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Formulation and evaluation of dexlansoprazole extended-release tablet

Shubham Santosh Sharma * and Pooja Ganesh Bhutada

Department of Quality Assurance, Vidyabharati College of Pharmacy, Amravati, (MH), Pin 444602 India.

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Abstract

Dexlansoprazole (DSP) is a proton pump inhibitor, it used to treat GERD and ulcer colitis. DSP works by decreasing the volume of acid in the stomach. DSP is an acid-labile medication that may be destroyed in the stomach's acidic pH. A coating technique was used to postpone drug release in the stomach, which can extend pharmacological activity. Shellac can be used to develop the sustain release tablet of dexlansoprazole as retardation of the drug (dexlansoprazole) was observed in the acidic pH of the stomach, and hence a sustain coated dexlansoprazole tablet was prepared and evaluated. The coating's primary function is to allow for the delayed, immediate, and prolonged delayed release of DSP. DSP coating with different polymers inhibits faster degradation in the acidic pH of the stomach, therefore increasing pharmacological action. DSP coating with different polymers inhibits fast degradation in the stomach's acidic pH, enhancing pharmacological action. The major function of the coating is to enable for the delayed, immediate, and prolonged delayed release of DSP. DSP coating with different polymers inhibits fast breakdown in the stomach's acidic pH, enhancing pharmacological action.

Keywords: Dexlansoprazole; Gastroesophageal reflux disease; Proton pump inhibitor; Sustain release tablet

1. Introduction

Gastroesophageal reflux disease (GERD) is a persistent symptom of mucosal injury caused by stomach acid refluxing into the esophagus from the stomach. “Changes in the barrier between the stomach and the esophagus, including abnormal relaxation of the lower esophageal sphincter, cause GERD. The most common symptoms include heartburn and regurgitation. Medications such as proton pump inhibitors, H2 receptor blockers and antacids are used in the treatment of GERD. DSP is a proton pump inhibitor drug used in the treatment of GERD” (1). However, it is degraded in acidic stomach pH, thus lacking in pharmacological action of the drug. Palletization of DSP and coating of various polymers prevents rapid degradation and also produces prolonged action Pellets are fine powder or granules of bulk medicines and excipients agglomerated together (2). It offers a number of advantages, including enhanced product appearance, reduced dosage dumping, increased safety and efficacy, and free dispersion in the gastro-intestinal tract. Shellac, hydroxypropyl methylcellulose phthalate-55, Eudragit (RSPO and RLPO). The major objective of coating is to extend the delay in DSP release. DSP coating with different polymers inhibits fast breakdown in the stomach's acidic pH, enhancing pharmacological action.

2. Material and methods

dexlansoprazole (API) has been a gift sample from ZIM laboratories, Nagpur, Maharashtra. Excipients like Microcrystalline cellulose and Shellac were purchased from Thermosil fine chem. Ind. Pune, HPMC Phthalate, Calcium Carbonate, Magnesium stearate, Talc were purchased from S.D. Fine Chem Lab Mumbai. This study's ingredients were all of analytical reagent grade.

* Corresponding author: SS SHARMA

Department of Quality Assurance, Vidyabharati College of Pharmacy, Amravati, (MH), Pin 444602 India..

2.1 Identification of drug:

Organoleptic study

Organoleptic properties of pure dexlansoprazole powder were checked.

2.2 Maximum absorbance of drug

The solution of dexlansoprazole in the concentration of 10mg/ml was prepared using water. It was scanned using a double beam U.V spectrophotometer using water as a blank over the wavelength range of 200-400nm.

2.3 Melting point

The open capillary technique was used to determine the melting point. Powdered drug (Dexlansoeprazole) was put into the open end of thin capillary of about 5cm length with uniform diameter (1mm width), by tapping gently. Capillary was then placed into the orifice of the melting point apparatus (veggo model: VMP-D). The temperature at which substance started to convert liquid and the temperature at which solid disappears and completely converted into liquid was noted from the digital display as the melting point range of the drug. Average triplicate reading was taken.

2.4 Solubility

Solubility of dexlansoprazole was determined by dissolving the small amount of drug in various solvents like water, chloroform, ether etc.

2.5 Calibration curve of DSP in pH 6.8 Phosphate buffer:

A standard DSP solution was produced by dissolving 100 mg of DSP in a pH 6.8 phosphate buffer solution in a 100 mL volumetric flask and adjusting the volume with pH 6.8 phosphate buffer to a concentration of 1000 g/Ml. To get the concentration of 100 g/mL, 10 mL of this solution was remove and diluted to 100 mL.. Aliquots of 1 mL, 2 mL, 3 mL, 4 mL, and 5 mL were pipetted into 10 mL volumetric flasks from 100/mL. The volume was filled with pH 6.8 phosphate buffer to achieve final concentrations of 10, 20, 30, 40, and 50 g/mL. A UV-Visible spectrophotometer is used to measure absorbance at 286 nm in comparison to pH 6.8 phosphate buffers as a blank. Experiment. Experiment was repeated for six times in order to obtain a consistent and graph plot.

2.6 FT-IR (Fourier transform infrared spectroscopy) studies:

The method of comparing infrared spectra was utilized to identify any probable chemical interaction between the drug and the polymer. The drug, drug polymer, and polymer were combined with the appropriate amount of potassium bromide. Using a hydraulic press at 15 tons pressure, 100 mg of this combination was crushed to create a clear pellet. A Perkin Elmer FTIR spectrophotometer was used to scan it from 4000 to 400 cm-1. Using the FTIR peak matching approach, the IR spectra of the physical combination was compared to that of pure medicine and polymers, which were matched to identify any presence or removal of peaks.

3. Preparation of extended delayed release Coating Tablet (3)

Table 1 Formulation of factorial batches of enteric coated tablet

Ingredients	Factorial Batches								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dexlansoeprazole	30	30	30	30	30	30	30	30	30
Microcrystalline Cellulose	100	100	100	100	100	100	100	100	100
Lactose	60	60	60	60	60	60	60	60	60
HPMC K100	32.5	17.5	20	22.5	25	27.5	30	32.5	17.5
HPMC Pthalate	17.5	32.5	30	27.5	25	22.5	20	17.5	32.5
Magnesium Stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5

Desired quantity of ingredients (Microcrystalline Cellulose, Lactose,HPMC Pthalate,HPMCK100, Magnesium Stearate and Talc) and drug (Dexlansoeprazole) were mixed (Shown in Table 1) in stepwise manner and then compress it by

rotary compression machine to prepare the tablet. After that 5% shellac coating solution was prepared and the tablets were coated.

F1 were selected as an optimized purpose in all over batches. The formulation (F1) of dexlansoprazole, HPMC K100, HPMC Pthalate, MCC, Magnesium state, Talc and having dissolution (%CDR) and drug content of this batch considered to be most satisfactory delay release tablet formulation.(4)

4. Results

4.1 Identification of Dexlansoprazole

The present study was undertaken to prepare an enteric coated tablet by using polymers. Preformulation studies of drugs and excipients are also carried out.

4.2 Organoleptic study of Dexlansoeprazole:

The organoleptic character of Dexlansoeprazole were observed physically, the observed properties comply with USP and the results are as in Table 2

Table 2 Organoleptic character of Dexlansoprazole

Organoleptic character	Properties
Colour	Yellow
Odour	Odourless
Physical appearance	Amorphous

4.3 Melting point

The procured reference standard of Dexlansoprazole was found to melt in the range of 139-140^{0}C and the results are described in Table 3

Table 3 Melting point of Dexlansoeprazole

Melting Point	Average
139	
140	140
140	

4.4 Solubility

The drug was shown to be freely soluble in methanol practically soluble in water, and freely soluble in organic solvents.

5. UV Spectroscopy

5.1 Determination of λ_{max} and selection of Analytical Wavelength

The typical Dexlansoprazole solution is scanned at wavelengths ranging from 200 to 400 nm. The absorption wavelength was determined to be 283.0 nm. As a result, the wavelength used for Dexlansoprazole determination is 283.0 nm (Figure 1)

5.2 Scan for absorption maxima of DSP using pH 6.8 phosphate buffer:

The absorption maxima of DSP were determined using a UV-Visible spectrophotometer with 0.1N HCl as the blank at 286 nm and pH 6.8 PB as the blank at 286 nm, respectively. For analysis, a drug concentration of 1 - 5 g/mL was utilized (Figure2) shows the usual graph and pH 6.8 phosphate buffer values.

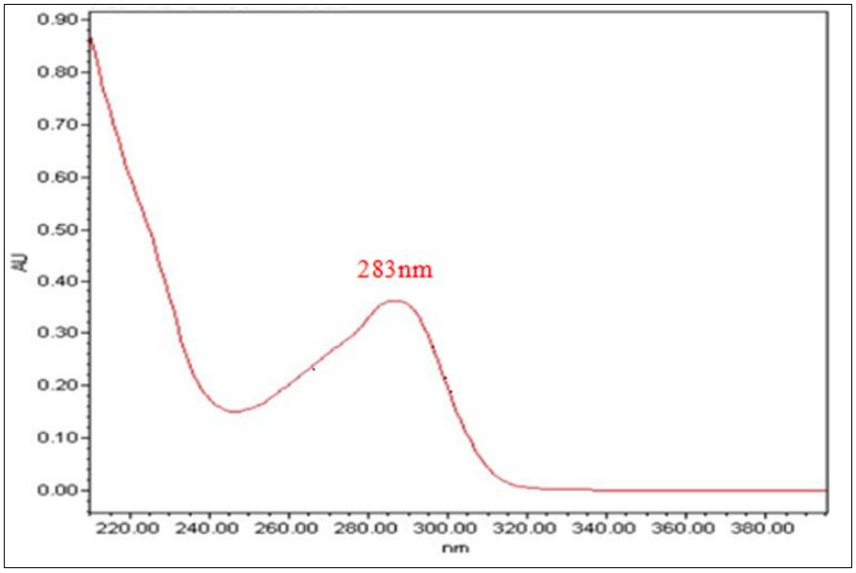

Figure 1 UV Spectrum of DEXLAN

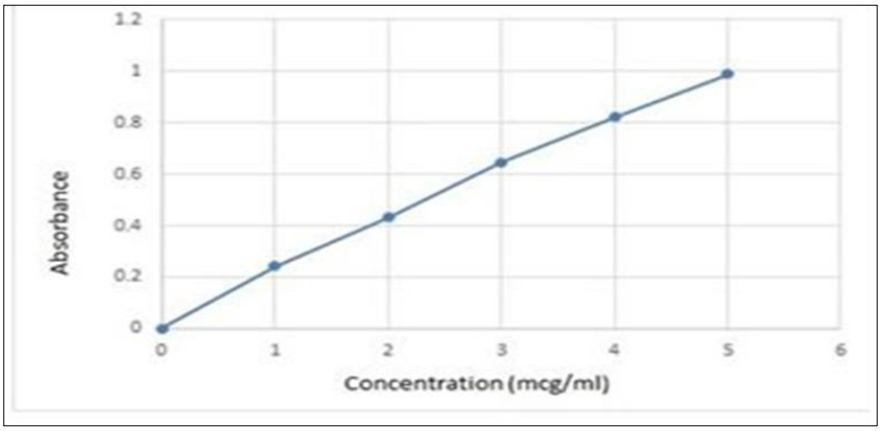

Figure 2 Standard graph of DSP using 6.8 phosphate buffers

5.3 FT-IR Compatibility studies:

The spectra of the drug, the drug-polymer, and the polymer were obtained. As shown in Table 5, the distinctive peaks at 3448 (N-H stretching), 1638.58 (C=N stretching), 1358.97 (S = O stretching), 1467 (C-H bending), and 1244 cm-1 (C-N vibrations) indicate that there are no interactions between the medication and excipients.

Table 4 Interpretation of IR-Spectra of Drugs and Drug-Excipients

Functional group	Region in cm-1
C-H stretching in hetero aromatic ring	3076.36
C-C stretching of phenyl ring	1474.63
C-C out of plane bending in aromatic ring	754.51
N-H stretching in hetero cyclic ring	3446.91
S=O stretching	1044.49
C-S stretching	611.45
C-F stretching of poly fluorinated compound	1110.17

5.4 Preformulation studies

All the preformulation parameter's Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio, for example, are all within the limit and meet the requirements. They are given as in Table 5

Table 5 Tapped density, Bulk density and weight variation for DSP

Formulation	Angle of Repose	Bulk density (gm/mL)	Tap density (gm/mL)	Carr's index	Hausner's Ratio
F1	25.96±0.23	0.66 ± 0.03	0.675 ± 0.02	13.05±0.2	1.15±0.4
F2	24.56±0.78	0.694 ± 0.03	0.714 ± 0.03	12.60±0.2	1.13±0.2
F3	26.96±0.44	0.704 ± 0.04	0.724 ± 0.04	13.24±0.2	1.13±0.3
F4	26.12±0.28	0.714 ± 0.04	0.735 ± 0.03	14.42±0.2	1.14±0.7
F5	26.44±0.95	0.719 ± 0.03	0.740 ± 0.02	12.05±0.1	1.14±0.5
F6	26.06±0.38	0.724 ± 0.04	0.740 ± 0.02	13.07±0.3	1.15±0.3
F7	26.87±0.84	0.729 ± 0.03	0.751 ± 0.04	14.42±0.1	1.13±0.4
F8	26.02±0.98	0.733 ± 0.03	0.753 ± 0.03	12.05±0.4	1.15±0.9
F9	26.06±0.18	0.740 ± 0.02	0.753 ± 0.04	13.07±0.6	1.14±0.5

6. Characterization Studies for delay release DSP tablet

6.1 Dissolution studies

Formulation (F8 - F14) using HPMC Pthalate, HPMC K100) as polymer in a 1:1 ratio, and it was found that the F1 formulation (HPMC Pthalate, HPMC K100) had the highest drug release. At 12 hours, drug release was determined to be 94.1 percent in the buffer stage and 2.5 percent in the acidic stage. Because of the rise in hydrophobic concentration of polymer drug retardation, it was used for longer delayed release coating. (Fig 3) depicts the in-vitro drug release profile of formulations F1–F9. (Table 5) depicts in vitro drug release values for barrier coated, immediate coated, and extended delayed release. (Figures 3&4) (5)

Table 6 Dissolution profile of F1-F9 (extended delayed release coating optimization) with comparison of dissolution pH-6.8 buffer

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1	7.200	6.858	5.455	6.823	6.994	6.310	5.626	6.652	6.994
2	9.635	12.371	10.994	9.291	9.942	8.912	11.303	10.146	9.874
3	19.031	20.653	19.782	21.525	20.058	18.611	15.541	18.415	18.997
4	23.996	25.010	25.709	26.093	24.960	23.403	25.106	22.315	24.714
5	31.485	29.118	31.873	32.910	31.908	30.034	31.712	29.351	31.421
6	40.898	42.281	39.098	39.114	40.844	40.568	40.066	38.820	40.423
7	47.967	50.727	49.476	46.206	46.646	46.574	48.327	47.007	48.070
8	55.758	57.506	56.899	56.246	53.882	55.863	56.223	54.211	54.014
9	61.880	65.691	65.799	65.280	64.442	64.244	63.956	64.670	63.685
10	73.167	76.657	72.831	75.183	74.340	72.944	72.791	75.323	73.306
11	83.489	79.127	83.971	85.002	82.581	79.021	78.422	80.558	81.609
12	94.208	92.901	90.860	93.265	94.937	90.776	89.763	90.782	91.154

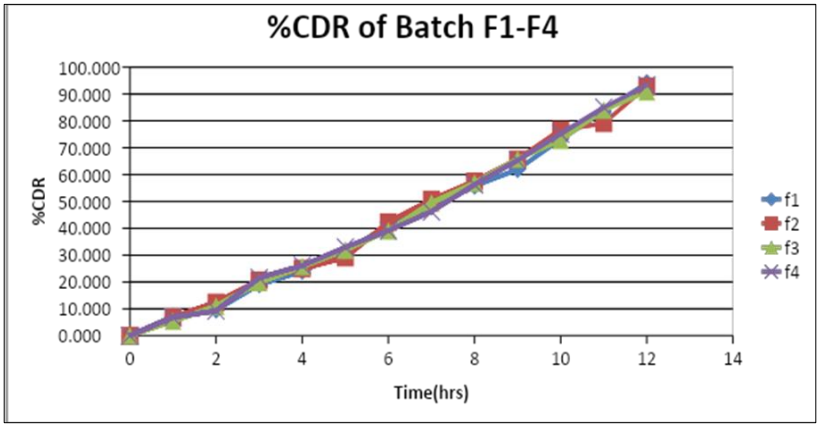

Figure 3 Extended delayed release batch in vitro release profile F1-F4

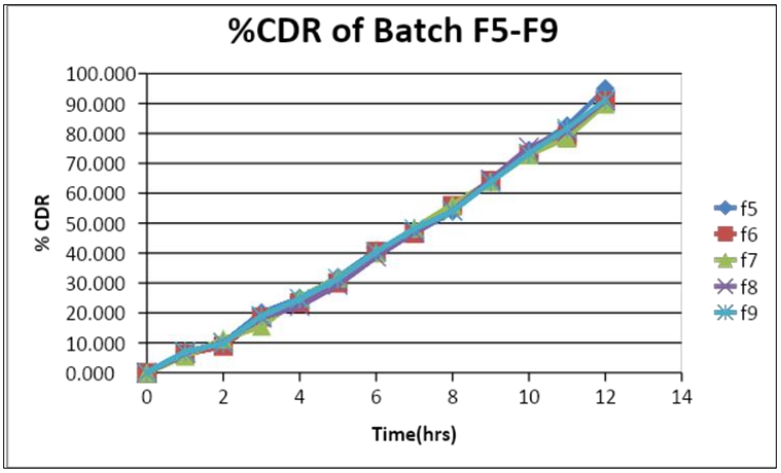

Figure 4 Extended delayed release batch in vitro release profile F5-F9

6.2 Kinetic analysis

The Korsmeyer Peppas and Higuchi models were used to analyze the findings of in vitro drug release experiments.(6)the n value of the F14 formulation was discovered to be 0.755, and drug release was discovered to follow anomalous diffusion. A mechanism for the connection of diffusion and erosion was discovered. Drug release was expected to follow first order release with r2 = 0.874, then Higuchi's equation with r2 =0.514, indicating diffusion as a mechanism. The values of the kinetic model used for percent drug release of all formulations are shown in Table 7.

Table 7 Model dependent kinetic analysis for the dissolution profile of different

Batch	Zero order r2	First order r2	Higuchi r2	Korsemeyer-Peppas r2
F1	0.844	0.947	0.643	0.962
F2	0.804	0.959	0.584	0.925
F3	0.930	0.898	0.791	0.988
F4	0.826	0.955	0.618	0.943
F5	0.852	0.806	0.798	0.958
F6	0.851	0.847	0.728	0.958
F7	0.725	0.814	0.555	0.741
F8	0.900	0.824	0.822	0.964
F9	0.885	0.911	0.686	0.969

7. Discussion

According to the present study, dexlansoprazole delayed release tablets were prepared using Shellac coating. From the results obtained it was concluded that dexlansoprazole delayed release tablet shows optimum in vitro dissolution time (%CDR) and drug content pattern. Optimization was done by making a minitab with a full factorial design paradigm Delay release tablets containing polymers especially HPMC Pthalate and HPMC K100 in a desired proportion can be used to delay release tablet formulation. dexlansoprazole and other excipient used in formulation are compatible with each other conclude from FTIR spectroscopy and it is also conclude that HPMC Pthalate at higher concentrations shows delay dissolution time slow release of drug from preliminary trials it was concluded that batch F1 which contains HPMC Pthalate and HPMC K100 shows better release than other trial batches, from full factorial batches response surface it is concluded that measured response i.e. % cumulative drug release and drug content after 12 h are broadly affected by independent variables batch F1 with HPMC Pthalate and HPMC K100 are much more significant in optimized area concluded from overlay plot. From this work it is finally concluded that optimized formulation of delay release tablets by using delay release enteric coated polymer were prepared which have better dissolution time (%CDR) and drug content. Hence the set objectives of this research worked has been achieved successfully. As the above study shows that delay release dexlansoprazole tablet have much more benefit than the current available marketed capsule and immediate release dexlansoprazole formulation. It was found that delay release tablet has a much more pharmacological and pharmacokinetic effect and the other shortcomings of the current marketed formulation can be overcome by developing the delay release tablet of dexlansoprazole which will help in prolonged effect and less dose dumping and also can help in curing the GERD in less time and might show greater pharmacological effect in less time.

8. Conclusion

From the above study it was concluded that the developing the dexlansoprazole sustain release tablet is possible and it can be an crucial development in curing the GERD and Ulcerative colites by decreasing the dose frequency increasing bio-availability and also reducing the dose dumping which might help in curing the disease effectively.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest by both the authors.

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