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Research article

Formulation and in-vitro Evaluation of orodispersible Tablets of Lansoprazole

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Abstract

Lansoprazole a proton pump inhibitor used in the short term treatment of gastric and duodenal ulcer, reflux esophagitis, structuring and erosive esophagitis. The ulcer is an acute condition and requires an immediate treatment. An Orodispersible tablet disperses readily in saliva and the drug is available in solution or suspension form for the immediate absorption and resulting in rapid onset of action. In the present research work Lansoprazole orodispersible tablets were prepared by direct compression method using varying concentrations of Croscarmellose sodium, Sodium Starch Glycolate, Crospovidone as superdisintegrants. The formulations prepared were evaluated for various parameters like, hardness, weight variation, Friability, *in vitro* dispersion time, water absorption ratio, drug content uniformity and in vitro drug release. The tablets prepared were dispersed in the range of 8.3±0.6-23.7±1.5seconds, the water absorption ratio was 24.9±4.2-186.8±3.2% and the drug was uniformly dispersed in all the formulations in the range of 95.6±0.4-102.5±0.8%. Among the formulation prepared the tablet containing 7.5% of Crospovidone 99.736±0.763% of the drug within 18 min. The overall result indicated that the formulation F6 containing Crospovidone 7.5% is better and fulfilling of the needs of the orodispersible tablets.

Key words: Orodispersible tablets, Lansoprazole, Croscarmellose sodium, Crospovidone, Sodium Starch Glycolate, superdisintegrant**.**

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1. Introduction

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. In addition, the oral medication is generally considered as the first avenue investigated in the discovery and development of new drug entities and pharmaceutical formulations, mainly because of patient acceptance, convenience in administration, and cost-effective manufacturing process [1]. For the last few decades, researchers have been developing intraoral delivery systems (IDS) that can produce desirable drug exposure for optimum therapeutic effect. As a result, as evident from the

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abundance of scientific and patent literature over the last twenty years, nontraditional oral dosage forms (e.g., buccal, sublingual, etc.) have been or are being developed with emphasis on pre gastric absorption by the various tissues of the oral cavity with the intention to avoid first-pass and gut-wall metabolism, to enhance bioavailability, or improve convenience of dosing. The target sites for local drug delivery in the oral cavity include the following: buccal, sublingual, periodontal, periodontal pocket, peribuccal, perilingual, tongue (i.e., lingual), and gum (i.e., gingival) [2].

Orodispersible tablets

Orally Disintegrating tablets (ODTs) rapidly disintegrate in the mouth without chewing upon oral administration and without the need for water, unlike other drug delivery systems and conventional oral solid immediate-release dosage form. ODT dosage forms, also commonly known as fast melt, quick melts, fast disintegrating, and orodispersible systems have the unique property of disintegrating the tablet in the mouth in seconds. For acute conditions, this dosage form is easier for patients to take anytime, anywhere those symptoms occur. For chronic conditions, it is assumed to improve compliance [3].

Market needs

The application of a drug delivery technology (DDT) to any molecule is based on market needs, product differentiation, and patient compliance. Owing to the increased costs of getting a product to market and focus on clinical advancement, new chemical entities (NCEs) typically do not go through an extensive evaluation of DDT. The goal is to get the product through the clinical studies with a stable formulation that can achieve the safety and efficacy required for Food and Drug Administration (FDA) approval.

A detailed survey was conducted to determine the proportion of patients having difficulty in swallowing tablets and to identify the reasons for the difficulty. More than 26 percent of patients mentioned problems in swallowing tablets. A prominent complaint was the size of the tablet, followed by the surface, form, and taste of the tablets. Twice as many women as men experienced swallowing problems. Elderly patients (>70 years) had less difficulty than younger patients in swallowing tablets. Pediatric and geriatric patients in particular experienced the greatest difficulty in swallowing tablets as well as people who are ill and supine in bed and those patients who are busy traveling without having access to water [4].

To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating tablets (ODTs) or Fast disintegrating tablets (FDTs) or mouth melting tablets(MMTs) or mouth dissolving tablets(MDTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water [5, 6].

Recently the European Pharmacopoeia adopted the term orodispersible tablet as a tablet to be placed in the oral cavity where it disperses rapidly before swallowing and which disintegrates in less than 3 min. There was nospecification concerning neither the hardness nor the friability of this kind of tablets. That is why we findcertain ODT in the market that disintegrate in less than 1 min or maybe 30 s. Commercially available ODT are prepared by various techniques, mainly lyophilisation , moulding and direct compression. The lyophilisation and molding techniques produce ODT which disintegrate within about 30 s, but that

have low physical resistance and high friability. On the other hand, tablets obtained by direct compression are less friable but disintegrate in a longer time [7].

Salient features of orally disintegrating tablets [8]

1. Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and, psychiatric patients.
2. Convenience of administration and accurate dosing as compared to liquids.
3. No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
4. Good mouth feels properly of ODTs helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
5. Rapid dissolution of drug and absorption which may produce rapid, onset of action.
6. Some drugs are absorbed from the month pharynx and esophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
7. Ability to provide advantages of liquid medication in the form of solid preparation.

Limitations of orally disintegrating tablets [9]

Drugs with relatively larger doses are difficult to formulate into MDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug. Patients who concurrently take anticholinergic medications may not be the best candidates for MDT. Similarly patients with Jorgen's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.

2. Experimental Materials and Methods

Materials

The materials used for preparing the orodispersible tablets were Croscarmellose Sodium (CCS), Sodium starch glycollate (SSG) and Crospovidone (CP) (Gift sample from Ajanta Pharma, Aurangabad) The model drug was Lansoprazole (Lee Pharma Limited, Hyderabad.) All other ingredients used were of analytical grade.

Methods

Preparation of mixed blend of drug and excipients: Blend of drug, CCS, CP and SSG for direct compression

All the ingredients were passed through mesh no. 60. Required quantity of ingredients were weighed as given in Table 1 and coground in mortar and pestle. The powder blend was evaluated for flow property and compressibility behavior.

Compression of Tablets

Lansoprazole Orodispersible tablets were prepared by direct compression method using various formulation additives in varying concentrations and the detailed composition was shown in the Table 1.

All the ingredients were powdered separately in a clean and dry porcelain mortar and then they were passed through # 60 mesh sieve. The drug and the additives were mixed thoroughly in an inflated polyethylene pouch in a geometric ratio of their weight. Then the powder mixture was compressed in to tablets of 100 mg weight using 6 mm flat round punches.

Evaluation of Tablets

Hardness

The hardness of tablet was measured using Monsanto hardness tester; it has graduated scale which gives the reading in kg/sq.cm [10].

Friability test [4, 11]

The friability test was performed to evaluate the ability of the tablet to withstand wear and tear in packaging, handling and transporting. The apparatus used to perform this test is known as "Friabilator". Twenty tablets were weighed and placed in the plastic chamber. The chamber is rotated at a speed of 25 rpm for 4minutes (for 100 revolutions). During each revolution the tablets falls from a distance of 6 inches, the loss in weight indicates the friability. The tablets were considered to be of good quality if the loss in weight is less than 0.8% (=1%). The results were shown in Table 4.

Weight variation (Uniformity of weight) Test [12]

Twenty tablets were selected randomly from each batch, weighed them and the average weight was determined. The tablets are also weighed individually and the percentage deviation was calculated for each tablet. Not more than two tablets may deviate from the percentage deviation given in the table and none should be deviate by more than twice that percentage.

Drug content uniformity [13]

Five tablets were weighed and powdered; a quantity of powder equivalent to 10 mg of Drug was dissolved in 100ml of methanol (1000µg/ml). From this solution 0.9ml solutions were pippetted and volume was made to 10 ml using methanol to concentration 9 µg/ml. the drug content was determined by measuring the absorbance at 285.5nm.the drug content was calculated using the standard calibration curve. The mean percentage drug content was calculated as an average of three determinations. The results were shown in Table 4.

Wetting time and water absorption ratio [11, 14]

The wetting time of the tablets were measured by using the simple procedure. Five circular tissue paper of 10cm diameter were placed in a petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet was noted as the wetting time.

For measuring water absorption ratio the weight of the tablet before keeping in the petridish was noted (wb). The wetted tablet from the petridish was taken and reweighed (wa).

In Vitro Disintegration Time [15, 16]

The disintegration time of the tablets was determined as per Indian Pharmacopoeial monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37 ± 0.5ºC using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted.

In VitroDissolution Studies [17, 18]

In vitro dissolution of orodispersible tablets of Lansoprazole was studied using USP XXIII type-II dissolution apparatus (Electro lab TDT-06N) by employing a paddle stirrer at 50 rpm. 900 ml of pH 6.8 phosphate buffer using 5ml SLS was used as dissolution medium. The temperature of dissolution medium was maintained at 37 ± 0.5o C throughout the experiment. One tablet was used in each test. Samples of dissolution medium (5ml) were withdrawn by means of syringe fitted with

pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 285.5 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent drug released was calculated and plotted against time.

Table 1. Composition of Orodispersible Tablets of Lansoprazole

Sr. No	Ingredient (mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Lansoprazole	30	30	30	30	30	30	30	30	30
2	Croscarmellose Sodium	2.5	5	7.5	-	-	-	-	-	-
3	Crospovidone	-	-	-	2.5	5	7.5	-	-	-
4	Sodium starch glycolate	-	-	-	-	-	-	2.5	5	7.5
5	Microcrystalline cellulose	35.5	33	30.5	35.5	33	30.5	35.5	33	30.5
6	Mannitol	30	30	30	30	30	30	30	30	30
7	Mg.Stearate	1	1	1	1	1	1	1	1	1
8	Talcum	1	1	1	1	1	1	1	1	1
9	Total	100	100	100	100	100	100	100	100	100

3. Results and Discussion

Formulations were prepared by direct compression are shown in Table 1. The data obtained for IR spectra is shown in table 2. The data obtained for precompressional parameters such as bulk density, tapped density, Hausner's ratio, Carr's index and angle of repose are shown in Table 3 and found within acceptable Pharmacopoeial limits. While post-compressional parameters like hardness, friability, weight variation, drug content, wetting time, water absorption ratio, in vitro dispersion time, in vitro disintegration time are mentioned in Table 3. The tablets measured hardness was found to be in the range of 2.1± 0.12 to2.5 ± 0.11 kg/cm2. The percentage friability was less than 1% for all formulations ensuring mechanical stability of the formulated tablets.

Table 2. Data obtained for IR spectra of Lansoprazole along with Excipients

Ingredients	PEAKS (cm^{-1})			
Functional groups	**C-H Structure**	**N-H Structure**	**C-F Structure**	**C=o Structure**
Pure drug	1265.13	1575.61	1170.32	1680.12
Drug and CP	1267.27	1575.82	1172.16	1683.91
Drug and SSG	1267.78	1576.03	1172.82	1683.91
Drug and CCS	1267.11	1575.91	1172.61	1683.68

All formulations then evaluated for variation in weight and results indicated that for all formulations exhibit very low weight variation which lies within the Pharmacopoeial limits i.e. ± 7.5%. The percentage drug content in all formulations was found in the range of 96.03 ± 0.69 to 102.53±0.07 indicating the

compliance with the Pharmacopoeial limits. According to the Pharmacopoeial standards the dispersible tablet must disintegrate within 3 min. but all formulated batches have shown very low disintegration time i.e. 8.3 to 23.3 seconds indicating suitability of formulation for fast dissolving tablet. Also evaluated for wetting time, in vitro dispersion time and water absorption ratio and found to be faster for the formulation F6.

Table 3. Physical Characteristics of Powder Blends.

Tablet code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Angle of repose (degree) ± SD,	23.04 ±0.3	23.77 ±0.4	23.53 ±0.5	23.37 ±0.4	22.16 ±0.2	23.44 ±0.4	23.31 ±0.3	22.83 ±0.4	22.44 ±0.2
Bulk density (gm./cc) ± SD,	0.54 ±0.01	0.55 ±0.01	0.55 ±0.02	0.53 ±0.03	0.48 ±0.02	0.50 ±0.01	0.47 ±0.02	0.43 ±0.03	0.58 ±0.01
Tapped density (gm./cc) ± SD,	0.57 ±0.01	0.59 ±0.02	0.61 ±0.03	0.58 ±0.04	0.55 ±0.01	0.58 ±0.01	0.55± 0.03	0.50± 0.02	0.66± 0.01
Carr's index (%)± SD,	5.26 ±2.0	6.78 ±2.0	9.84 ±2.0	8.62 ±2.2	12.14 ±4.9	14.96 ±2.2	14.23 ±2.0	13.2± 2.0	11.81 ±2.2
Hausner's ratio ± SD,	1.06 ±0.02	1.07 ±0.03	1.11 ±0.03	1.09 ±0.03	0.65 ±0.23	1.17± 0.03	1.16± 0.23	1.15± 0.02	1.13± 0.02

Table 4. Evaluation of Orodispersible Tablets

Sr. No	Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Weight Variation (mg)	99.5	997	99.6	99.8	99.3	99.1	99.3	99.4	99.6
2	Diameter (mm)	6	6	6	6	6	6	6	6	6
3	Hardness (Kg/cm2)	2.4 ±0.1	2.3 ±01	2.1 ±0.1	2.5 ±0.1	2.3 ±0.1	2.4 ±0.1	2.3 ±0.1	2.3 ±0.1	2.2 ±0.1
4	Friability (%)	0.69	0.2	0.81	0.89	0.90	0.95	0.87	0.75	0.81
5	% Drug Content	101.2 ±18	96.3 ±0.5	99.2 ±0.9	98.7 ±1.5	100 ±1	100 ±1	99.9 ±0.5	102.5 ±0.8	100.5 ±0.9
6	Water Absorption Ratio (%)	45.1 ±3.2	76.6 ±2.2	109 ±4.3	100.5 ±2.3	132.9 ±1.5	186.8 ±3.2	39.5 ±2.1	59.5 ±1.6	107.6 ±3.2
7	Wetting Time(sec)	27.7 ±0.5	22.7 ±0.5	19.7± 0.58	17.7± 0.58	14.7± 0.58	12.7± 0.58	26.7± 0.57	24.6± 0.58	20.7± 0.57
8	*In-Vitro* Disintegration Time (sec)	23.3 ±0.5	18.3 ±0.5	14.7 ±0.6	13.3 ±0.6	10.3 ±0.6	8.3 ±0.6	22.3 ±0.6	18.7 ±0.6	15.7 ±0.6

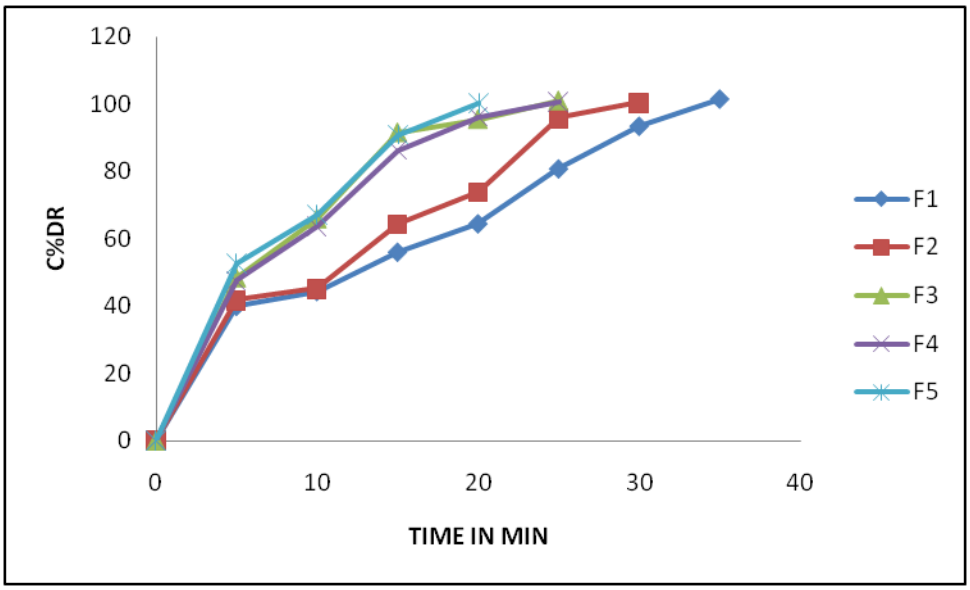


Figure 1. In-vitro zero order plots of Lansoprazole orodispersible tablets of formulation F1, F2, F3, F4, F5.

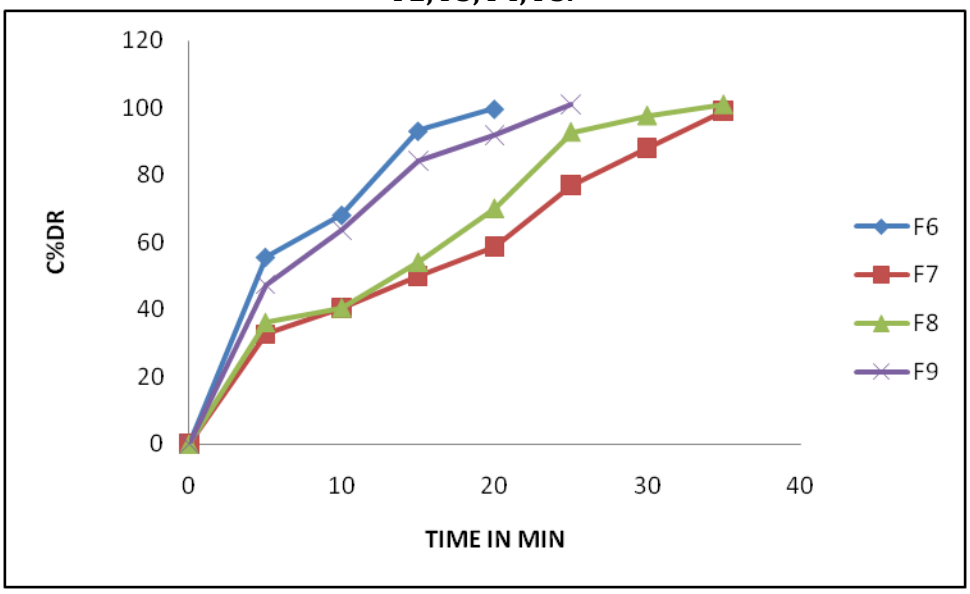


Figure 2. In-vitro zero order plots of Lansoprazole orodispersible tablets of the formulation F6, F7, F8, F9.

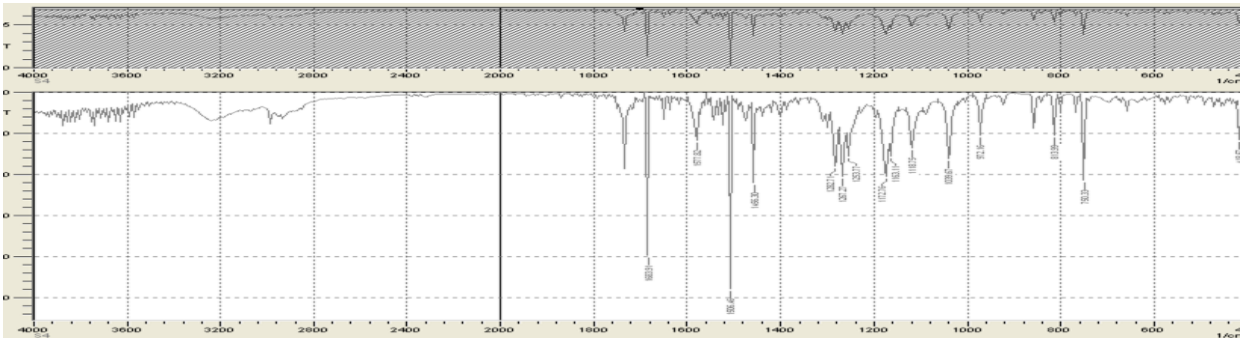


Figure 3. IR spectrum of Lansoprazole pure drug

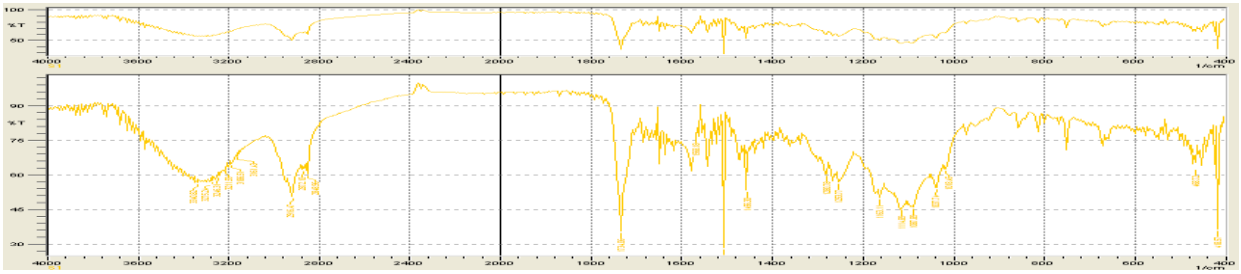


Figure 4. IR spectrum of Formulation F2 (containing 5% Croscarmellose sodium)

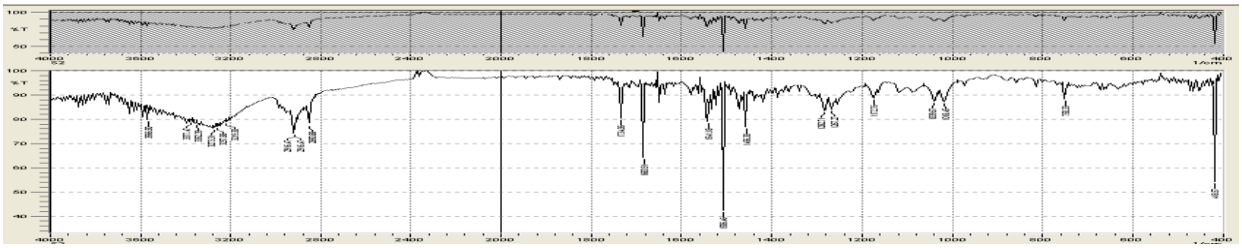


Figure 5. IR spectrum of formulation F6 (contaning Crospovidone 5%)

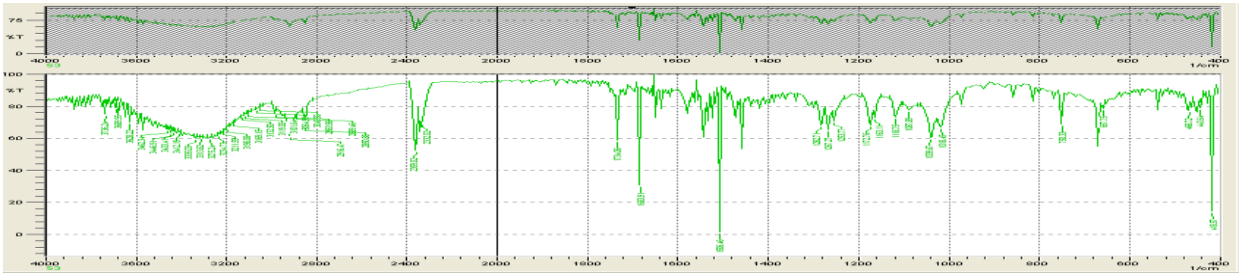


Figure 6. IR spectrum of formulation F8 (containing 5% Sodium Starch Glycolate)

Conclusion

Overall, the results suggest that suitably formulated mouth-dissolving tablets of lansoprazole containing crospovidone (F6) can be achieved. The tablets exhibited good i*n vitro* dispersion and wetting properties in presence of superdisintegrants. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption, leading to increased bioavailability.

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