RESEARCH ARTICLE

Formulation and Evaluation of Lansoprazole Fast Dissolving Buccal Films

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Abstract

Aim: The aim of the study deals with the formulation and evaluation of fast dissolving buccal films of which is an effective and well-tolerated treatment option in the management of acid-related disorders. Lansoprazole fast dissolving buccal films are a new, patient-friendly, and more convenient formulation of which can be taken with or without water. **Materials and Methods**: In the present investigation, polyvinyl alcohol and polyvinylpyrrolidone were used as film-forming agents, and polyethylene glycol 400 is taken as plasticizer. Solvent casting method was used for the preparation of fast dissolving buccal films. **Results and Discussion:** The films were prepared and evaluated for film thickness, folding endurance, dispersion test, drug content, and dissolution. The *in vitro* dissolution studies were carried out using simulated salivary fluid (pH 6.8 phosphate buffer). **Conclusion:** Among all the formulations, formulation L7 was released up to 99.8% of the drug from the film within 5 min of time which exhibits faster absorption and also shows desirable characteristics of the film. The drug-excipient interaction studies carried out by Fourier-transform infrared studies, differential scanning calorimetry analysis–X-diffraction studies, and scanning electron microscopic studies, and the results revealed that there were no major interactions between the drugs and excipients used for the preparation of films.

Key words: Fast dissolving buccal films, Lansoprazole, Polyethylene glyol 400, Polyvinyl alcohol, Polyvinylpyrrolidone, Solvent casting method

INTRODUCTION

Lansoprazole is a proton-pump inhibitor (PPI) which inactivates the final step in the gastric acid secretion pathway in gastric parietal cells in a dose-dependent manner. Bioavailability is 85% after the first dose - the highest among PPIs,[1-5] and acid inhibition is swift, resulting in rapid relief of symptoms.[6] Lansoprazole also exhibits antibacterial activity against *Helicobacter pylori in vitro*.[7–9] 17 years of clinical experience worldwide have shown lansoprazole to be an effective and well-tolerated treatment option in the management of acid-related disorders, including gastric and duodenal ulcers and gastroesophageal reflux disease and the treatment or prevention of gastroduodenal lesions induced by non-steroidal anti-inflammatory drugs.[10] Lansoprazole is also effective in combination with different regimens for *H. pylori* eradication and is included in the first-line PPI-based options for this purpose.[7,8,11-13]

Lansoprazole fast dissolving buccal film (LFDBF) is an orally dissolving film and is a new, patient-friendly, and more convenient formulation of lansoprazole which can be taken with or without water. LFDBF, which has an artificial strawberry flavoring, disintegrates rapidly in the mouth and is swallowed easily with the patient's saliva. It is the first PPI that can be taken orally without water. This formulation represents an improved alternative presentation for all patients requiring lansoprazole, offering the benefits of a choice of administration options. LFDBF maintains the same pharmacological properties as lansoprazole capsules and can be taken by any patient who is currently prescribed lansoprazole. The ability to take a tablet either

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with or without water will offer increased convenience and flexibility, particularly when patients are traveling, and may help to improve compliance in some patients. In addition, LFDBF may be suitable for certain groups of patients, such as those with dysphasia associated with gastroesophageal reflux disease,[14] dynophagia or strictures, and the elderly or long-term care patients.[15] LFDBF is available in Japan and the UK and will soon become available in the rest of Europe and the USA for use in all lansoprazole indications. This article summarizes the development of LFDBF and current clinical experience with the formulation.

MATERIALS AND METHODS

Lansoprazole was procured as gift sample from M/S Aurobindo Pharmaceuticals, Hyderabad. Polyvinyl alcohol (PVA) and polyvinylpyrrolidone (PVP) were commercially procured from M/S Yarrow Chem Products, Mumbai. Polyethylene glycol (PEG) was procured commercially from Sisco Research Laboratories Pvt., Ltd., Mumbai. Saccharin sodium was procured commercially from M/S Yarrow Chem Products, Chennai. All the materials used in the formulation were of pharmacopoeial standards.

Preparation of LFDBF

Fast dissolving buccal films of lansoprazole were prepared by solvent casting method. Film-forming agents such as PVA and PVP were prepared in the form of aqueous solutions individually in 100 ml beakers to attain clear solutions. Then, the solution of PVP was added to PVA aqueous solution and stirred well to get homogenous solution which is marked as solution A. Accurate quantities of lansoprazole and saccharin sodium were weighed individually and dissolved in suitable quantity of PEG 400 (PEG 400) to get a drug and plasticizer solution which is marked as solution B. The solution B was added to aqueous solution A and mixed continuously. The obtained solution was drawn on the non-adhesive base plate and dried under infrared (IR) lamp for 24 h. After drying, the films were cut into suitable sizes. Various trials were conducted to carried out optimize formula for the preparation of LFDBFs. The various compositions and schematic representation of LFDBFs are given in Table 1 and Figure 1.

In vitro dissolution study using Franz diffusion cell

In vitro dissolution studies were performed on all the film formulation using an apparatus called Franz diffusion cell apparatus which maintaining a volume capacity of 15 ml was used for dissolution study. The film equivalent to 15 mg of lansoprazole was placed in between the two compartments of an apparatus, and pipette 15 ml of 6.8 pH buffer (pH of saliva) was added to receptor compartment. Cell is kept on magnetic stirrer and bead in the cell is maintained at a speed of 50 revolution per minute (RPM), and medium maintained at a temperature of nearly 32°C ± 0.5°C and withdraw 1ml of samples at various time intervals and the samples were diluted with 6.8 pH phosphate buffer and measured the absorbance at 284 nm against 6.8 pH Buffer as Blank. The various dissolution profiles for films are shown in Figure 2. The *in vitro* dissolution parameters are given in Table 2.

Evaluation of fast dissolving films

Film thickness

The film thickness was measured using screw gauge with a least count of 0.01 mm at different locations on the film. The film thickness was measured at three different locations, and the average weight was determined. The obtained results are given in Table 3.

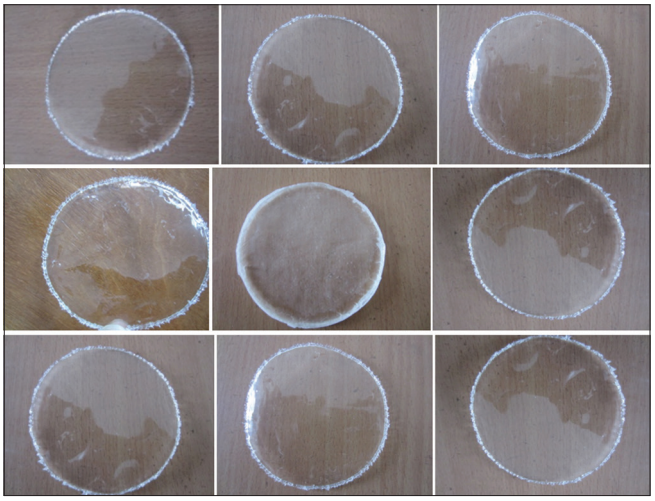

Figure 1: Lansoprazole fast dissolving buccal films

Table 1: Composition of LFDBF

Ingredients (%W/W)	L1	L2	L3	L4	L5	L6	L7	L8	L9
Lansoprazole	150	150	150	150	150	150	150	150	150
PVP	250	250	250	250	250	250	250	250	250
PVA	300	350	400	450	500	500	500	500	500
PEG 400	100	100	100	100	100	120	140	160	180
Sodium saccharin	20	20	20	20	20	20	20	20	20
Methanol	10	10	10	10	10	10	10	10	10

LFDBF: Lansoprazole fast dissolving buccal film, PVP: Polyvinyl pyrrolidine, PVA: Polyvinyl alcohol, PEG 400: Polyethylene glycol 400

Folding endurance

Folding endurance was determined repeatedly by folding a small strip of the film at the same place till number of times the film could be folded at the same place without cracking which was noted as folding endurance. The film was folded at an angle of 180^0 at the same place till it broke or folded up to 100 times without breaking. The studies were performed in trice and the average mean was calculated.

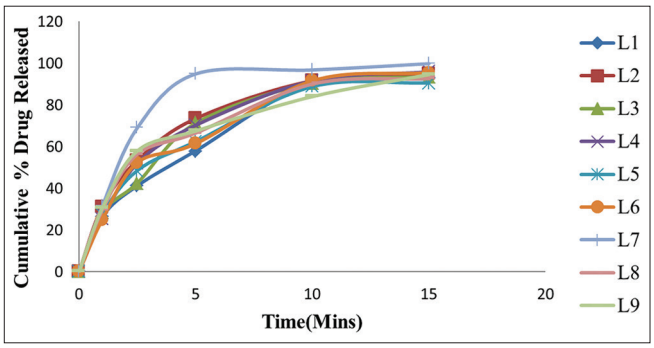

Figure 2: Drug release profiles for lansoprazole fast dissolving buccal film

Table 2: Evaluation of *in vitro* dissolution parameters for LFDBF

Formulation	T_{50} (min)	T_{90} (min)	$DE_{5\%}$	First order	
				K (min^{-1})	R^2
L1	5.5	>15	19.8	0.156	0.946
L 2	2.5	>15	19.6	0.234	0.954
L 3	2.5	14.5	18.6	0.367	0.922
L 4	2.0	9.5	25.9	0.216	0.906
L 5	2.0	8.0	36.8	0.211	0.915
L 6	2.1	9.5	34.5	0.207	0.945
L 7	0.5	4.5	22.8	0.267	0.994
L 8	1.8	10	23.2	0.138	0.935
L 9	1.9	10	25.6	0.188	0.927

LFDBF: Lansoprazole fast dissolving buccal film

Uniformity of drug content

The content of drug uniformity of the films was tested by ultraviolet -visible spectrophotometric method. The absorbance values were determined at a wavelength of 284 nm. The percentage drug content of various films was determined and is given in Table 2.

Dispersion test

A film equivalent to 5 mg of lansoprazole was placed in 200 ml of 6.8 pH phosphate buffer and was stirred for 3 min. Then, the resulting solution was passed through sieve number 22. The film passed the dispersion test only when no residue is left on the screen.

Evaluation of various dissolution parameters

Based on dissolution data obtained, various dissolution parameters were calculated such as T_{50}, T_{90}, $DE_{5\%}$ first-order rate constant, and Hixson–Crowell as shown in Table 2.

Characterization

Dissolution studies were performed on all the formulations; among these, formulation L7 were further evaluated by Fourier-transform IR (FTIR) spectroscopy and differential scanning calorimetry (DSC).

FTIR spectroscopy

The FTIR spectra of lansoprazole, PVP, and PVA were obtained using Brucker FTIR spectrophotometer to study the interaction between drug and carrier in films. The samples were prepared in KBr discs (2 mg sample in 200 mg KBr), and the sampling range was 400-4000/cm and the resolution was 4/cm. The FTIR spectra are shown in Figures 3-5.

Table 3: Evaluation of physical parameters for LFDBF

Formulation	Weight uniformity (mg)	Drug content (mg/film)	Film thickness (mm)	Dispersion test	Folding endurance (%)	Curling
L1	93	13.25	0.032	Passed	94	Absent
L2	96	14.22	0.033	Passed	96	Absent
L3	90	13.88	0.034	Passed	95	Absent
L4	74	10.55	0.030	Passed	71	Absent
L5	78	11.47	0.032	Passed	70	Absent
L6	88	12.88	0.031	Passed	83	Absent
L7	101	14.99	0.034	Passed	99	Absent
L8	97	13.88	0.031	Passed	94	Absent
L9	95	11.33	0.032	Passed	81	Absent

LFDBF: Lansoprazole fast dissolving buccal film

DSC

DSC measurements were performed on lansoprazole and film-forming agents such as PVP and PVA using differential scanning calorimeter (SHIMZDO and DSC-60). The samples were placed in a sealed aluminum crucible and evaluated with a heating rate of 20°C/min at a temperature range of 25–250°C. The thermograms were recorded and are shown in Figures 6-9.

Scanning electron microscopic (SEM) analysis

The SEM photographs were taken for the optimized film formulation L7 and lansoprazole pure drug. The SEM

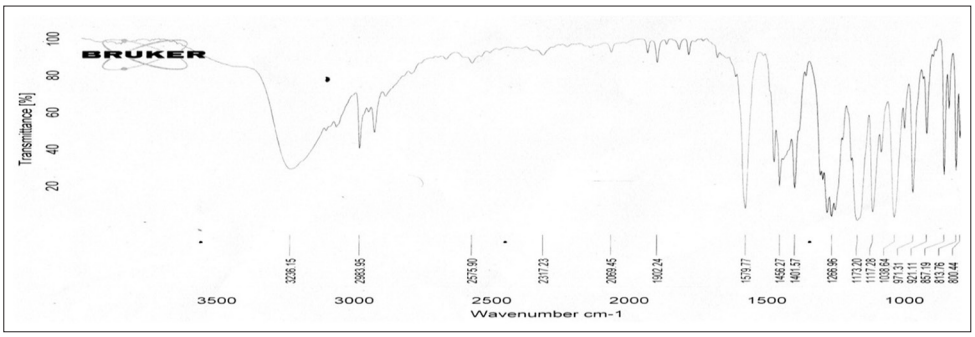

Figure 3: Fourier-transform infrared spectrum of lansoprazole pure drug

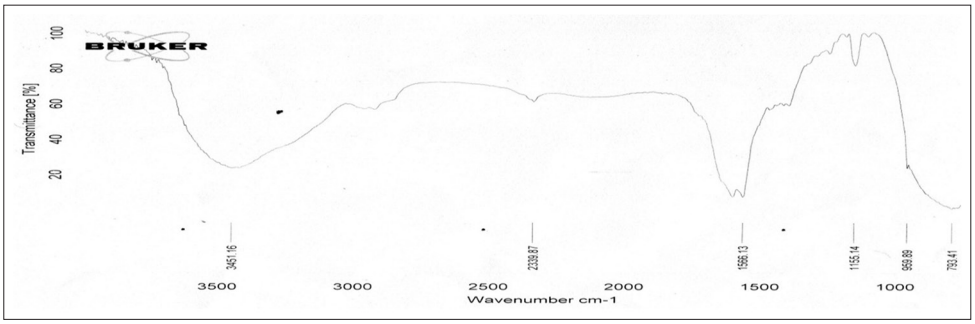

Figure 4: Fourier-transform infrared spectrum of polyvinylpyrrolidone

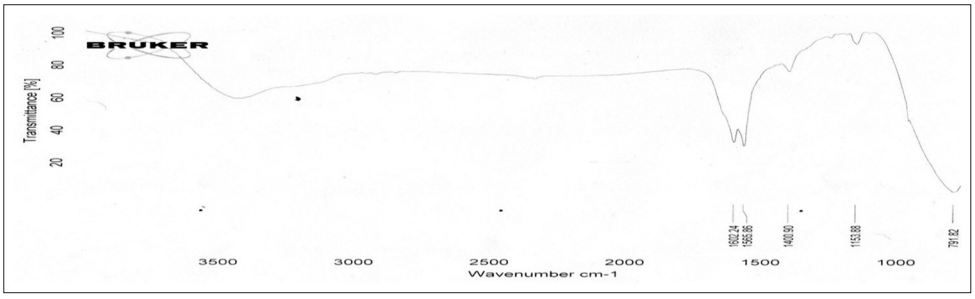

Figure 5: Fourier-transform infrared spectrum of polyvinyl alcohol

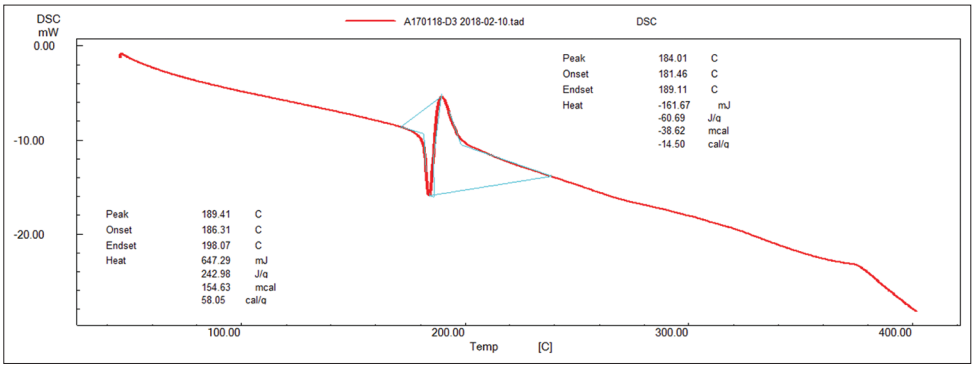

Figure 6: Differential scanning calorimetry thermogram of lansoprazole pure drug

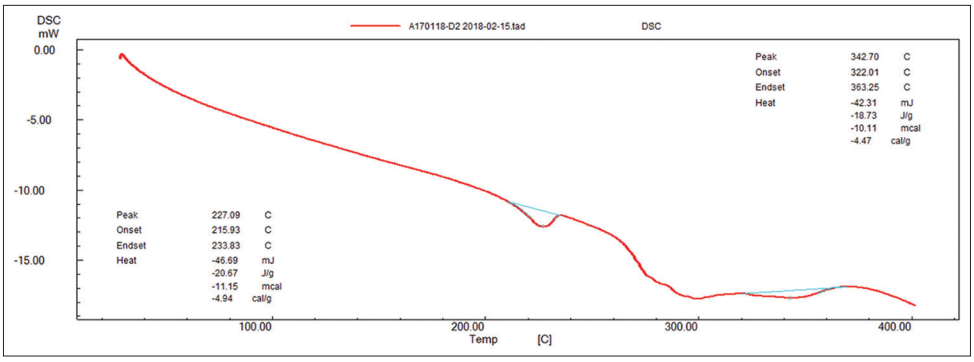

Figure 7: Differential scanning calorimetry thermogram of polyvinylpyrrolidone

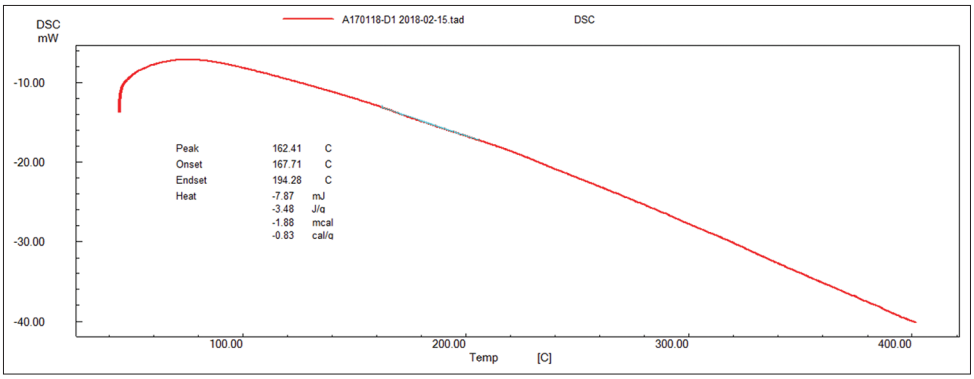

Figure 8: Differential scanning calorimetry thermogram of polyvinyl alcohol

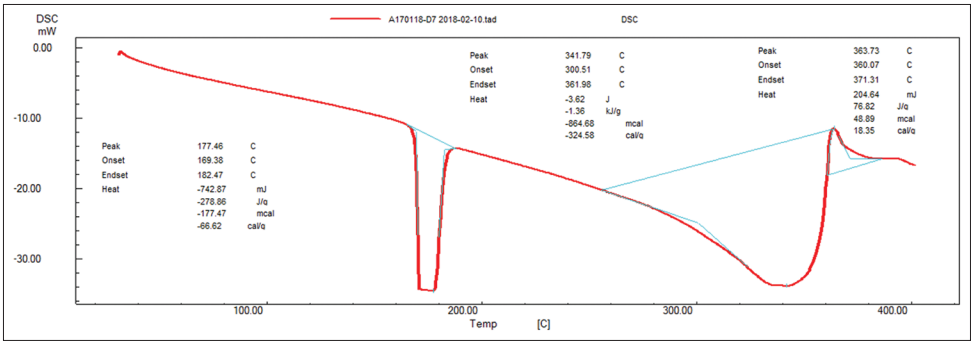

Figure 9: Differential scanning calorimetry thermogram of optimized formulation L7

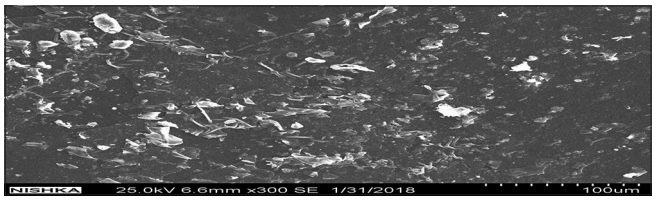

Figure 10: Scanning electron microscopic photograph of lansoprazole pure drug

photographs are shown in Figures 10-11. The L7 formulation showed smooth even surface.

X-ray powder diffraction (XRD)

The powder crystalline of the lansoprazole and the optimized formulation L7 was determined using SHIMADZO XRD -7000 with copper target instrument. The conditions were maintained at 40 Kv voltages, with 40 MA at room temperature. The scanning rate employed was 0.1°/s over a range of two values from 3° to 45°. The diffractograms are shown in Figures 12-15.

RESULTS AND DISCUSSION

The present investigation deals with the formulation and evaluation of fast dissolving buccal films of lansoprazole which is used for the treatment of acid-related disorders. The main focus of this study was to select the best combination of polymer and excipients to formulate lansoprazole fast dissolving buccal films. Lansoprazole fast dissolving buccal films were prepared by solvent casting method using PVP and PVA which were used at different concentrations as

film forming polymers. PEG 400 was used as plasticizer to make the pliable and flexible in nature. Saccharin sodium was used as artificial sweetener in the formulation. The films were prepared under identical conditions to minimize processing variables and evaluated for various physical properties such as thickness of a film, folding endurance, and content of drug uniformity, and dispersion test is used to ensure the stability of films. The composition of various fast dissolving buccal films of lansoprazole is given in Table 1.

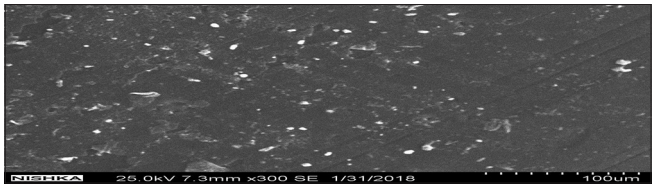

Figure 11: Scanning electron microscopic photograph of optimized film formulation (L7)

The prepared films were further evaluated for thickness, folding endurance, dispersion test, drug content, and *in vitro* diffusion studies. The thickness of a film was found in the range of 0.031 ± 0.003–0.034 ± 0.003 mm. The optimized formulation L7 film is having thickness 0.0342 mm. The folding endurance values of all prepared films ranged from 30 to 100%. The optimized formulation L7 film was found to have folding endurance of 100% which is highly beneficial or agreeable. The drug uniformity was found in the range of 14.99 ± 1.6 mg. The optimized formulation L7 film was found to have 14.99 mg. The films were further subjected to dispersion test as per the Indian Pharmacopoeial standard. All the prepared film formulations were found to disperse in 6.8 pH phosphate buffer within 3 min. No inert fibrous or

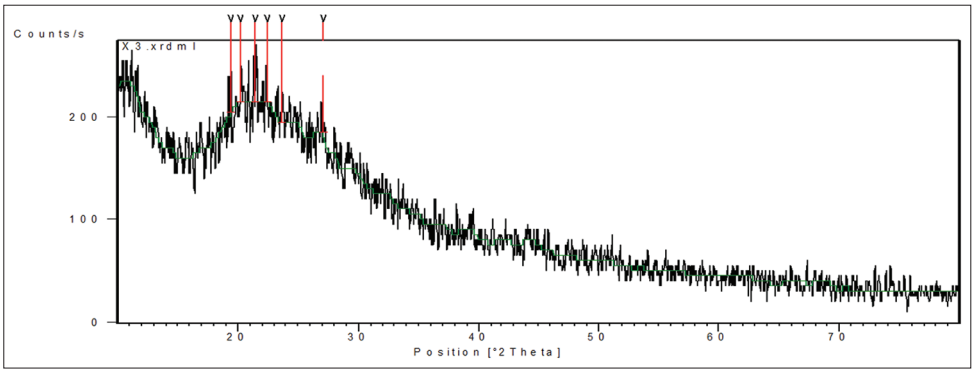

Figure 12: X-ray powder diffraction spectrum of lansoprazole pure drug

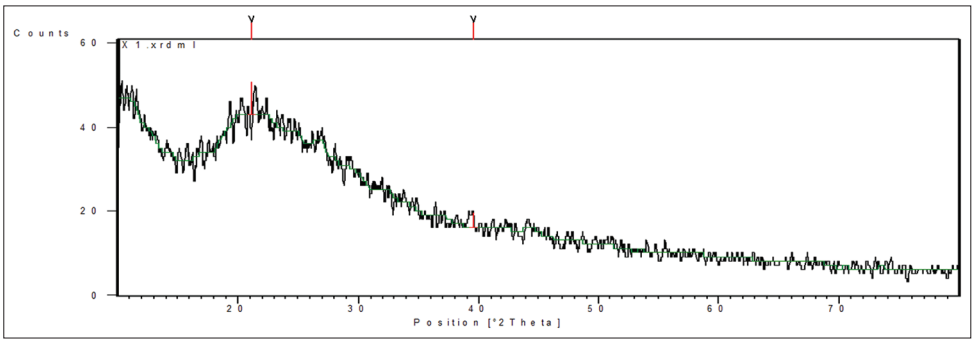

Figure 13: X-ray powder diffraction spectrum of polyvinylpyrrolidone

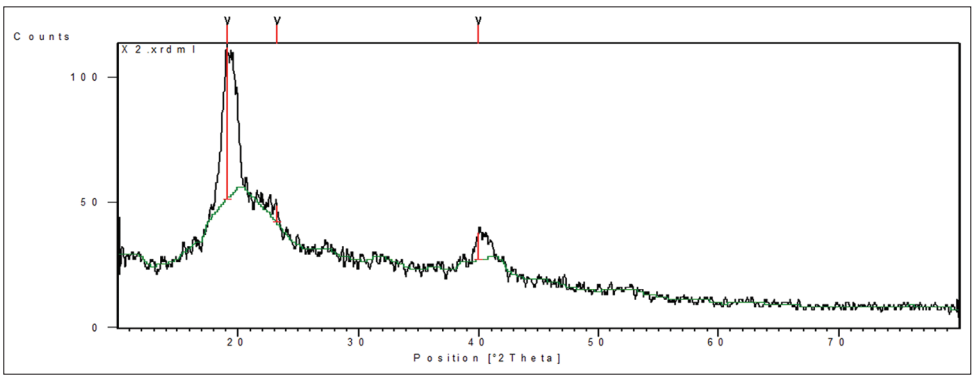

Figure 14: X-ray powder diffraction spectrum of polyvinyl alcohol

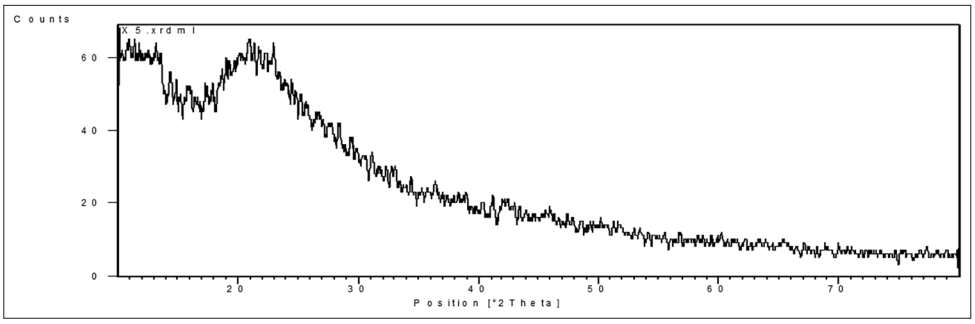

Figure 15: X-ray powder diffraction spectrum of optimized formulation (L7)

insoluble material was left on the 22-mesh screen when the dispersion was passed through it. The prepared films were subjected to a thickness of a film, drug content, and folding endurance, and dispersion test values obtained for various fast dissolving buccal films are given in Table 2.

Fast dissolving buccal films of lansoprazole were further subjected to *in vitro* dissolution studies using Frantz diffusion cell with 15 ml of 6.8 pH phosphate buffer as a medium which is maintained at a temperature 32°C. The dissolution medium in the cell was maintained to rotate at 50 rpm using magnetic stirrer. The samples were withdrawn at various time intervals and were consequently diluted with 6.8 pH phosphate buffer, and absorbance values were noted at 284 nm using ELICO double beam spectrophotometer. The obtained dissolution profiles are given in Table 2 and are shown in Figure 1. Formulations L1, L2, L3, L4, L5, L6, L8, and L9 were found to release more than 90% of the drug within 15 min. The formulations L7 were found to be best suitable for fast dissolving, and also, this film should possess all the physical characteristics required for the fast dissolving buccal film. The film formulations L7 containing 25% of PVP and 50% of PVA were found to exhibit the best film forming properties with 100% folding endurance value. These L7 formulations with 10–15% of PEG were found to exhibit rapid dispersion in the dissolution media and dissolved readily in the same medium which indicated fast dissolving characteristics of the film. The first-order graphs for various fast dissolving buccal films were found to be linear with correlation coefficient values obtained which were in the range of 0.906–0.994. It indicated that the drug release from the films was found to be concentration dependent. This indicated that the dissolution of the drug from the film was greatly dependent on weight uniformity of the film that undergoes dissolution per unit time. The *in vitro* dissolution parameters are given in Table 2. The pure drug and film-forming agents were subjected to characterized FTIR studies. The FTIR spectra of the commercial sample of lansoprazole displayed bands at 3236/cm due to N-H Stretch and 2983/cm due to C=C Stretching. The IR spectra of drug and film-forming agents indicated that there are no interactions between drug and excipients used. DSC thermographic studies were carried out on lansoprazole pure drug and film-forming agents. The exothermic peak for pure lansoprazole drug was obtained at 189.41°C. The short broad exothermic peak for PVP was obtained at 227.07°C. The short exothermic peak for PVA was obtained at 161.41°C. The short endothermic peak for optimized formulation L7 was obtained at 177.1°C. Hence, no interaction between drug and excipients was observed with DSC studies. The XRD patterns of lansoprazole and film-forming agents such as PVP and PVA and optimized formulation (L7) diffraction patterns of pure lansoprazole showed characteristic high diffraction peaks. On the other hand, the diffraction patterns of optimized formulation (L7) showed a decrease in the peak intensity.

CONCLUSION

Fast dissolving buccal films of lansoprazole prepared in the present study should exhibit good film properties as indicated by film thickness and folding endurance was measured. All the films prepared were found to be stable uniform, flexible, and pliable and 99% of drug was released from optimized film L7 within 5 min of time. This was advisable for fast absorption. Hence, fast dissolving buccal films of lansoprazole were found to be suitable for effective and well-tolerated treatment option in the management of acid-related disorders**.**

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