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RESEARCH ARTICLE

Formulation and evaluation of Lansoprazole delayed release orally disintegrating tablets

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Abstract: The objective of present study was an attempt to formulate and evaluate delayed release orally disintegrating tablets for Lansoprazole, which is a benzimidazole anti-ulcer agent and is one of the most widely, used drugs for treating mild and severe ulcers. Successful delivery of drugs specifically to the intestine requires the protection of drug from being release in stomach. The present study demonstrates that the lansoprazole enteric-coated granules could be successfully intestine targeted by using pH dependent polymers in different concentrations. By observing the dissolution profile for all the formulations F5c was better formulation of all the formulation. Formulation F5c was formulated as lansoprazole delayed release orally disintegrating tablets by using HPMC E5, Eudragit L30 D-55 and Eudragit NE 30D. Formulated tablets showed delayed *in vitro* dissolution behavior, probably due to optimized concentration of polymers. The value of regression correlation coefficient (R^2) was calculated for all the formulations F1-F8 that values were close to 1. Among regression correlation coefficient (R^2) values of Higuchi's equation, Korsmeyer-Peppas equation and Hixson-Crowell equation, R^2 values of Korsmeyer-Peppas equation was found to be higher and the n values was found to be ($n<0.45$) release mechanism. Similarly, between Zero order and First order equation, R^2 values of zero order equation was found to be higher. Hence, the drug release followed zero order release kinetics with fickian diffusion mechanism. The optimized formulation F5c was stable at 25°C/60% RH and 40°C/75% RH as per ICH guidelines, after 2 months.

Keywords: Lansoprazole; HPMC E5; Eudragit L30 D-55; Eudragit NE 30D.

1. Introduction

Lansoprazole is an anti-ulcer agent, used for treatment of mild and severe ulcers. The present study demonstrates that the Lansoprazole enteric-coated granules could be successfully intestine targeted by using pH dependent polymers in different concentrations. Development of additional la mode pharmaceuticals & meds is target of analysts over world. With particular finished objective to achieve satisfying results, pharmaceutical must be honest to goodness depicted in genuine estimations structure. Standard vivacious release drug advancement structures when taken as frequently as would be prudent in day can keep up pharmaceutical obsession levels in remedially capable degree. Regardless this results in significant changes in plasma drug levels [1,2].

The stability of lansoprazole a proton pump inhibitor is a function of pH and it rapidly degrades in acidic medium of the stomach, but has acceptable stability in alkaline conditions. Hence in order to deliver lansoprazole into the intestine, delayed release formulation was developed by enteric coating of the drug loaded sugar spheres [3]. ODT formulation was developed as water is not required to swallow the dosage form, which is highly convenient feature for patients, who are traveling and do not have immediate access of water

2. Experimental Methods

2.1 Drug-Polymers Compatibility Study:

The study was carried out to find out the compatibility among the drug, polymers.5percentage w/w of sample was mixed with dry KBr, [4] and each disc was scanned at a speed of 4 mm/sec at a resolution of 400-4500 cm^{-1}.

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2.2. Preparation of Lansoprazole Delayed Release Orally Disintegrating Tablets:

2.2.1. Drug Loading:

Sugar pellets (850-1000µm) were sieved through 18 mesh and 33% of pellets were taken for drug loading from total batch size. Dispersed in specified ml of purified water and stirred for 10 minutes. The required quantity of HPMC E5 was taken and dispersed in specified ml of purified water and stirred for 10 minutes to obtain a clear solution. Purified water containing drug was mixed with dispersed HPMC E5 solution with stirring. Pellets were loaded using dispersion both into FBC bowl and coated [5]. The composition of pellets, barrier coating is shown in Table 1 and the operation conditions are shown in the Table 2

Table no 1 Formulation and preparation of Drug Loading and Barrier coating of pellets

Drug loading	**mg/ tablet**
Lansoprazole	30
Sugar sphere	75
Tween 80	0.25
HPMC E 5	5.50
Dibasic sodium phosphate	0.75
Water	q. s
Barrier coating	
HPC	7.5
Mannitol	26
Water	q. s

Table no 2 Fluidized Bed Coater operation Conditions for Drug Loading

Parameters	**Operation conditions**
Air pressure	2lb/in^2
Inlet temperature	48 ^oC
Bed temperature	42 ^oC
Spray RPM	3-6
Blower RPM	299

2.2.2. Barrier Coating:

Required quantity of Drug loaded pellets was taken for Barrier coating. Required quantity of hydroxy propyl cellulose and mannitol was taken and dissolved in specified ml of purified water and stirred until a clear solution was obtained and coating was done [6] by following the operation parameters shown in (Table no 3).

Table no 3 Spray Coater operation conditions for Barrier coating

Sl.no	**Name of parameters**	**Operation parameter**
1	Pump RPM	35
2	Air pressure	2 Psi
3	Pan RPM	10-13
4	Inlet temp	65^oC
5	Outlet temp	38 ^oC
6	Gun distance	20

2.2.3. Enteric Coating:

Specified quantity of Barrier coated pellets were taken for Enteric coating. Required quantity of Eudragit L30 D-55, Eudragit NE 30-D, triethyl citrate, tween 80, talc, glyceryl monostearate, were taken and dispersed in purified water and stirred for 10 minutes until a clear solution was obtained [7] and coating was done according to the operation parameters shown in the (Table no 4).

Table no 4 Spray Coater operation parameters for Enteric coating

Sl.no	Name of parameters	Operation parameter
1	Pump RPM	35
2	Air pressure	2 Psi
3	Pan RPM	10-13
4	Inlet temp	65^{o}C
5	Outlet temp	38 ^{o}C
6	Gun distance	20

2.3. Evaluation of prepared pellets

2.3.1. Scanning Electron Microscopy Analysis

This study was performed to observe the morphological changes and the particle size changes that occurred due to the formulation variation [8].

2.3.2. In vitro Dissolution Study

Dissolution studies of samples were performed according to USP XXIII type II apparatus in acidic and phosphate buffer of pH 1.2 and 6.8 respectively, with temperature 37+ 0.5^{0}C and the rotation speed was 75 rpm. Samples were withdrawn at various time intervals and analyzed spectrophotometrically [9].

2.3.3. Drug Release kinetics

Studies were performed to observe the release kinetics of lansoprazole delayed release orally disintegrating tablets [10].

3. Results and Discussion

The present study was undertaken to formulate Lansoprazole delayed release oral dispersible tablets. The study involves preformulation studies of drug and excipients, formulation and processing development along with evaluation of tablets made with the optimized formulation. Finally, tablets were evaluated by *in vitro* methods [11].

3.1 Drug excipient incompatibility

FTIR spectroscopy study was carried out to find out the possible interaction between selected drug lansoprazole and enteric coating polymers. The resultant graphs are shown in the Figure 1 and Figure 2

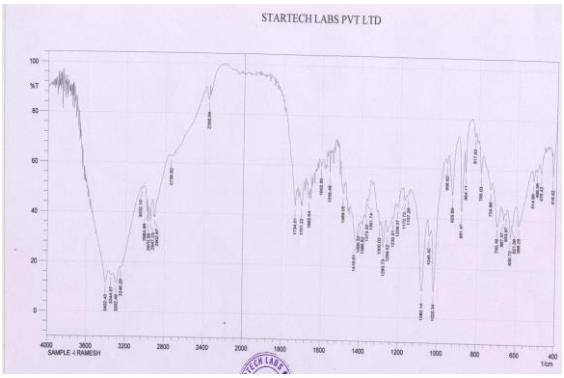

Figure 1: FTIR Spectroscopy of Pure Drug Sample

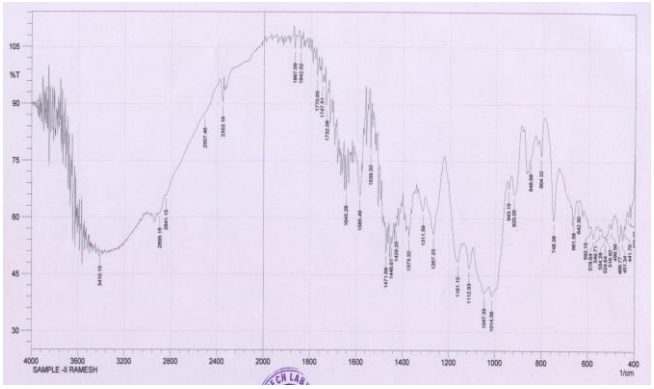

Figure no 2 FTIR Spectroscopy of optimized Formulation F5c

3.2 Scanning electron microscopy (SEM)

The surface characteristics of the enteric coated pellets were observed by scanning electron microscopy (SEM) in Figs 12 (a) and 12 (b). SEM was performed to determine spherical nature of pellet. Cross section of the pellet showed the clear individual coated layers. Non-aggregated pellets with smooth surface and spherical shape were observed.

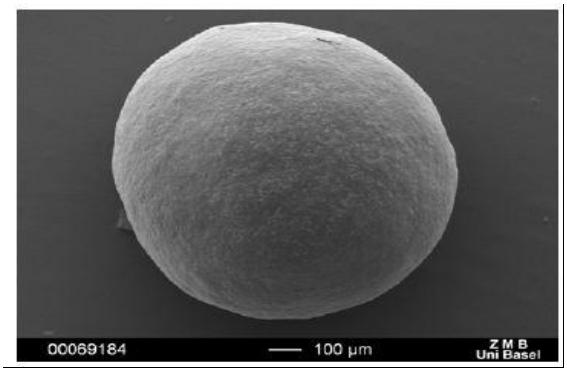

Figure 3. Surface of Enteric Coated Pellet

3.3 Drug release studies

Based on the observations, it can be concluded that the formulated delayed release oral disintegrating tablets of lansoprazole using widely accepted and physiologically safe polymers and other excipients was capable of exhibiting delayed release properties for a period of 2hrs (Figure 4 and 5). Delayed release pellets were prepared by dispersion layering palletization technique on sugar spheres. These drugs layered pellets were seal coated and then enteric coated to protect the drug from gastric fluid [10, 11].

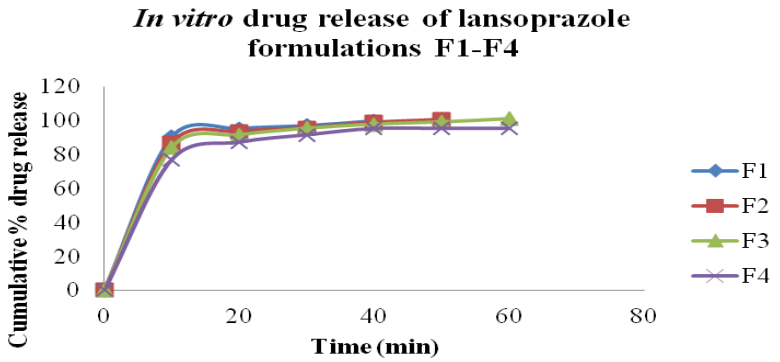

Figure 4: *In vitro* Drug Release Profile of Lansoprazole from Formulations (F1 to F4)

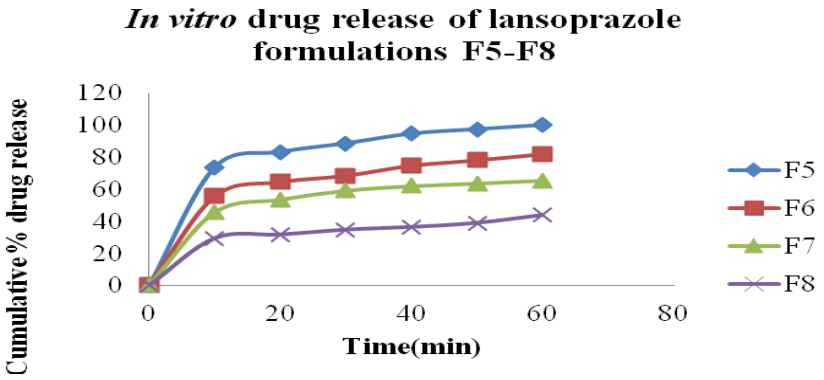

Figure 5: *In vitro* Drug Release Profile of Lansoprazole from Formulations (F5 to F8)

3.3 Drug release kinetics

The *in vitro* drug release data when modelled into various mathematical equations revealed that the drug release followed first order kinetics and Fickian mechanism of drug release as evident from the higher R^2 values [12-14] and the results are shown in Table

Table 5. Release kinetics Profile of Formulation (F1-F8)

Formulation	Zero order		First order		Higuchi		Korsmeyer - peppas		Hixson -crowell	
	R^2	K	R^2	K	R^2	K	R^2	N	R^2	K
F1	0.957	-0.301	0.920	0.138	0.981	2.897	0.988	0.138	0.935	0.049
F2	0.935	-0.325	0.924	0.0875	0.976	3.419	0.992	0.178	0.977	0.042
F3	0.929	-0.310	0.901	0.0736	0.961	3.527	0.991	0.199	0.996	0.038
F4	0.969	-0.412	0.894	0.0690	0.957	4.698	0.986	0.279	0.995	0.036
F4a	0.977	-0.407	0.903	0.069	0.960	5.336	0.985	0.321	0.883	0.053
F4b	0.987	-0.515	0.920	0.064	0.968	5.817	0.986	0.354	0.896	0.051
F5	0.978	-0.516	0.947	0.0690	0.987	5.804	0.997	0.346	0.996	0.040
F 5a	0.9655	-0.513	0.8366	0.0898	0.9929	5.7303	0.9949	0.3422	0.9388	0.046
F 5b	0.9678	-0.570	0.8782	0.0831	0.9961	6.3371	0.9982	0.3872	0.9598	0.0465
F 5c	0.953	-0.591	0.950	0.0644	0.981	6.606	0.982	0.405	0.920	0.052
F6	0.974	-0.511	0.881	0.0230	0.993	5.691	0.995	0.428	0.992	0.018
F7	0.900	-0.378	0.769	0.0138	0.961	4.297	0.986	0.406	0.928	0.010
F8	0.975	-0.273	0.765	0.0069	0.911	2.494	0.938	0.414	0.965	0.005

4. Conclusion:

In this study lansoprazole delayed release oral dispersible tablets were prepared by using Eudragit L 30 D 55 as an enteric coating polymer. The study successfully formulated delayed-release oral dispersible tablets of lansoprazole using Eudragit L 30 D 55 as an enteric coating polymer, demonstrating sustained delayed release for up to 2 hours through a well-established dispersion layering palletization technique.

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