.86	4.1±0.52	0.62±0.55	3.24±0.53	101±0.12
F7	250±0.55	4.3±0.63	0.59±0.17	3.59±0.62	99.26±0.09
F8	249±0.77	4.4±0.42	0.67±0.82	3.57±0.41	101.1±0.62
F9	250±0.24	3.8±0.74	0.78±0.26	3.11±0.26	100±0.25
F10	249±0.03	3.9±0.79	0.69±0.82	3.27±0.67	99.2±0.01
F11	248±0.75	4.4±0.62	0.65±0.16	3.52±0.16	98.13±0.02
F12	249±0.52	4.1±0.14	0.79±0.04	3.78±0.97	99.3±0.17
F13	250±0.51	3.9±0.84	0.67±0.43	3.21±0.46	100±0.46
F14	248±0.35	4.1±0.37	0.55±0.84	3.74±0.48	99.1±0.74
F15	249±0.37	4.4±0.52	0.78±0.32	3.7±0.03	100±0.45
F16	251±0.82	4.3±0.43	0.66±0.15	3.55±0.64	98.8±0.89
F17	250±0.47	3.8±0.48	0.81±0.54	4.24±0.45	99.5±0.54
F18	249±0.49	4.2±0.2	0.76±0.88	3.55±0.76	98.9±0.98
F19	249±0.98	3.9±0.14	0.55±0.53	3.66±0.35	99.3±0.87
F20	251±0.65	3.6±0.34	0.61±0.43	3.37±0.79	100±0.98
F21	250±0.95	4.1±0.53	0.71±0.65	4.3±0.64	99.8±0.42
F22	249±0.95	4.7±0.75	0.62±0.88	3.76±0.31	99.6±0.65

Discussion:

Appearance:

The tablets were observed visually and did not show any defect such as capping, chipping and lamination.

Physical characteristics:

The physical characteristic of Dexlansoprazole Controlled release tablets (F1 to F22) such as weight variation, hardness, friability, thickness, and drug content were determined and results of the formulations (F1 to F22) found to be within the limits specified in official books.

Weight Variation:

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet. Average weight of the tablet is approximately in range of 248±0.35 to 251.6±0.86, so the permissible limit is ± 5% (more than 250mg). The tablet weights were within the Pharmacopoeial specifications.

Tablet Hardness:

Hardness of the three tablets of each batch was checked by using Monsanto hardness tester. The results showed that the hardness of tablets was found to be in the range of 3.6±0.34 to 4.9±0.89kg/cm2. This indicates good tablet strength.

Percent Friability:

Percentage friability of all the formulations was found to be in between 0.55±0.53 to 0.79±0.04%. This indicated good handling property of the prepared CR tablet.

Dimension (Diameter and Thickness):

Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness and diameter can result in problems with packaging as well as consumer acceptance. The size (diameter) of the tablets of all formulations were found to be 8.0±0.0 mm and thickness ranged between 3.11±0.26 to 4.3±0.64.

Drug content:

The content of active ingredients in the formulation was found to be between 98.13±0.02 to 101.2±0.07%w/w, which is within the specified limit as per IP (i.e. 90-110% w/w). All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

IN-VITRO DRUG RELEASE STUDIES OF DEXLANSOPRAZOLE CONTROLLED RELEASE TABLETS:

Table 13: *In-Vitro* drug release studies of Dexlansoprazole Controlled Release tablets (F1-F8)

Time	CUMULATIVE % DRUG RELEASE							
(hours)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	32.48±0.78	6.23±0.86	10.45±0.61	19.13±0.82	16.76±0.68	17.49±0.75	21.76±0.78	8.23±0.74
2	56.87±1.24	9.64±0.51	19.59±0.29	35.64±0.33	24.43±0.74	36.38±0.43	38.46±1.06	10.75±0.34
4	71.09±1.22	27.13±0.86	25.11±0.48	47.56±0.38	38.96±0.98	42.76±0.34	41.03±1.08	16.42±0.76
6	82.86±1.09	39.80±0.11	29.67±0.14	59.43±0.92	51.29±1.02	58.96±0.28	53.49±0.98	21.31±0.84
8	94.86±0.75	48.18±0.18	37.53±0.12	69.49±0.46	58.46±0.84	61.22±0.56	57.84±0.84	31.47±0.98
10	97.32±.68	55.17±0.13	54.22±0.18	84.63±0.36	63.86±0.98	64.76±0.98	61.98±0.68	41.75±0.91
12	98.82±.54	63.36±0.65	66.53±0.27	88.68±0.63	69.16±0.48	69.23±0.84	70.72±0.73	52.46±0.1
14	99.94±0.74	71.24±0.69	72.3±0.44	96.75±0.79	74.69±0.68	71.46±0.67	74.39±0.25	58.69±0.77
16	-----	79.92±0.31	83.41±0.48	99.57±0.35	75.46±0.84	73.34±0.68	78.67±0.43	61.32±0.72
18	-----	86.18±0.77	85.96±0.89	-----	79.47±0.56	74.31±0.84	83.38±0.57	64.46±0.67
20	-----	90.17±0.14	87.43±0.11	-----	82.46±0.76	76.69±0.76	85.64±0.48	63.78±0.58
22	-----	95.86±0.22	88.39±0.18	-----	84.76±0.84	78.46±0.48	88.46±0.74	65.82±0.84
24	-----	98.79±0.48	90.31±0.74	-----	86.16±0.67	80.23±0.78	91.23±0.66	68.49±0.67

Table 14: *In-Vitro* drug release studies of Dexlansoprazole Controlled Release tablets (F9-F15)

Time	CUMULATIVE % DRUG RELEASE						
(hours)	F9	F10	F11	F12	F13	F14	F15
0	0	0	0	0	0	0	0
1	6.72±0.84	23.88±0.94	17.82±0.35	9.57±0.84	14.86±0.35	14.12±0.71	15.62±0.36
2	14.16±0.71	49.32±1.32	18.9±0.48	22.68±0.72	32.28±0.73	16.25±0.16	22.27±0.13
4	18.46±0.67	53.92±0.84	31.13±0.78	26.1±0.98	44.32±0.15	28.43±0.86	30.45±0.75
6	28.56±0.87	63.07±0.67	60.84±1.01	28.09±1.04	55.75±0.29	37.35±1.97	37.72±1.21
8	37.44±0.67	71.77±1.24	75.6±1.28	55.8±1.32	67.16±0.88	46.54±0.55	45.47±0.18
10	45.12±0.78	77.85±0.98	84.49±0.37	69.3±0.37	74.43±0.96	58.18±0.82	53.63±0.53
12	50.54±0.32	83.76±1.09	92.7±0.68	76.5±0.67	84.59±0.13	66.31±0.33	69.78±0.82
14	59.4±0.49	86.34±0.98	93.18±1.38	80.45±0.32	89.66±0.49	75.18±0.88	72.93±0.63
16	60±0.97	89.43±0.65	94.08±0.84	83.1±0.84	94.34±0.21	79.22±0.15	78.35±0.46
18	61.2±0.54	93.6±1.24	94.59±1.24	83.6±0.47	99.46±0.87	83.73±0.87	81.92±0.37
20	62.25±0.78	93.67±1.42	95±0.84	84.6±1.24	-----	88.26±0.21	84.28±0.64
24	65.86±0.49	96.9±0.82	96.24±0.84	85.79±0.78	-----	92.68±0.53	90.98±0.89

Table 15: *In-Vitro* drug release studies of Dexlansoprazole Controlled Release tablets (F16-F22)

Time (hours)	CUMULATIVE % DRUG RELEASE						
	F16	F17	F18	F19	F20	F21	F22
0	0	0	0	0	0	0	0
1	11.26±0.86	26.63±0.29	7.26±0.35	12.34±0.87	15.12±0.65	6.35±0.41	21.89±0.36
2	16.28±0.63	43.27±0.82	17.87±0.76	17.53±0.54	28.35±0.44	15.74±0.26	36.43±0.35
4	21.54±0.86	58.57±0.61	23.65±0.34	26.89±0.35	37.54±0.76	22.83±0.34	39.67±0.67
6	27.87±0.29	67.43±0.25	31.44±0.98	38.67±0.86	49.76±0.82	30.55±0.98	44.65±0.98
8	35.27±0.18	77.25±0.82	40.34±0.65	47.52±0.56	51.14±0.59	38.75±0.65	59.83±0.42
10	48.46±0.65	80.62±.14	48.82±0.76	56.89±0.87	59.98±0.34	45.97±0.76	64.99±0.23
12	56.38±0.72	85.82±.62	56.76±0.43	65.53±0.34	62.15±0.98	53.42±0.45	70.65±0.87
14	61.46±0.14	89.26±0.53	60.35±0.78	70.98±0.65	67.45±0.39	61.76±0.78	75.98±0.19
16	67.74±0.36	94.71±.65	64.55±0.57	76.57±0.89	74.68±0.62	67.41±0.57	81.76±0.54
18	74.55±0.81	99.36±0.16	71.36±0.34	80.65±0.45	79.25±0.45	74.43±0.34	85.33±0.21
20	79.37±0.92	-----	77.73±0.32	84.25±0.32	80.87±0.85	81.76±0.32	89.23±0.56
22	86.47±0.75	-----	85.13±0.87	86.73±0.76	84.54±0.56	88.98±0.87	90.54±0.87
24	91.04±0.14	-----	92.66±0.54	89.36±0.45	87.35±0.37	93.56±0.54	92.36±0.44

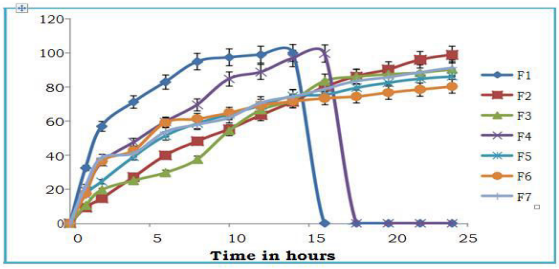

Fig. 10: Dissolution graphs for the formulations F1 to F7

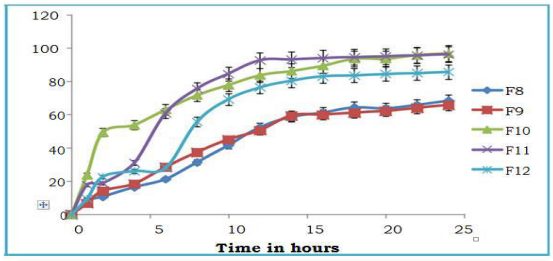

Fig. 11: Dissolution graphs for the formulations F8 to F12

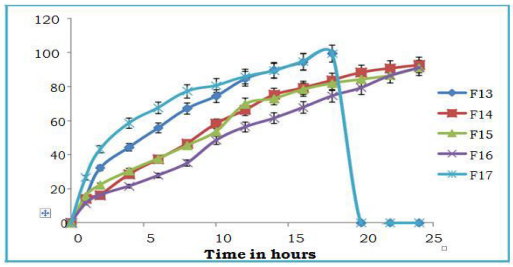

Fig. 12: Dissolution graphs for the formulations F13 to F17

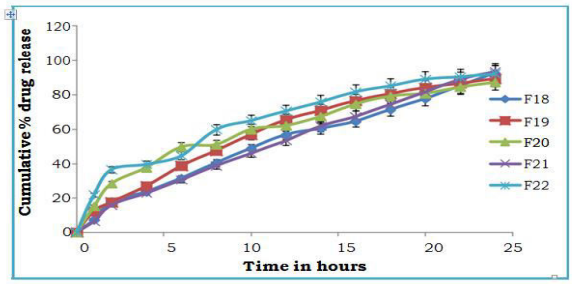

Fig. 13: Dissolution graphs for the formulations F18 to F22

Discussion:

The prepared Dexlansoprazole CR tablets were evaluated for the dissolution studies in acid buffer (pH-1.2) for 2 hrs, 4.5 pH acetate buffer for 2 hrs, 6.8 pH phosphate buffer for 8 hrs and 7.4 pH phosphate buffer for 12 hrs % Drug release was calculated at various time intervals. The results were shown in the **Table: 13-15 and Fig.10-13**.

To prepare the different controlled release formulations of Dexlansoprazole tablets with different polymers such as acrylic acid polymer such as Carbopol-974P, HPMC grades for prevalence HPMC K4M, K15M, K100M, Natural Polymers akin to Xanthan gum, Guar gum, Sodium CMC, and Pectin, aerosil is glidant, magnesium stearate is lubricant and Micro Crystalline cellulose was used as diluents by Direct Compression method.

Formulations of F1, F2, F3 and F4 containing Carbopol-974P alone and combination of Carbopol-974P and HPMC K4M. The Formulation F1 has shown cumulative % drug release of 99.94±0.74 % at the end of 14th hr, Formulation F2 has shown release 98.79±0.48% at the end of 24th hr, Formulation F3 has shown release 90.31±0.74 % at the end of 24th hr, Formulation F4 has shown release 99.57±0.35 % at the end of 16th hr.

Formulations F5, F6, and F7 containing combination of Carbopol-974P and HPMC K15M. The Formulation F5 has shown cumulative % drug release of 86.16±0.67 % at the end of 24th hr,

Formulation F6 has shown release 80.23±0.78 % at the end of 24th hr, Formulation F7 has shown release 91.23±0.66 % at the end of 24th hr. Formulation F8 containing combination of Carbopol-974P and HPMC K4M. The Formulation F8 has shown cumulative % drug release of 68.49±0.67 % at the end of 24th hr. Formulation F9 containing HPMC K15M alone.

The Formulation F9 has shown cumulative % drug release of 65.86±0.49% at the end of 24th hr. Formulations F10, F11, and F12 containing

combination of HPMC K15M and Sodium CMC. The Formulation F10 has shown cumulative % drug release of 96.9±0.82 % at the end of 24th hr, Formulation F11 has shown release 96.24±0.84 % at the end of 24th hr, Formulation F12 has shown release 85.79±0.78 % at the end of 24th hr. Formulation F13, F14 containing Xanthan gum alone. The Formulation F13 has shown cumulative % drug release of 99.46±0.87 % at the end of 18th hr, The Formulation F14 has shown release of 92.68±0.53 % at the end of 24th hr. Formulation F15 containing combination of Xanthan gum and Guar gum. The Formulation F15 has shown cumulative % drug release of 90.98±0.89 % at the end of 24th hr.

Formulation F16, F17, F18, F19, F20 and F21 containing Guar gum, Pectin and HPMC K100M alone. The Formulation F16 has shown cumulative % drug release of 91.04±0.14% at the end of 24th hr, The Formulation F17 has shown release of 99.36±0.16% at the end of 18th hr, The Formulation F18 has shown release of 92.66±0.54% at the end of 24th hr, The Formulation F19 has shown release of 89.36±0.45 % at the end of 24th hr, The Formulation F20 has shown release of 87.35±0.37% at the end of 24th hr, The Formulation F21 has shown release of 93.56±0.54% at the end of 24th hr. Formulation F22 containing combination of Pectin and HPMC K100M. The Formulation F22 has shown cumulative % drug release of 92.36±0.44% at the end of 24th hr.

The results of cumulative % drug release shown that the Dexlansoprazole was released in a controlled behaviour from all the formulations where formulation F-2 showed maximum cumulative % drug release i.e. 98.79±0.48 at the end of 24th hour which was the intent of the finalized formulation (to prolong the drug release up to 24 hrs) while others being not reached to the time point of maximum release still extending the release.

Comparison of *In-Vitro* Drug release studies of Optimized Dexlansoprazole CR Formulation (F-2) with Innovator Product:

Table 16: Comparative *In-vitro* drug release studies of optimized formulation of Dexlansoprazole (F-2) with Innovator product

Time (Mins)	F-2	Innovator Product
0	0	0
10	---	38.25±0.36
20	---	47.34±0.69
30	---	55.71±0.12
45	---	66.62±0.27
60	---	74.48±0.81
75	---	89.87±0.65
90	---	98.43±0.76
120	9.64±0.51	---
220	27.13±0.86	---
340	39.80±0.11	---
460	48.18±0.18	---
580	55.17±0.13	---
700	63.36±0.65	---
820	71.24±0.69	---
940	79.92±0.31	---
1060	86.18±0.77	---
1180	90.17±0.14	---
1300	95.86±0.22	---
1420	98.79±0.48	---

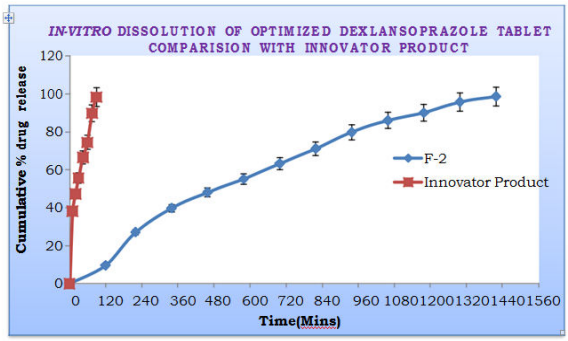

Fig. 14: Comparative *In-vitro* drug release studies of optimized formulation of Dexlansoprazole (F-2) with Innovator product

Discussion:

Dexlansoprazole is available as conventional immediate release tablet dosage form as in the brand name of Dexilant 30mg Tablets.

In the present research work Dexlansoprazole Controlled Release Tablets 30mg was formulated and the composition was optimized with an objective of prolonging the drug release capable of 24 hrs and the *in-vitro* drug release of optimized Dexlansoprazole Controlled Release Tablets 30mg was evaluated and was compared against the *in-vitro* drug release of corresponding Innovator product.

The drug release from Dexilant 30mg tablets was about 98.43±0.76 cumulative % drug release in 90 minutes, whereas finalized Controlled release tablet dosage containing Drug to Polymer (Carbopol-974 P: HPMC K4M) at 1:1 ratios (F-2) has shown the cumulative % drug release of 98.79±0.48 at the end of 24 hours. The formulation which has shown the drug release at Zero order / constantly for the preferred time period of time was deliberate as optimized formulation. **Table.16**

Based on *in-vitro* release studies, it was clearly manifest that the drug release from finalized Controlled release tablet dosage form has been prolonged for 24 hours, whereas marketed Innovator product has shown almost complete cumulative % drug release in 90 minutes. Based on the results, it can be concluded that the innovator product needs to be administered 2 to 3 times in a day, while the Dexlansoprazole Controlled release tablet can be administered once daily is sufficient to continue the therapeutic concentration.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model. **Table. 17**

Table 17: Dexlansoprazole Release Kinetic Parameters for Optimized Formulation

F. Code	Zero Order	First Order	Higuchi	Best fit	Korsmeyer-Peppas		Release Mechanism
	R^2	R^2	R^2		R^2	n-Valve	
F2	0.984	0.874	0.969	zero order	0.997	0.792	Anomalous Diffusion

Optimized Formulation (F-2) for Release Kinetics Graphs:

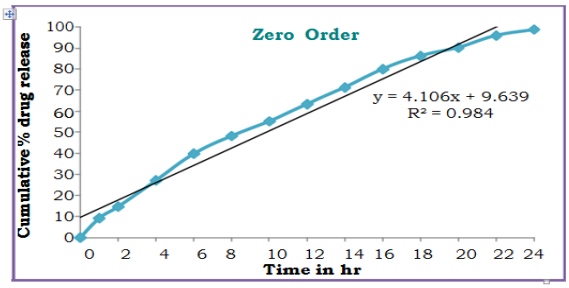

Fig. 15: Zero order release kinetics of Dexlansoprazole optimized Formulation (F-2)

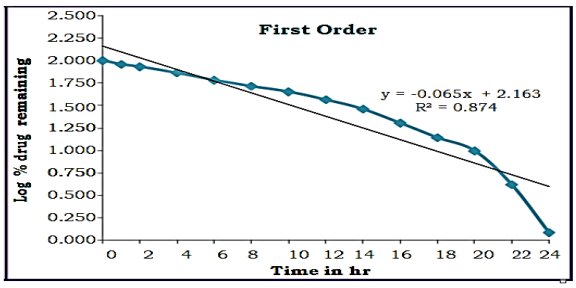

Fig. 16: First order release kinetics of Dexlansoprazole optimized Formulation (F-2)

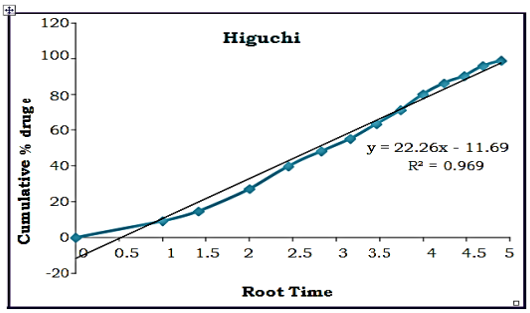

Fig. 17: Higuchi model kinetics of Dexlansoprazole optimized Formulation (F-2)

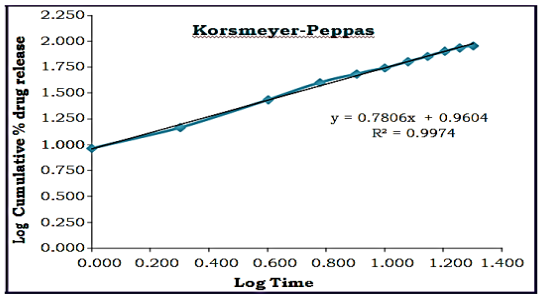

Fig. 18: Korsmeyer-Peppas model kinetics of Dexlansoprazole optimized Formulation (F -2)

Discussion:

In-vitro dissolution kinetic parameter from optimized formulation of Dexlansoprazole controlled release tablet was calculated and the reports are given in **Table.17 and Fig.15-18**. It was examined the drug dissolution kinetic from the formulation was followed zero order as the R2 value of zero order was establish to be 0.984 and the mechanism of drug release was found to be following Anomalous Diffusion as the n value of korsemeyer-peppas was found to be 0.792.

Stability studies of Dexlansoprazole optimized formulation (F-2):

After storage the formulation was analyzed for various physical parameters, results are showed in **Table 18**.

Table 18: Stability study of Optimized formulation (F-2) of Controlled release Dexlansoprazole tablets at Accelerated temperature 40^0 C ± 2^0 C / 75% RH ± 5%.

Parameter	Initial	Accelerated temperature (40^0 C ± 2^0 C / 75% RH ± 5 %)			
		1st Month	2nd Month	3rd Month	6th Month
Weight variation (mg)	250±0.67	249±0.45	248±0.23	249±0.55	250±0.29
Thickness (mm)	3.98±0.71	3.37±0.28	3.25±0.78	3.37±0.28	3.23±0.31
Hardness(kg/cm2)	4.9±0.89	4.8±0.79	4.9±0.54	4.8±0.62	4.9±0.48
Friability (%)	0.59±0.53	0.58±0.45	0.59±0.37	0.58±0.21	0.59±0.54
Drug content (%/tablet)	99.98±0.03	99.57±0.12	98.78±0.53	99.42±0.63	99.11±0.47
In-vitro drug release at 24th hour	98.79±0.48	98.35±0.19	97.98±0.25	98.32±0.41	98.43±0.24

All the values are expressed as mean± SE, n=3

Discussion:

Accelerated Stability studies of optimized formulation were performed for a period of 6 months as per ICH guidelines. The reports of various evaluation parameters such as Weight variation, Thickness, hardness, friability, Drug content, *In-vitro* dissolution at 24th hour of Dexlansoprazole at various predetermined time intervals. The results are obtained in table. 18. No major segregation was initiate between evaluated parameters before and after storage and all are in acceptable limits. The tablets showed satisfactory at Accelerated temperature 400C ± 20C / 75% RH ± 5%.

CONCLUSION:

Dexlansoprazole is a proton pump inhibitor used to treat heartburn caused by gastroesophageal reflux disease (GERD), and to heal erosive esophagitis (damage to the esophagus from stomach acid). It is a short biological half-life (1to2 hrs), bioavailability (60%) and narrow therapeutic index. because of all these parameters Dexlansoprazole was preferred as a good aspirant for controlled drug delivery systems.

1. Preformulation studies were execute for Dexlansoprazole with polymers used were initiate compatable as per FTIR and DSC study interpretation.
2. By using Direct Compression method Dexlansoprazole controlled release tablets were formulated with contradictory polymers such as Acrylic acid polymer such as Carbopol-974P, HPMC grades for prevalence HPMC -K4M, HPMC-K15M, HPMC-K100M, Natural Polymers akin to Xanthan gum, Guar gum, Sodium CMC, and Pectin.
3. Prepared formulations were evaluated for different physico-chemical properties resembling pre and post compression parameters. Results were concluded that values were within the pharmacopoeial limits, then these formulations were evaluated for *in-vitro* drug release and kinetics & mechanism of drug release.
4. Based on *In-vitro* dissolution studies and release kinetics F-2 formulation was preferred as an optimized amongst the all. This optimized formulation was compared with the innovator product; results showed increase the release profile.
5. Stability studies were performed for optimized formulation F-2 for 6 months according to the ICH guidelines and found to be stable.

ACKNOWLEDGEMENTS

The authors are thankful to Astra Zeneca Pharma Ltd, Bangalore for providing a gift sample and the authors are also thankful to V. V. Institute of Pharmaceutical Sciences, Gudlavalleru for their encouragement towards the success of the work.

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Cite of article: Deepika K, Vishnu MS, Rao AL. (2024). Development of controlled release formulations of Dexlansoprazole to improve bioavailability. International Journal of Medical Laboratory Research. 9(1):1–20. http://doi.org/10.35503/IJMLR.2024.9101

CONFLICT OF INTEREST: Authors declared no conflict of interest
SOURCE OF FINANCIAL SUPPORT: Nil