FORMULATION AND EVALUATION OF SUBLINGUAL TABLETS OF LANSOPRAZOLE

Vishal B. Mahajan [1*], Trusha P. Shangrapawar [2], Sujit S. Kakade[2], Ashok V. Bhosale [3], Pramod S. Biradar[1], Sandesh B. Nagargoje[1].

[1] Research Scholar, Department of Pharmaceutics, PDEA's Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Kharadi, Pune, Maharashtra, India.

[2] Assistant Professor, Department of Pharmaceutics, PDEA's Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Kharadi, Pune, Maharashtra, India.

[3] Principal, PDEA's Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Kharadi, Pune, Maharashtra, India.

Corresponding Author Email: mahajanvishal044@gmail.com

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Abstract: *The main objective present research work was to establish the sublingual tablet of Lansoprazole. Lansoprazole uses as a Peptic ulcer disease. Lansoprazole is a BSC class-II drug, it has low solubility and high permeability, hence need to enhance the solubility of Lansoprazole by using a solid dispersion method with a hydrophilic carrier such as Polyethylene glycol-6000 and selecting the 1:4 is the best ratio for solid dispersion. FTIR were used to conduct a compatibility examination on the drug and excipient of a particular solid dispersion. According to this investigation, there is no interaction between the drug and the carrier. The direct compression process was used to create the Sublingual tablet. Sublingual tablets are prepared by using various natural and synthetic super-disintegrant such as Cross povidone, Kyron T-314 and Banana Powder. The pre-compression study was performed and the results were reported. Angle of repose, bulk density, tapped density, Hausner's ratio, and Carr's index were all calculated in the pre-compression investigation, and the findings demonstrated good compliance with IP specifications. The tablets parameters were evaluated by testing thickness, hardness, weight variation, friability test etc. The disintegration time for sublingual tablets was found to be 27±1.16 to 52±1.12 sec. The formulation F8 showed the best results of the dissolution study containing Crospovidone and Banana Powder respectively. The formulation F8 showed 99.14±1.98 of cumulative drug release within 30min. These unique formulation Lansoprazole sublingual tablets demonstrated a rapid onset of action and may be useful and practical for pediatric, geriatric, and psychiatric patients as well as those who have trouble swallowing and in circumstances where water is not readily available.*

Keywords: *Sublingual Tablet, Lansoprazole, Solid Dispersion, Crospovidone, Kyron T-314, Banana Powder*

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INTRODUCTION

A specific category of solid dosage form known as sublingual tablets is designed to be put under the tongue and deliver medication through the mucosal lining of the mouth directly beneath the tongue, resulting in an immediate systemic response. The medicine that the stomach absorbs travels to the mesenteric circulation, which connects to the stomach via the portal vein, and is often metabolised by the liver, also known as first pass metabolism. However, medications absorbed through the oral cavity do not undergo first-pass metabolism because the oral cavity's highly vascularized mucosal lining, which is followed by the jugular veins and superior vena cava, has direct arterial circulation connections. (1)

The proton pump inhibitor class of antisecretory drugs, which includes Lansoprazole, prevents the final stage of acid generation by blocking the H+/K+ ATPase enzyme system known as the proton pump in the upper layer of the stomach parietal cell. For acid-related disorders such as gastroesophageal reflux disease (GERD), Zollinger-Ellison syndrome, peptic ulcer, and lesions caused by non-steroidal anti-inflammatory drugs (NSAIDS), Lansoprazole is a safe and effective treatment option. It is also useful when combined with various regimens for the eradication of H. pylori. (2)

According to a market study, Lansoprazole is offered as enteric coated pellets that are packed inside of capsules because it is acid labile. Although an enteric coating can postpone the drug's release, the procedure is time-consuming and expensive. As a result, this article aims to manufacture Lansoprazole sublingual tablets after using the solid dispersion method to increase its solubility. [3]
Therefore, in this study, efforts are made to increase Lansoprazole's solubility using a solid dispersion approach and to create a sublingual Lansoprazole tablet that will have a quicker beginning of action as a Peptic Ulcer medication.

MATERIAL AND METHOD

A gift sample of Lansoprazole was received from Murli Krishna Pharma Pvt. Ltd. Pune. Crospovidone was received from Prachin Chemical, Ahmedabad. Kyron T-314 was received from Corel Pharma Chem, Ahmedabad. Banana Powder was received from GJ Foods, Dhule. Lactose, Magnesium Stearate, Talc was received from Signet Excipients Pvt. Ltd. Mumbai and Aspartame was received from Beloorbayir Biotech Limited, Bangaluru.

Solubility Study of Lansoprazole [4]
Different conical flasks with 10 ml of various media and an excess amount of Lansoprazole were added, sealed properly, and placed in a REMI incubator shaker for 24 hours at 50 rpm at 37 ^{0}C. The flasks were then removed and filtered using Whatmann filter paper. In order to test absorbance at 284 nm, a clear solution was prepared, diluted appropriately with the proper media, and used as a blank solution.

Preparation of calibration curve of Lansoprazole in phosphate buffer solution pH 6.8[5]
In a 100 ml volumetric flask with phosphate buffer solution at pH 6.8, 10 mg of Lansoprazole that had been precisely weighed was added to create the stock solution. The volume was then increased to 100 ml by obtaining a 100 g/ml solution using a phosphate buffer solution with a pH of 6.8. A range of concentrations of 10–50 ug/ml were produced by diluting various aliquots from the stock solution in series of 1, 2, 3, and 4 and 5 ml in a 10 ml volumetric flask with phosphate buffer solution pH 6.8. A UV spectrometer was used to test the solutions' absorbance at 284 nm. The absorbance vs. concentration calibration curve was plotted, and the slope, intercept, and coefficient of correlation values were computed.

Drug – Excipient Compatibility Study [6]
Fourier Transform Infrared Spectroscopy (FTIR)
FT-IR spectrum of Lansoprazole was obtained on an FTIR spectrophotometer (FTIR 8400S, Shimadzu) using the KBr powder press technique to check its purity. Using dried potassium bromide, the baseline correction was carried out. With a resolution of cm-1 over the range 4000-400 cm-1, the instrument was operated in dry air purge. The scans were examined for principal drug peak existence. The reported IR spectrum's primary peaks and the detected peaks were compared.

Preparation of Solid Dispersion of Lansoprazole [7]
In different ratios, such as Lansoprazole + PEG 6000 (1:1), (1:2), (1:3), and (1:4), solid dispersions of the medicine and polymer were made using the kneading process. These solid dispersions were labelled S1, S2, S3, and S4 correspondingly.

Preparation of solid dispersion of Lansoprazole by Kneading method.
The PEG-6000 was put in a mortar, mixed with water (10% w/w) to make a paste, and then the drug was progressively added to the mixture in the kneading manner. To get the appropriate consistency, a reasonable amount of water was sporadically added while the mixture was physically kneaded for an hour. The mixture was dried in an oven (Electronic India) set to 50°C for 24 hours. The dried compound was ground with a grinder and pestle. The compound was filtered through a 65-mesh screen before being kept in a closed container.

Table 1: Formulation of solid dispersion of Lansoprazole by kneading method

Formulations / Batches	Composition	Method
S1	Lansoprazole+PEG6000(1:1)	Kneading Method
S2	Lansoprazole+PEG6000 (1:2)	Kneading Method
S3	Lansoprazole+PEG6000 (1:3)	Kneading Method
S4	Lansoprazole+PEG6000 (1:4)	Kneading Method

Evaluation of Solid Dispersion of Lansoprazole [8]

Solubility Study of solid dispersion of Lansoprazole

An excessive amount of solid dispersion powder was poured to several conical flasks with 10 ml of various media, sealed properly, and shaken for 24 hours at 50 rpm at 37 0C in a REMI incubator shaker. The flasks were then removed and filtered using Whatmann filter paper. In order to test absorbance at 284 nm, a clear solution was prepared, diluted appropriately with the proper media, and used as a blank solution.

Drug Content

Accurately weighed physical mixes and solid dispersions corresponding to 10 mg of Lansoprazole are dissolved in 10 ml of ethanol. The solution is filtered, appropriately diluted, and its drug content is measured using a UV spectrophotometer at a wavelength of 284 nm.

% Drug Content = WA/WT x 100

Where,

WA= Actual Drug content,

WT= Theoretical drug content.

Percentage Yield

created a solid dispersion from raw materials and compared the sample weight achieved to the theoretical weight of the sample, Use the formula to calculate the yield in percent.

The percentage yield was determined in relation to the dry product. The following formula was used to compute the percentage yield based on the calculated theoretical yield (T.Y) and the practical yield (P.Y) that was attained.

% Yield = Practical Yield / Theoretical Yield x 100

In-vitro dissolution study of solid dispersion of Lansoprazole by Kneading Method [9]

Dissolution profiles of solid dispersions of Lansoprazole by kneading method [S1, S2, S3, S4] were determined using the USP Type II Dissolution test apparatus (Electro lab Model TDT-08L) set with a paddle speed of 100 rpm. Dissolution was performed in 900 ml of phosphate buffer pH 6.8 maintained at 37± 0.5^0C. The complex of solid dispersion containing 15mg of Lansoprazole and PEG 6000 (1:1, 1:2, 1:3, 1:4) [S1, S2, S3, S4] was taken in a muslin cloth and tied to the rotating paddle kept in vessel of dissolution apparatus, the paddle was rotated at 100 rpm. Aliquot of dissolution medium, 5 ml was withdrawn at specified time and filtered through Whatmann filter paper. The amount of drug dissolved was determined by UV-Visible spectrophotometer by measuring the absorbance of the sample at 284 nm. An equal volume of fresh medium, prewarmed at 37^0C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Three trials for each batch were performed and average percentage drug release.

X-ray Diffraction (XRD)

The X-ray diffraction (X-RD) of Lansoprazole were obtained using X-RD instrument Bruker AXS, D8 Advance with Ni-filtered Cu radiation, at a voltage of 45kV and current of 40mA.

Formulation Of Sublingual Tablet Of Solid Dispersion Of Lansoprazole

Table 2: Formulation of Sublingual Tablet of Lansoprazole

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Ingredients	**Unit Formula (mg per tablet)**									
Lansoprazole SD	75	75	75	75	75	75	75	75	75	75
Crospovidone	5	10	-	-	-	-	5	7	-	-
Kyron T-314	-	-	5	10	-	-	-	-	5	7
Banana Powder	-	-	-	-	5	10	5	3	5	3
Avicel 101	50	50	50	50	50	50	50	50	50	50
Lactose	62	57	62	57	62	57	57	57	57	57
Aspartame	4	4	4	4	4	4	4	4	4	4
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200	200

Pre-Compression Evaluation Of Tablet Blend Of Sublingual Tablets Of Solid Dispersion Lansoprazole

Angle of repose (10)

The funnel method was used to determine the angle of repose of the powder blend. Powder mixtures that had been precisely weighed were put in a funnel. The funnel's height was adjusted such that the tip of the funnel barely (2 cm) touched the top of the pile of powder mixes. On the surface of the funnel, the powder mixtures were permitted to freely flow through. The powder cone's diameter was measured, and the following formula was used to determine the angle of repose.

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

whereas,

θ = angle of repose,

h = height of pile,

r = average radius of the powder cone.

Bulk density (11)

It was carried out by pouring powder blend in 100 ml graduated cylinder. The sample occupied volume has been recorded. Bulk density was calculated by following formula.

Bulk density (g/ml) = Weight of the powder / Volume of the powder ---eq

Tapped density (12)

It was carried out by pouring powder blend in 100ml graduated cylinder. The cylinder was tapped mechanically by Tap density apparatus until a constant volume was obtained. Volume occupied by the sample after tapping were recorded and tapped density was calculated by using following formula:

Tapped density (g/ml) = Weight of the powder / Tapped volume of the powder ---------eq

Hausner's ratio (13)

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula;

Hausner′s ratio = Tapped density / Bulk density---------- eq

Compressibility index (14)

It was one of the simple techniques to determine flow property of powder. In which the bulk density and tapped density was compared and % Compressibility index was calculated from following formula.

Carrs index = Tapped density −Bulk density / Tapped density × 100 ----- eq

Manufacturing Of Sublingual Tablet Of Solid Dispersion Of Lansoprazole By Direct Compression Method

The best batch of solid dispersion of Lansoprazole was chosen and formulated into sublingual tablet. Accurate quantity of drug and all ingredients were weighed according to formula powders except talc and magnesium stearate was blended homogeneously in mortar and pestle for 15 minutes. Prepared powder blend was passed through sieve no. #60. Finally, Talc and Magnesium stearate passed from sieve no. #30 added and was further mixed for10 minutes.

Accurately weighed 200 mg homogeneously mixed powder blend was fed manually and compressed with constant compression force and hardness on 16 stations tablet compression machine with 9 mm, breakthrough, and flat faced punches.

Total ten formulations were prepared.

Post-Compression Evaluation Of Sublingual Tablets Of Lansoprazole

Thickness (15)

Vernier callipers were used to measure the thickness of 10 tablets, which were then converted to millimetres (mm).

Hardness (16)

Hardness indicates the ability of a tablet to with stand mechanical shocks while handling. The hardness of the tablets was determined using Digital hardness tester. It is expressed in Kg/cm^2.Digital hardness tester was used to measure hardness of the tablet. In which the tablet was placed in the tester and pressure needed to break the tablet was measured.

Weight Variation (17)

Twenty tablets are ingested and their individual and collective weights are calculated on an electronic weighing scale in accordance with the I.P. protocol for uniformity of weight. One tablet's average weight was determined using the entire weight.

The weight variation test would provide a reliable way to assess the uniformity of the medication content.

Friability (18)

Friability is the measure of tablet strength. It was carried out by using Roch friability apparatus, in which the accurately weighed 20 tablets was allowed to rolling and free fall at 25 rpm, after 100 revolutions weight of tablet was again measured and % friability was calculated by following formula

% Friability = Wint – Wfinal / Wint × 100 ---eq

Where,

Wint = Initial weight of the tablets

Wfinal =Final weight of the tablets

Disintegration Time (19)

Disintegration times for sublingual tablets were determined using USP tablet disintegration apparatus with saline phosphate buffer of pH 6.8 as medium. Maintained the medium temp at 37± 2° C. The time in minute taken for complete disintegration of the tablets with no palatable mass remaining in the apparatus was measured.

Wetting Time (20)

In that the tissue paper has been folded twice and placed in petri dish above that tablet is placed and 6 ml water was added. The time required to get the tablet completely wet was measured.

Water Absorption Ratio
In this method, A piece of tissue paper folded twice was placed in a small petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed too completely wet. The wetted tablet was then weighed. Water absorption ratio was determined using following equation.
Water absorption ratio = Wa−Wb\ Wb ×100
Where,
Wa – weight of tablet after absorption
Wb – weight of tablet before absorption.

Drug Content (21)
This method is performed as per Indian Pharmacopoeia. Two tablets were crushed and added to 30 ml of 0.1M NaOH in 100 ml volumetric flask sonicated to disintegrate, then diluted by acetonitrile and then this solution was filtered and diluted the filterate with a mixture of seven volumes acetonitrile and three volumes of 0.1M NaOH. Absorbance was measured by UV spectroscopy at 284nm

In-vitro Dissolution Study (22)
The in-vitro drug release study of formulated sublingual tablets F1-F10 was carried out using USP dissolution apparatus type II (Electro Lab Dissolution Tester USP II) at 50 rpm. A temperature of 37±0.5 ^{0}C was maintained throughout the study. The dissolution test was carried out using 900ml of saline phosphate pH 6.8. A sample (5 ml) of the aliquot was withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25and 30min. The samples were replaced with fresh dissolution. The samples were filtered through Whattman filter paper and analysed using UV-visible spectrophotometer (UV-1800, Shimadzu, Japan) at 284nm and the percentage drug release was calculated.

Stablity Study (23)
The manufactured sublingual tablet of solid Lansoprazole dispersions was put in plastic tubes with desiccant and kept at ambient temperatures, such as room temperature at 37^{0}C 2^{0}C/40% RH 5% for a period of 90 days. Each tablet is weighed, wrapped in aluminium foil, and packed in a dark-coloured PVC bottle. It is then heated to a humidity level above the specified level for 3 months. At the end of that time, it is evaluated for its physical attributes, including its hardness, disintegration time, and drug content.

RESULTS AND DISCUSSIONS

Solubility Study of Lansoprazole
The solubility study of Lansoprazole was performed and it was found to be **practically insoluble** in Distilled water, Phosphate buffer pH 6.8, Phosphate buffer pH 7.2.

Table 3: solubility of Lansoprazole

Sr. No.	Medium	Solubility (mg/ml)
1.	Distilled Water	0.041±0.10
2.	Phosphate buffer pH 6.8	0.089±0.15
3.	Phosphate buffer pH 7.2	0.055±0.09

Results are mean of three determinations
Calibration Curve of Lansoprazole in Phosphate Buffer 6.8
The UV spectroscopy method was selected as an analytical tool for Lansoprazole to calculate the solubility data and percent (%) release data of prepared formulation. Calibration curve of Lansoprazole in acidic media do not showed linearity for this reason calibration curve of Lansoprazole in phosphate buffer pH 6.8 was developed at 284 nm and it showed good linearity. The calibration curve's linear regression equation

and correlation coefficient was found to be y = 0.0098x + 0.0015 and R^2 = 0.9992. Calibration curve of Lansoprazole depicted in Figure 1

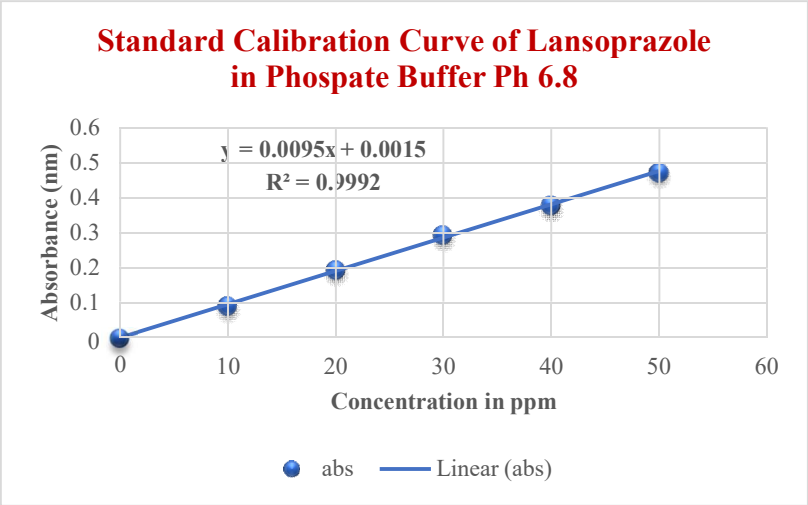


Figure 1: Standard Calibration curve of Lansoprazole in Phosphate Buffer 6.8

Drug – Excipient Compatibility Study

Fourier Transform Infra-Red Spectroscopy (FTIR) Interpretation of Lansoprazole

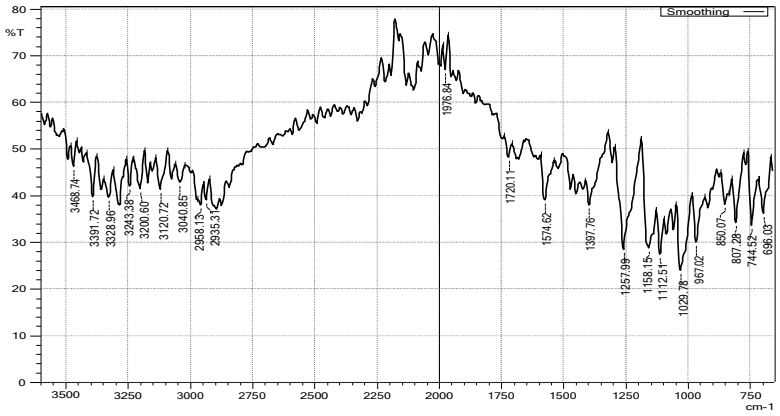


Figure 2: FTIR Studies of Lansoprazole

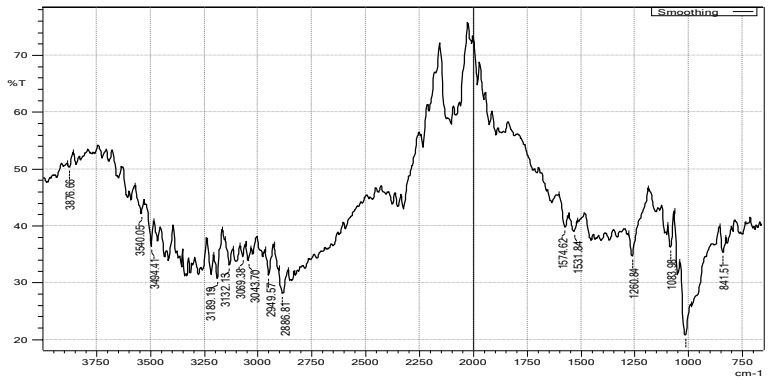
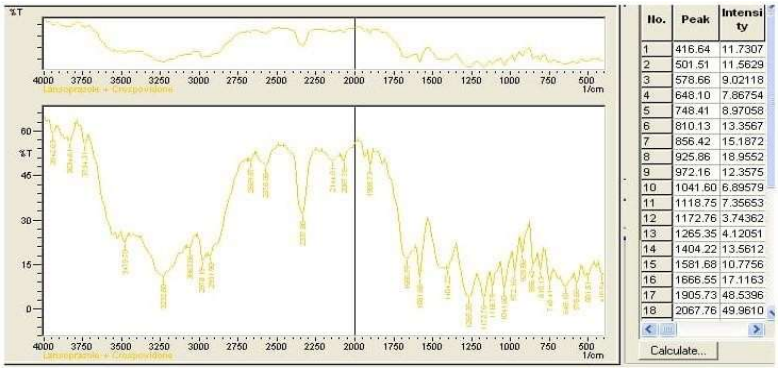


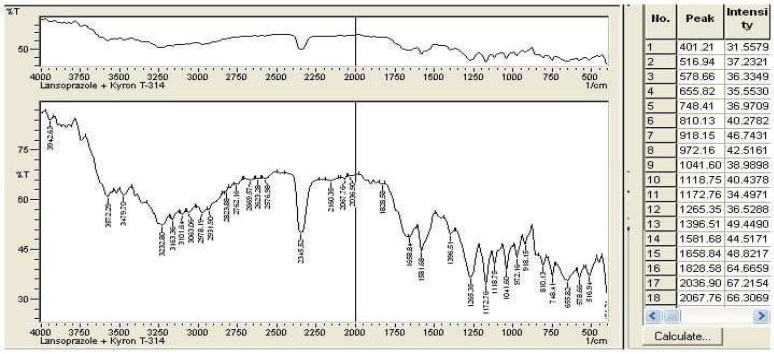
Figure 3: FTIR Peak of Lansoprazole + PEG-6000



No.	Peak	Intensity
1	416.64	11.7307
2	501.51	11.5629
3	578.66	9.02118
4	648.10	7.86754
5	748.41	8.97058
6	810.13	13.3567
7	856.42	15.1872
8	925.86	18.9552
9	972.16	12.3575
10	1041.60	6.89579
11	1118.75	7.35653
12	1172.76	3.74362
13	1265.35	4.12051
14	1404.22	13.5612
15	1581.68	10.7756
16	1666.55	17.1163
17	1905.73	48.5396
18	2067.76	49.9610

Calculate...

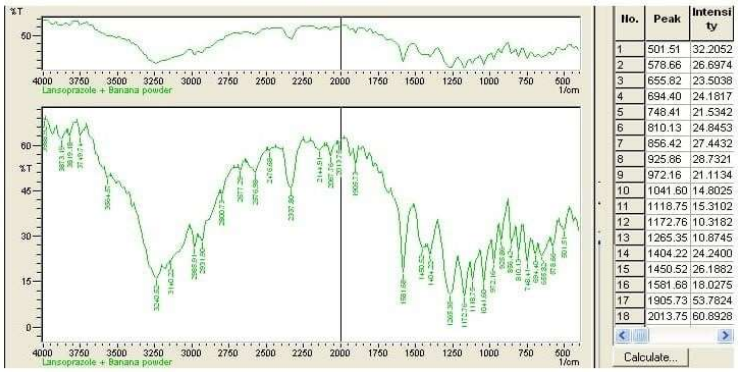
Figure 4: FTIR Studies of Lansoprazole + Cropsovidone



No.	Peak	Intensity
1	401.21	31.5579
2	516.94	37.2321
3	578.66	36.3349
4	655.82	35.5530
5	748.41	36.9709
6	810.13	40.2782
7	918.15	46.7431
8	972.16	42.5161
9	1041.60	38.9898
10	1118.75	40.4378
11	1172.76	34.4971
12	1265.35	36.5288
13	1396.51	49.4490
14	1581.68	44.5171
15	1658.84	48.8217
16	1828.58	64.6659
17	2036.90	67.2154
18	2067.76	66.3069

Calculate...

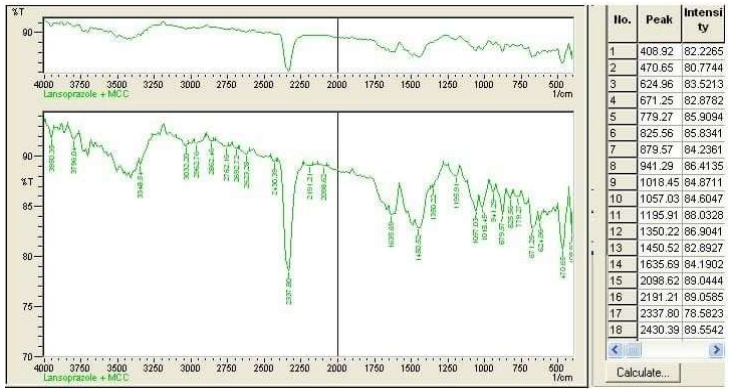
Figure 5: FTIR Studies of Lansoprazole + Kyron T-314



No.	Peak	Intensity
1	501.51	32.2052
2	578.66	26.6974
3	655.82	23.5038
4	694.40	24.1817
5	748.41	21.5342
6	810.13	24.8453
7	856.42	27.4432
8	925.86	28.7321
9	972.16	21.1134
10	1041.60	14.8025
11	1118.75	15.3102
12	1172.76	10.3182
13	1265.35	10.8745
14	1404.22	24.2400
15	1450.52	26.1882
16	1581.68	18.0275
17	1905.73	53.7824
18	2013.75	60.8928

Calculate...

Figure 6: FTIR Studies of Lansoprazole + Banana Powder



No.	Peak	Intensity
1	408.92	82.2265
2	470.65	80.7744
3	624.96	83.5213
4	671.25	82.8782
5	779.27	85.9094
6	825.56	85.8341
7	879.57	84.2361
8	941.29	86.4135
9	1018.45	84.8711
10	1057.03	84.6047
11	1195.91	88.0328
12	1350.22	86.9041
13	1450.52	82.8927
14	1635.69	84.1902
15	2098.62	89.0444
16	2191.21	89.0585
17	2337.80	78.5823
18	2430.39	89.5542

Calculate...

Figure 7: FTIR Studies of Lansoprazole + MCC pH 101

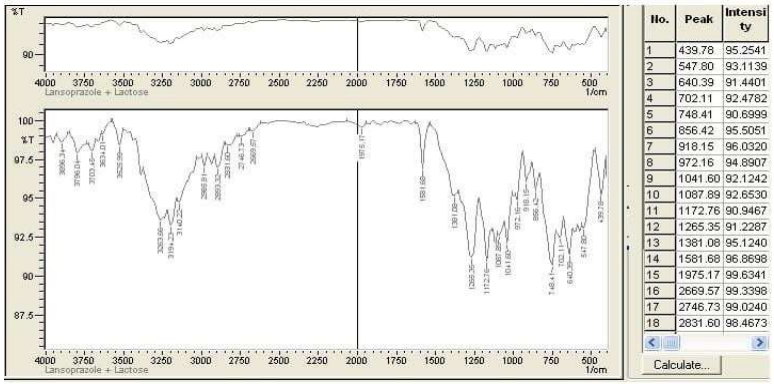


Figure 8: FTIR Studies of Lansoprazole + Lactose

Solubility Study of solid dispersion of Lansoprazole

Table 4: Solubility Study of solid dispersion of Lansoprazole

Sr. No.	Method	Drug : Carrier (Ratio)	Solubility (mg/ml)
1.	Kneading Method	Pure drug	0.089
2.	Kneading Method	Lansoprazole + PEG 6000 (S1)	0.163
3.	Kneading Method	Lansoprazole + PEG 6000 (S2)	0.310
4.	Kneading Method	Lansoprazole + PEG 6000 (S3)	0.472
5.	Kneading Method	Lansoprazole + PEG 6000 (S4)	0.546

Drug Content

The drug content was found to be within the range of to indicating uniform distribution of drug in the formulated tablets as per pharmacopeia specification.

Table 5: Drug Content

Sr. No.	Formulation	% Drug content
1	S1	98.63±0.99
2	S2	99.05±0.50
3	S3	98.42±0.35
4	S4	99.47±0.80

Results are mean of three determinations

Percentage Practical Yield Study of Solid Dispersion

Percentage practical yield was calculated to know about % yield or efficiency of any method which will help in selection of appropriate method. The practical yield for each batch is reported below.

Table 6: Percentage Yield Study of Solid Dispersion

Formulation	Theoretical Yield	Practical Yield	% Practical Yield
S1	0.240	0.215	89.58±0.83
S2	0.300	0.275	91.66±0.60
S3	0.400	0.375	94.75±0.75
S4	0.500	0.480	96±0.90

Results are mean of three determinations

Different trial batches of solid dispersion show % practical yield from range 89.58% to 96%. Batch S4 Showed 96% practical yield.

Dissolution of Solid Dispersions

Dissolution study of solid dispersion prepared by Kneading method S1, S2, S3, S4 was carried out in phosphate buffer pH 6.8 and analysed spectrophotometrically at 284nm. Each preparation was tested in triplicate and then mean values were calculated. The table 10.18 indicates the % drug release of each formulation at the end of 30 min. The graph was plotted to show % drug release which was represented in Table below.

Table 7: Dissolution of Solid Dispersions

Time (min)	Cumulative % of Drug Release			
	S1	**S2**	**S3**	**S4**
0	0	0	0	0
5	16.98±0.03	21.84±0.07	24.12±0.10	29.59±0.16
10	26.15±0.10	30.22±0.21	36.38±0.25	40.46±0.29
15	38.96±0.40	44.96±0.30	50.60±0.34	58.16±0.39
20	56.85±0.65	59.60±0.70	68.96±0.60	72.69±0.69
25	75.56±0.78	77.36±0.88	86.12±0.79	89.26±0.81
30	85.41±0.93	88.96±0.96	92.22±0.91	94.56±0.96

Results are mean of three determinations

Out of four formulations S4 shown maximum drug release i.e., 95.56%. Solid dispersion (S4) of Lansoprazole with PEG 6000 (1:4) prepared by Kneading method significantly improved its solubility and dissolution rate. Increased wetting and solubilizing effect of PEG 6000 as well as the molecular dispersion of drug in solid dispersion and alteration of surface properties of drug particle may be responsible for the enhanced dissolution rate of Lansoprazole from solid dispersion compared to pure Lansoprazole.

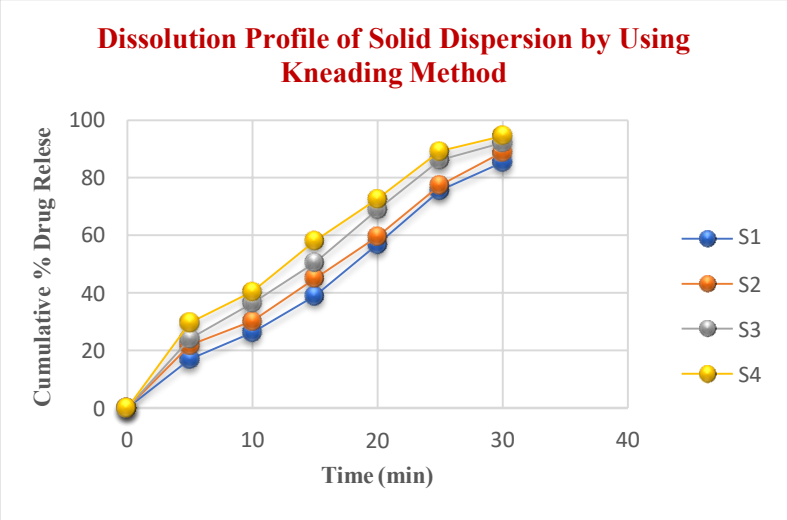


Figure 9: Dissolution of Solid Dispersion by Using Kneading Method

10.2.5 Drug Excipient Compatibility Studies of Solid Dispersion of Lansoprazole
Fourier Transform Infra-Red Spectroscopy (FTIR) Interpretation of Solid Dispersion Lansoprazole + PEG6000 (1:4) (S4) By Kneading Method

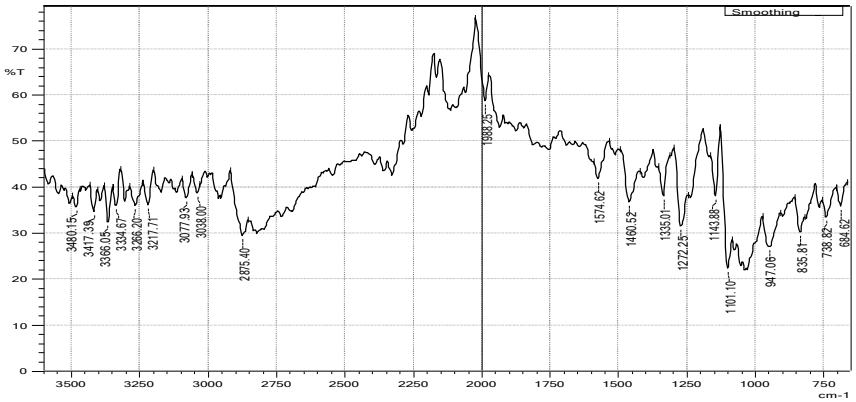


Figure 10: FTIR Studies of Solid Dispersion Lansoprazole + PEG6000 (1:4) (S4) By Kneading Method

X-ray Diffraction (XRD) of solid dispersion

The Diffraction Pattern of Lansoprazole revealed several sharp high-intensity. This angles 20 suggesting that the drug existed as crystalline material. There were few characteristic peaks of Lansoprazole with a considerable reduction in the peak intensity. This diminished peak suggests conversion of the drug into an amorphous form. This marked reduction in peak intensity provides may increase dissolution rate of solid dispersion preparation. It is indicated in figure.

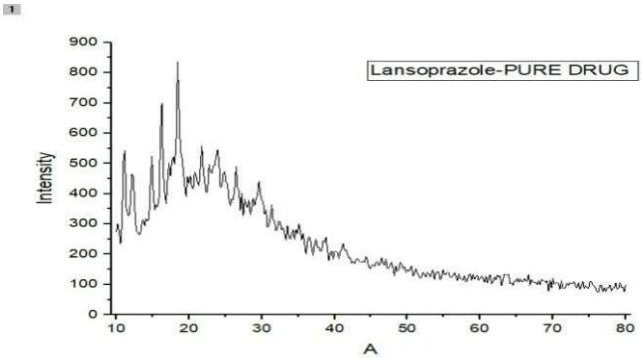


Figure 11: X-ray Diffraction (XRD) of Lansoprazole

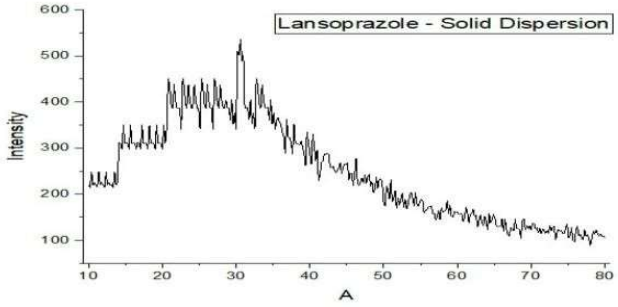


Figure 12: X-ray diffraction (XRD) of solid dispersion

Evaluation Of Tablet Blend Of Sublingual Tablets Of Lansoprazole

The characterization of mixed blend was done for determination of mass-volume relationship parameter. The evaluated parameter angle of repose, bulk density, tapped density, hausner's ratio and compressibility index was reported in table below

Table 8: Evaluation of tablet blend for sublingual tablets

Formulations	Angle of Repose (θ˚)	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Hauser's Ratio (HR)	Compressibility Index (%)
F1	27.47 ± 0.34	0.42±0.07	0.46±0.22	1.10±0.02	8.6±0.26
F2	30.75 ± 0.20	0.42±0.34	0.46±0.39	1.09±0.11	8.69±0.32
F3	27.02 ± 0.74	0.43±0.04	0.42±0.05	1.05±0.18	4.76±0.30
F4	27.74 ± 0.50	0.33±0.02	0.37±0.42	1.12±0.08	10.81±0.34
F5	29.63 ± 0.28	0.40±0.34	0.43±0.37	1.07±0.15	6.9±0.22
F6	26.10 ± 0.64	0.45±0.05	0.49±0.27	1.08±0.19	8.1±0.39
F7	29.37 ± 0.22	0.41±0.40	0.45±0.03	1.09±0.03	8.8±0.27
F8	26.56 ± 0.84	0.42±0.46	0.46±0.34	1.01±0.05	8.61±0.42
F9	27.47 ± 0.90	0.33±0.25	0.35±0.42	1.06±0.04	5.71±0.25
F10	28.81 ± 0.25	0.37±0.21	0.4±0.02	1.08±0.12	7.5±0.55

Results are mean of three determinations

10.4.1 Angle of Repose

Angle of repose of various powder mixed blends(F1-F10), prepared with different superdisintegrants, was measured by funnel method. Angle of repose was found in the range 26.10±0.64- 30.75±0.20. The excellent flow ability of powder blend was also evidence with angle of repose.

10.4.2 Bulk density

The bulk density of various powder mixed blends(F1-F10) prepared with different superdisintegrants was measured by graduated cylinder. The bulk density was found in the range 0.33 ± 0.02– 0.45 ± 0.05g/ml.

10.4.3 Tapped Density

The Tapped density of various powder mixed blends(F1-F10) prepared with different super-disintegrants was measured by using measuring cylinder. The tapped density was found in the range **0**.35± 0.42 - 0.49 ± 0.27g/ml. These values indicate good packing characteristics and the powder was not bulky.

10.4.4 Hauser's Ratio

The Hausner's ratio of various powder mixed blends(F1-F10), prepared with different super-disintegrants, it is calculated by using bulk density and tapped density data. It was found in the range of 1.01±0.05 – 1.12±0.08 reveals good flow properties (<1.25)

10.4.5 Compressibility Index

The Compressibility index of various powder mixed blends(F1-F9), prepared with different super-disintegrants, using bulk density and tapped density data, compressibility index was calculated. It was found in the range 4.76 ± 0.30 – 10.81± 0.34%. This indicates good flow properties.

Evaluation Of Sublingual Tablets

The Sublingual Tablet of solid dispersion of Lansoprazole were prepared & subjected to post-compression parameters like weight variation, thickness, hardness, friability, drug content, in vitro disintegration time, wetting time, water absorption ratio, in vitro dissolution studies were carried out. All the formulations were passed the parameter which was reported in Table below

Table 9: Post-Compression Evaluation of Sublingual Tablet of Lansoprazole

Formulations	Thickness (mm)	Hardness (kg/cm^2)	Weight Variation (mg)	Friability (%)	Disintegration time (Sec)	Wetting Time (Sec)	% Water Absorption Ratio	Drug Content
F1	3.23±0.15	3.1±0.3	201±1.22	0.15±0.2	52±0.12	48±1.02	52.64±0.22	98.36±0.22
F2	3.27±0.24	3.4±0.8	199±1.14	0.25±0.4	30±0.09	32±1.04	62.31±0.48	99.36±0.08
F3	3.13±0.23	3.5±0.1	200±1.00	0.50±0.8	48±1.22	42±1.08	55.88±0.67	98.21±0.45
F4	3.22±0.18	3.2±0.8	198±1.50	0.30±0.4	39±0.14	30±1.05	65.10±0.82	98.63±0.56
F5	3.26±0.46	3.1±0.4	199±1.30	0.25±0.1	58±1.05	45±1.04	54.35±0.89	99.89±0.30
F6	3.27±0.35	3.5±0.2	200±1.02	0.20±0.3	50±0.14	38±1.07	58.35±0.74	99.26±0.89
F7	3.20±0.28	3.1±0.9	201±2.10	0.50±0.5	45±0.16	35±1.02	60.96±0.65	98.78±0.99
F8	3.27±0.38	3.2±0.5	200±1.01	0.20±0.8	27±0.16	21±1.01	70.50±0.56	99.47±0.11
F9	3.22±0.18	3.3±0.1	199±1.20	0.30±0.2	41±0.19	39±1.01	56.22±0.35	99.47±0.79
F10	3.25±0.32	3.4±0.5	199±1.02	0.45±0.6	32±1.04	25±1.02	67.15±0.28	97.47±0.57

Results are mean of three determinations

10.5.1 Thickness

The thickness of the tablets was measured by using Vernier caliper by picking the tablets randomly. The values are almost uniform in all formulations. Thickness was found in the range from 3.13 ± 0.23 mm – 3.27 ± 0.35 mm. Uniform in the values indicates that formulations were compressed without sticking to the dies and punches.

10.5.2 Hardness

Tablets were evaluated by using Monsanto Hardness tester. Hardness of the tablets was in the range 3.1 ± 0.3 - 3.5 ± 0.2 kg/cm^2. Uniform hardness was obtained due to equal compression force. The obtained hardness range showed good mechanical strength with an ability to withstand physical and mechanical stress conditions.

10.5.3 Weight variation

Tablets were prepared using direct compression technique. Since the material was free flowing, tablets were obtained of uniform weight due to uniform die fill. Tablets were obtained in the range with acceptable weight variations as per Pharmacopoeia specifications, limit of ±5%. It was found to be from 198±1.00 - 201±1.22mg.

10.5.4 Friability

Tablets were evaluated by using Roche Friabilator and friability of tablets was observed in acceptable range. 0.15 ± 0.02 - 0.9 ± 0.117 (less than 1%) This indicated a good mechanical resistance of the prepared mouth dissolving tablets.

10.5.5 Drug content of Lansoprazole

Tablets were evaluated by using assay method. The drug content was obtained in the acceptable limit. The drug content was found in the range 90.18 ± 0.19 - 99.75 ± 0.09 %w/w. (i.e. 99-101% w/w). The found range was within the specified limit as per Pharmacopoeia.

10.5.6 Disintegration time

Tablets were subjected for the *in-vitro* disintegrate time in the USP Disintegrate test apparatus. The *in-vitro* disintegrate time for all ten formulations varied from 27±1.16 to 52±1.12 seconds. The rapid disintegrate was seen in the formulations containing Crospovidone and Banana Powder. This is due to rapid intake of the water from the medium, swelling and burst effect. It also noticed that the concentration of Crospovidone and Banana Powder increased, the time taken for the disintegrate was reduced. the formulations with highest concentration of Crospovidone and Banana Powder shown significant rapid disintegrate.
Disintegrate time was to be found very less for F8 formulation which contains highest concentration and efficiency of Crospovidone and Banana Powder.

10.5.7 Wetting time test

The values of wetting time for all formulations lie between 21±1.01- 48±1.02 and it was observed that as the concentration of disintegrant increases the time taken for wetting decreases.

10.5.8 Water absorption ratio

Water absorption ratio which is important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water. It was found in the range of **52.64±0.22 to 70.10±0.56%.** The Water absorption ratio (R) increases with the increased concentration of combination of natural and synthetic superdisintegrants.

10.5.9 In vitro % Drug Release of Drug from Tablet

All the ten tablet batches of sublingual tablet of solid dispersion of Lansoprazole were subjected for the in vitro dissolution studies using tablet dissolution apparatus (USP). phosphate buffer 6.8 was used as dissolution medium.

Table 10: In vitro Cumulative % Drug Release of Drug from Tablet

Time (mi	Cumulative % Drug Release									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
0	00	00	00	00	00	00	00	00	00	00
5	27.96±0.	41.67±1.	24.25±0.	32.91±1.	21.58±0.	29.62±1.	30.96±1.	46.71±1.	28.25±1.	37.26±1.
10	40.71±1.	50.54±1.	36.61±1.	45.09±1.	33.93±1.	42.09±1.	48.51±1.	58.61±1.	39.76±1.	50.03±1.
15	52.35±1.	64.84±1.	48.00±1.	58.72±1.	42.70±1.	56.13±1.	52.85±1.	71.91±1.	47.26±1.	60.42±1.
20	74.65±1.	79.03±1.	60.91±1.	71.94±1.	56.79±1.	67.03±1.	63.12±1.	86.21±1.	60.79±1.	72.97±1.
25	82.21±1.	92.52±1.	75.26±1.	88.84±1.	72.18±1.	79.79±1.	87.52±1.	93.36±1.	85.28±1.	87.65±1.
30	90.75±1.	98.18±1.	88.02±1.	95.99±1.	88.10±1.	92.41±1.	92.12±1.	99.14±1.	90.17±1.	96.43±1.

Results are mean of three determinations

The rapid dissolution was observed in formulation F8 releases **99.14%** at the end of 30 minutes. Formulations F1-F9 released **88.10±1.92** to **98.18±1.98** at the end of 30 min. Rapid dissolution might be due to fast breakdown of particles and rapid absorption of drugs. The drug release was completely achieved in shorter duration of time. In all the formulations the drug release within 30 minutes. High dissolution may occur due to faster breakdown.

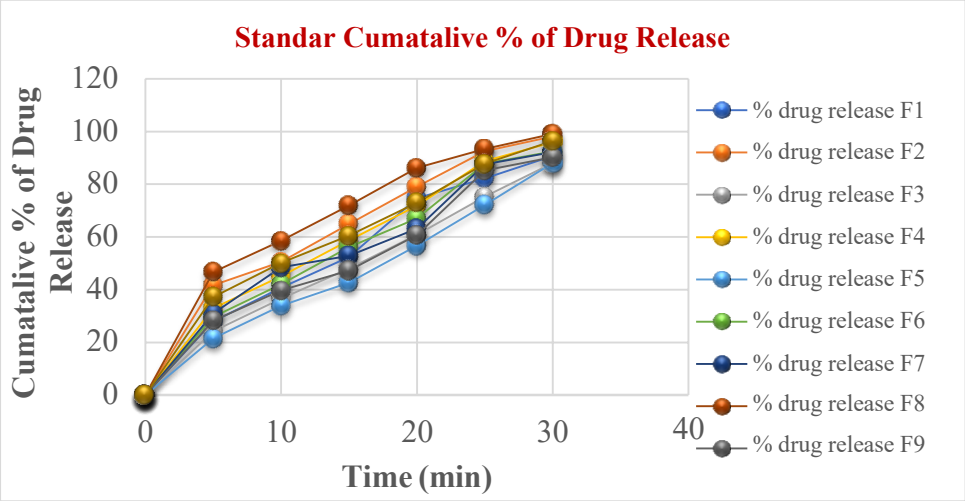


Figure 13: Cumulative % drug release of F1-F10 formulations

In comparative study F8 formulation gives higher percent drug release compare to other remaining nine formulations at the end of 30 minutes and graphical representation is shown in Figure 10.19. Therefore, it was concluded that the best optimized batch was found to be F8 because of lesser disintegration time and highest percentage drug release at the end of 30 min among all the formulations. Because it containing Crospovidone and Banana Powder super-disintegrant with fast wetting time and highest swelling property.

10.4. Stability Study

The formulation F8 was selected for stability studies on the basis of their high cumulative % drug release and also results of in vitro disintegration time studied. The stability studies were carried out at 37˚C±2˚C/40˚C±5% relative humidity for the selected formulation up to three months. For every 1-month time interval the tablets were analysed for drug appearance, hardness, disintegration time, content uniformity, % drug release up to three months. The results obtained in Table below

Table 11: Stability Study

Formulation	Parameters Evaluated	Initial	After 2 Months	After 3 Months
F8	Appearance	Brownish-white crystalline powder	Brownish-white crystalline powder	Brownish-white crystalline powder
	Hardness	3.2±0.5	3.1±0.2	3.0±0.4
	Disintegration	27±0.16	29±0.11	32±0.09
	Drug content (%)	99.47±0.11	98.92±0.16	98.12±0.09
	In vitro drug release	99.14±1.98	98.10±1.26	97.45±1.47

Results are mean of three determinations

CONCLUSION

Overall, the results showed that the solubility and dissolution rate of Lansoprazole were increased by a suitable formulation of solid dispersion of S4 with PEG 6000 generated by kneading. When compared to

pure Lansoprazole, the rate at which Lansoprazole dissolves from solid dispersion may be increased due to changes in the drug's surface properties.

Angle of repose, bulk and tapped densities, compressibility index, and Hausner's ratio of the powder blend were all assessed before compression. The weight variation, hardness, friability, drug content, disintegration time, wetting time, in vitro drug release, and stability investigations of the compressed tablets was also assessed.

Among all of the created solid dispersions, it was discovered that S4 was optimal. The study demonstrates that employing a solid dispersion approach and kneading can significantly increase the rate at which Lansoprazole dissolves. Thus, formulations for sublingual Lansoprazole tablets using the crospovidone, Kyron T-314, and banana powder systems could be taken into consideration. When compared to other formulations, Lansoprazole (F8) sublingual tablets showed a greater medication release. The solid dispersion technique can be used to increase the solubility, dissolution rate, and oral bioavailability of medications that are not water soluble, according to the results above.

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CONFLICT OF INTEREST

All authors declared no conflicts of interest.

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