Development and Characterization of Lansoprazole Fast Dissolving Tablets

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Running Title: Formulation and Evaluation of Oral Disintegrating Tablets for Lansoprazole

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Abstract

Objective: The purpose of presentinvestigation to formulate, characterize the fast dissolving tablets (FDT) for Lansoprazole. Lansoprazole,a proton pump inhibitor.It mainly used for the effective management of peptic ulcer. It is having very low solubility in GI fluid, which results in to poor bioavailability after oral administration. So there is a strong need to formulateLansoprazole Solid Dispersion. Where there is in imbalance between mucus layer and acid secretion it causes ulceration.In this condition, quick actions are required. Hence need to formulate suitable dosage forms likemouth dissolving/disintegrating tablet, to achieve reliable bioavailability and enhance patient compliance.

Methods:FDT formulations of Lansoprazole were prepared usingdifferent quantities of Ac-di-sol&Polyplasdone employed as Superdisintegrants by Direct Compression technique. Ninetrials were formulated and evaluated for Pharmaceutical Product Performance.

Results: Results shows that all the formulations were lie within the acceptance criterion and the *In-vitro* dissolution profiles were subjected to kinetic modeling.

Conclusion: Formulation (F_1) containing6 mg of Ac-di-sol&6mg of Polyplasdone was found to be best one among all and also similar to the Marketed product (**PREVACID-15**) (f2= 75.03, f1= 3.41) to marketed product. Formulation (F_1) follow zeroorder, whereas release mechanism found to be nonfickian type (n= 0.509).

Keywords: Lansoprazole, superdisintegrants, Polyplasdone , Ac-di-sol , Non-Fickian Diffusion.

1. INTRODUCTION

Oro Dispersible Tablets (FDT) occupy special role in pharmaceutical market. Oral dissolving tablets, melt-in mouth tablets were used frequently in the place of FDT (RK gunda et al., 2018).

Rapid disintegrating tablets can be readily available for disintegration, they breakdown in the mouth region within 60 seconds. Based on the method of manufacturing those exhibits variations in characteristic organoleptic properties such as sweetness/ taste masking and improved palatability. They also exhibit modulations in quality control; parameters such as breaking index, delivery of drug from formulation, stability, Clinical outcome. Many methods available for the preparation of FDTs , popular methods include cotton candy process, granulation techniques, named technologies (Durasolv, Orosolv), spray drying, trituration, molding, lyophilization/ freeze drying, mass extrusion (Raghavendra G et al.,2016).

Lansoprazole is a Proton Pump Inhibitor, anti-secretory agent. It was widely used in the management of Peptic Ulcers.

One of the major problems with this drug is its very low solubility in GI fluid, which results in to poor bioavailability after oral administration.63 so there is a strong need to formulate Lansoprazole Solid Dispersion. Where there is in imbalance between mucus layer and acid secretion it causes ulceration. In this condition, quick actions are required. Hence need to formulate suitable dosage forms like mouth dissolving/disintegrating tablet, to achieve reliable bioavailability and enhance patient compliance. (Amrutkar PP et al., 2010; VishalShelke et al., 2020; ArtiChourasiya et al., 2021)

An attempt was made to achieve enhanced drug release from the dosage form by employing various concentrations of combination super disintegrants (Ac-di-sol, Polyplasdone) by formulating the Fast dissolving tablets for Lansoprazole. Among variousmethods of manufacture techniques available, Tablets by Direct Compression techniques has unique nature in the form of less time consumption, rapid production, economy in the operational management (Gundaet al.,2016).

2. MATERIALS AND METHODS

2.1. Materials

Lansoprazole was a gift sample procured from Meditech Pharma Pvt Ltd, India. Avicel,Polyplasdone, Ac-di-solwere procured from National Scientifics, Guntur. Other excipients were procured from HighChemie Ltd,vadodara.

2.2.1*Preparation of Lansoprazole Solid Dispersion (SD) by Melting Method*

Lansoprazole FDT were manufactured as per direct compression method.PEG 6000 was melted in a beaker on a water bath maintained at 50- 60°C. Required amount (D: E in 1:1) of the drug was then added to molten PEG 6000 and mixed thoroughly for 5 min. The molten mixture was cooled rapidly by placing it in an ice bath for about 5 min and solidified. The hardened

mixture was powdered, sieved through an 80-mesh screen, packed and stored in desiccators for further estimation.

2.2.2*Preparation of Lansoprazole Fast Dissolving Tablets*

LansoprazoleFDTwere manufactured as per direct compression method. The formulae presented as Table 1. To obtain the uniform mixed fine blend, all the contents were subjected to sifting using 40 mesh (#40). Lubricants were screened through #80, mix them with above mixture and compressed to get FDT with the help of Tabletminipress (8 stations) using 8 mm circular punches. Obtained tablets were subjected to IPQC tests. Final tablets were transferred toairtight, light resistance containers for storage and further processing (Raghavendra Kumar Gunda et al., 2017).

2.3.Evaluation of Lansoprazolefast dissolving tablets

2.3.1.Hardness

It was carried out with the help of Monsanto Tablet Hardness Tester (Raghavendra Kumar Gunda et al., 2020).

2.3.2.Friability/ Durability

Twenty tablets were weighed (cumulatively) recorded as W_0 (Initial weight). Then the tablets were subjected to dedusting using Roche Friabilator for 4 min with a rotation rate of 25 rpm and weight was noted as Final weight (W). Percentage friability was determined from following equation. (%Friability ≤1).

$$\textbf{Friability (\%)} = (W_0 - W) / W_0 \times 100$$

2.3.3.Assay

20 tablets were selected on the unbiased manner andpulverized. The powder equivalent to 100 mg Lansoprazole was weighed and transferred to 100 mL volumetric flask containing 60 mL

ofmethanol and sonicated for 10 min to solubilise the drug completely then dilute the methanolic solution with water to make up the final volume. From that prepare further dilution of 2 mL aliquot in 100 mL of 0.1 N HCl. The obtained solution was filtered through Whatman filter paper and absorbance of solution as measured at 284 nm with the help of UV-Visible spectrophotometer.

2.3.4.Thickness

Thickness was determined with the help vernier calipers (Manchineni PR et al.,2020).

2.3.5.Wetting time

Tablets to be tested for Determination of wetting time were placed on a petridish containing paper soaked in 5mL of distilled water (2.5inch internal diameter). Time taken by the tablet to wet was recorded in seconds.

2.3.6.*In-vitro* Dissolution Study

LansoprazoleFDT subjected to dissolution test with the help of USP XXIII type-II tablet dissolution test apparatus using 900 ml of pH 6.8bufferas per official method specified in monograph. Absorbance for samples was noted at 284 nm using UV Visible spectrophotometer (after suitable dilutions if necessary).

2.3.7. Kinetic modeling of drug release

The dissolution profile of all the formulations was subjected to kinetic modeling (Higuchi et al., 1963; Peppas NA et al.,1985).

2.3.8. Disintegration test

This test was performed as per the provisions of modified disintegration test for tablets. A cylindrical vessel with 10 # was placed in such way that only 2 ml of medium would be placed below the sieve.Disintegration time was recorded (Raghavendra Kumar Gunda et al., 2016).

3. RESULTS AND DISCUSSION

9 Lansoprazolefast dissolving tabletsformulations were prepared by direct compression method using various proportions of super disintegrants combination as per the formulae presented in Table 1. Developed formulations were evaluated for pharmaceutical product performance tests. Data was presented in Table 2.

All tablets found to have good mechanical strength and less friable. The prepared tablets were within the standard limits for uniformity of weight as well as drug content uniformity.

Wetting time for all the formulations varied from 26.5±2.29 to 43±1.9 sec. The Disintegration Time of tablets was in the range of 33±1.75 to 63.5±1.29sec and the same was represented as Fig. 1-2.

Dissolution profiles of Lansoprazolefast dissolving tablets were well fit to kinetic modeling, results presented in Table 3 and the same was shown in Fig. 3-6 .

Based on the desirability, F_1 is considered as best formulation among all batches. F_1 composed of both Ac-di-sol and polyplasdone in equal quantity i.e6 mg each, produced promising dissolution characteristics, which helps in meeting the purpose of research by faster disintegration& rapid dissolution (optimum delivery of drug from dosageform). Data for derived kinetic parameters were summarized in Table 4.

The effect of combination superdisintegrants on the wetting time, release profile were studied with the help of Response surface methodology using Sigmaplot software. Contour plots were shown asFig. 7-11.F_1 is compared with Marketed product **(PREVACID-15)** tablets, shows similarity **f2= 75.03;f1= 3.41**and the same was presented as Fig. 12.**.**

4. CONCLUSION

The current research investigation focuses about influence of utilization of superdisinterants such as Polyplasdone and ac-di-sol for the development of LansoprazoleFDT.F_1 follows zero order type of kinetics, higuchi type model where as the mechanism of drug release follows nonfickian. On the basis of evaluation parameters, the optimized formulation F_1 may be used for the effective management of reflux esophagitis or gastroesophageal reflux disease (GERD), Zollinger Ellison syndrome.

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Table 1: Formulae for the Preparation of Lansoprazole Fast dissolving tablets

Name of Ingredients	Quantity of Ingredients per each Tablet (mg)								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Lansoprazole SD (Complex)	60	60	60	60	60	60	60	60	60
Avicel pH 102	62	64	66	64	66	68	66	68	70

Polyplasdone	6	6	6	4	4	4	2	2	2
Ac-Di-Sol	6	4	2	6	4	2	6	4	2
Aspartame	10	10	10	10	10	10	10	10	10
Aerosil	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Total Weight	150	150	150	150	150	150	150	150	150

Table 2: Post-Compression Parameters

S.No	Formulation Code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Average Weight (mg)	Drug Content (%)	Wetting Time (sec)	Disintegration Time (sec)
1	F_1	2.75±0.25	2.4±0.02	0.625±0.6	149.32±0.45	98.605±1.15	26.5±2.29	33±1.75
2	F_2	2.8±0.2	2.45±0.02	0.635±0.38	149.85±0.95	98.51±2.04	30±2.25	39±2.5
3	F_3	2.9±0.25	2.45±0.021	0.605±0.28	148.2±0.55	98.21±1.65	32.5±2.01	47±2.1
4	F_4	2.7±0.26	2.4±0.013	0.645±0.19	150.04±1.1	98.605±1.31	33±1.9	41±1.6
5	F_5	2.75±0.21	2.45±0.013	0.655±0.28	150.11±0.54	98.51±2.18	36.5±1.8	47±2.29
6	F_6	2.85±0.27	2.45±0.016	0.67±0.07	149.18±0.89	98.21±1.79	39±1.75	55±1.9
7	F_7	2.75±0.3	2.45±0.015	0.655±0.4	150.85±0.76	96.785±1.6	37±1.55	49.5±1.05
8	F_8	2.8±0.25	2.5±0.015	0.665±0.3	150.81±0.15	96.69±2.48	40.5±2.1	55.5±1.9
9	F_9	2.9±0.3	2.5±0.018	0.68±0.32	150.27±0.44	96.39±2.08	43±1.9	63.5±1.29

Table 3: Statistical Parameters

S.NO	Formulation Code	Statistical Parameters											
		Zero order			First order			Higuchi			Korsmeyer-peppas		
		a	b	r	a	b	r	a	b	r	a	b	r
1	F_1	16.422	1.512	0.961	2.144	0.027	0.938	0.729	12.774	0.999	1.087	0.509	0.997
2	F_2	16.253	1.486	0.961	2.087	0.023	0.963	0.642	12.563	0.999	1.082	0.508	0.997
3	F_3	15.874	1.461	0.961	2.053	0.020	0.979	0.702	12.343	0.999	1.072	0.509	0.997
4	F_4	15.968	1.475	0.962	2.083	0.022	0.958	0.732	12.457	0.999	1.076	0.509	0.997
5	F_5	15.799	1.449	0.961	2.054	0.020	0.971	0.645	12.246	0.999	1.072	0.507	0.997
6	F_6	15.423	1.424	0.962	2.032	0.018	0.982	0.703	12.025	0.999	1.061	0.509	0.997
7	F_7	15.927	1.450	0.960	2.060	0.020	0.963	0.555	12.257	0.999	1.077	0.505	0.997
8	F_8	15.757	1.424	0.960	2.038	0.019	0.972	0.469	12.046	0.999	1.073	0.503	0.997
9	F_9	15.378	1.399	0.960	2.021	0.017	0.982	0.530	11.825	0.999	1.061	0.505	0.997

Table 4: Dissolution/ Kinetic Parameters

S.NO	Formulation Code		Kinetic Parameters			
		$t_{10\%}$(Min)	$t_{1/2}$ (Min)	$t_{90\%}$(Min)	Wetting Time (Sec)	Disintegration Time (Sec)
1	F_1	1.696	11.160	37.085	26.5	33
2	F_2	1.990	13.091	43.501	30	39
3	F_3	2.256	14.839	49.310	32.5	47
4	F_4	2.051	13.492	44.834	33	41
5	F_5	2.285	15.036	49.965	36.5	47
6	F_6	2.526	16.616	55.215	39	55
7	F_7	2.235	14.707	48.871	37	49.5
8	F_8	2.456	16.160	53.700	40.5	55.5
9	F_9	2.690	17.698	58.810	43	63.5

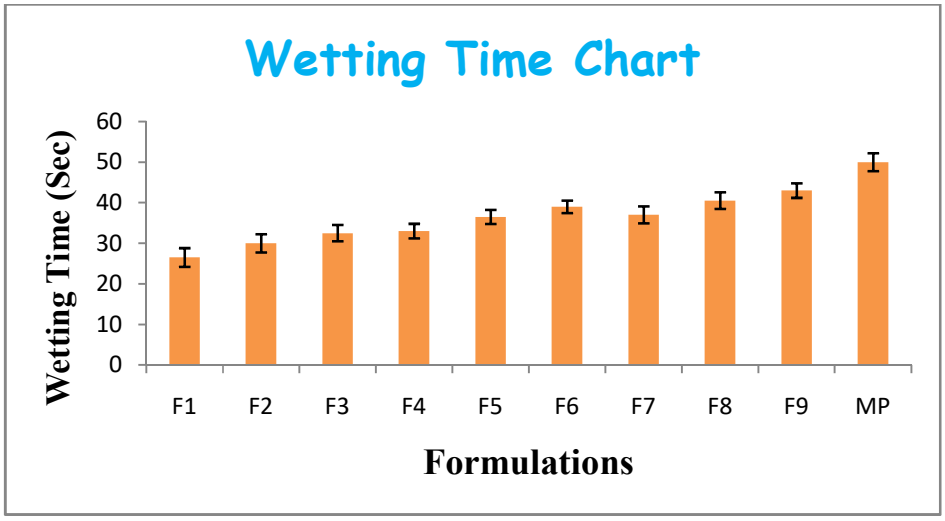

Fig.1 Wetting Time Chart

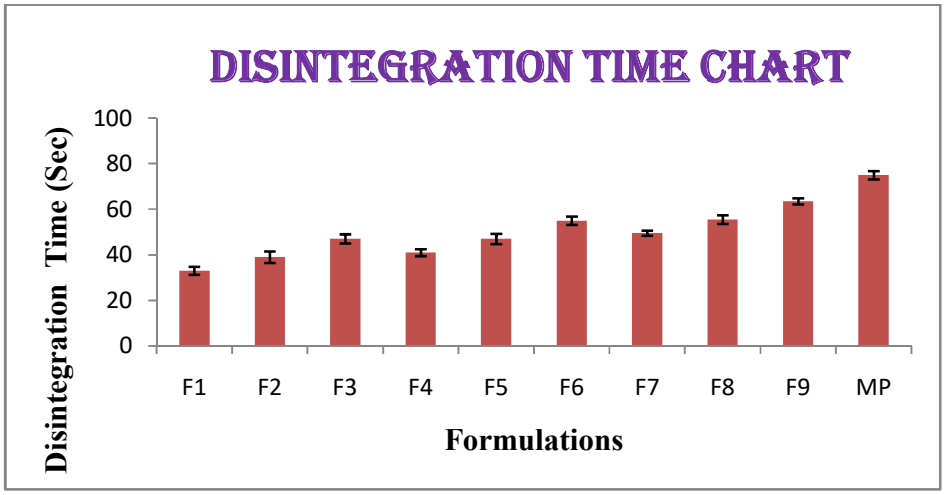

Fig.2 Disintegration Time Chart

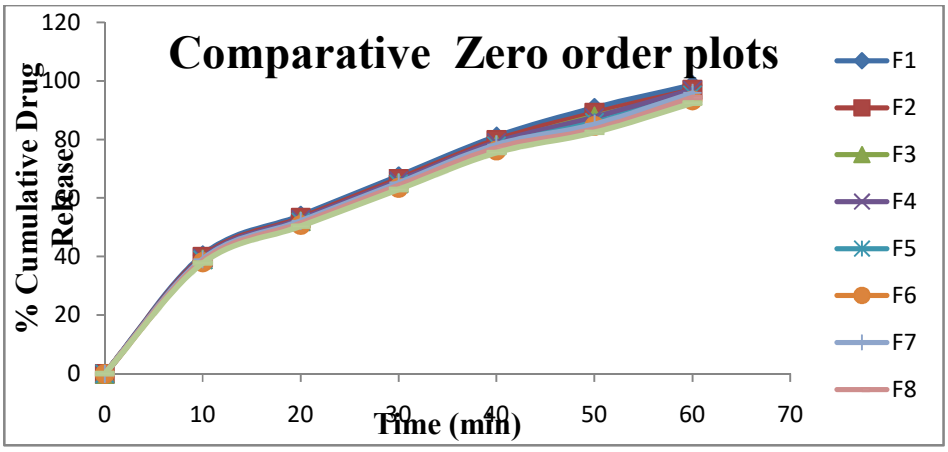

Fig.3 Comparative Zero order plots

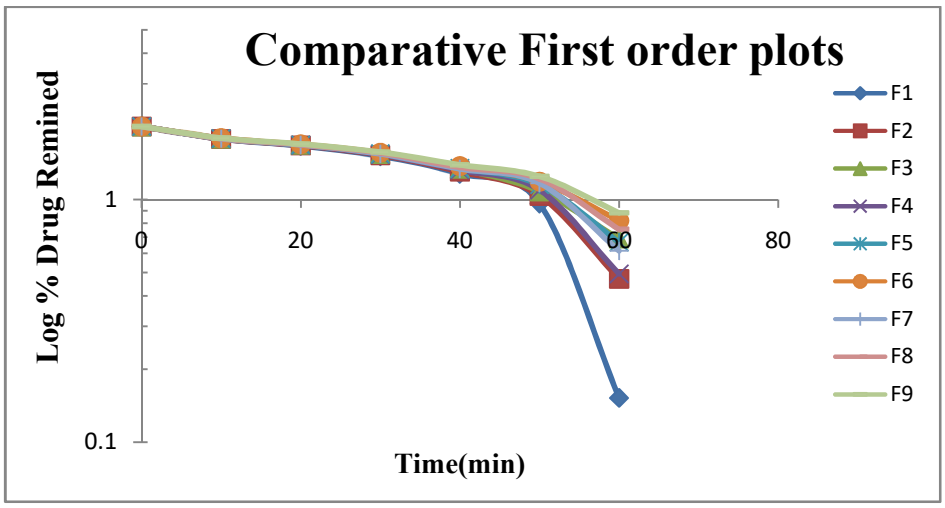

Fig.4 Comparative First order plots

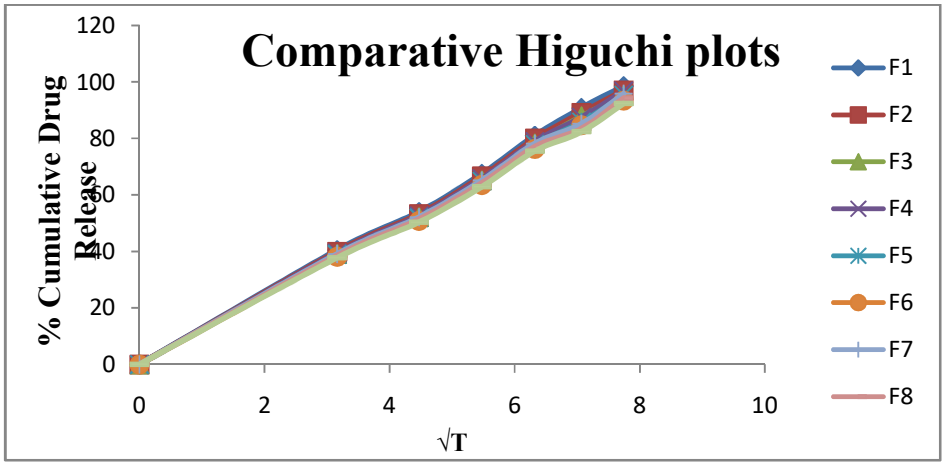

Fig.5 Comparative Higuchi plots

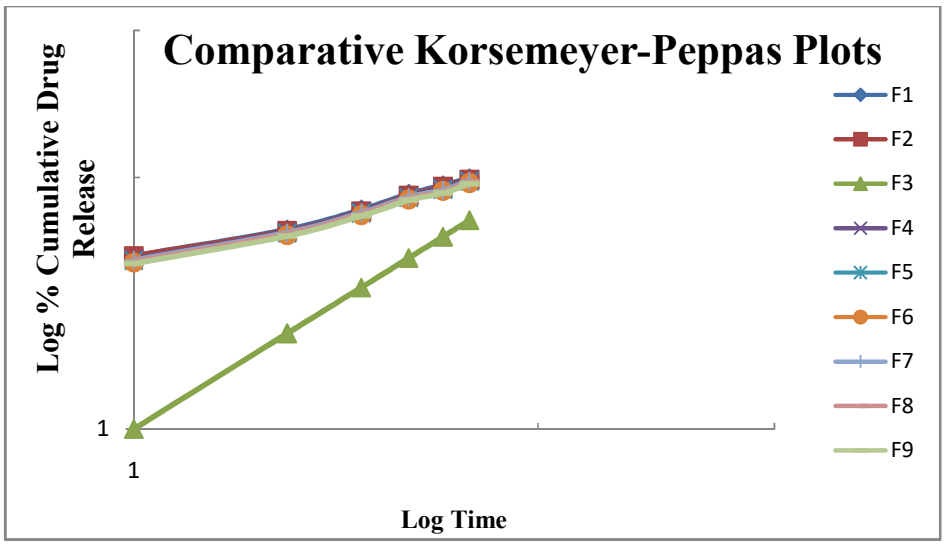

Fig.6 Comparative Korsmeyer-Peppas plots

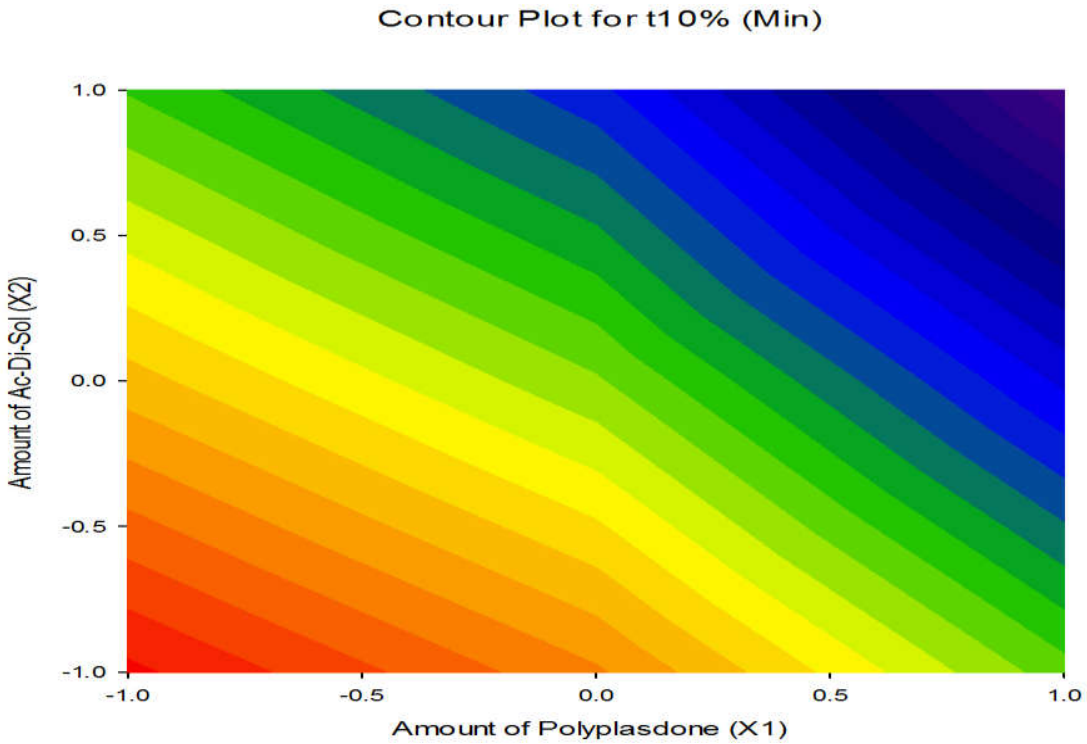

Fig.7 Contour Plot For $t_{10\%}$

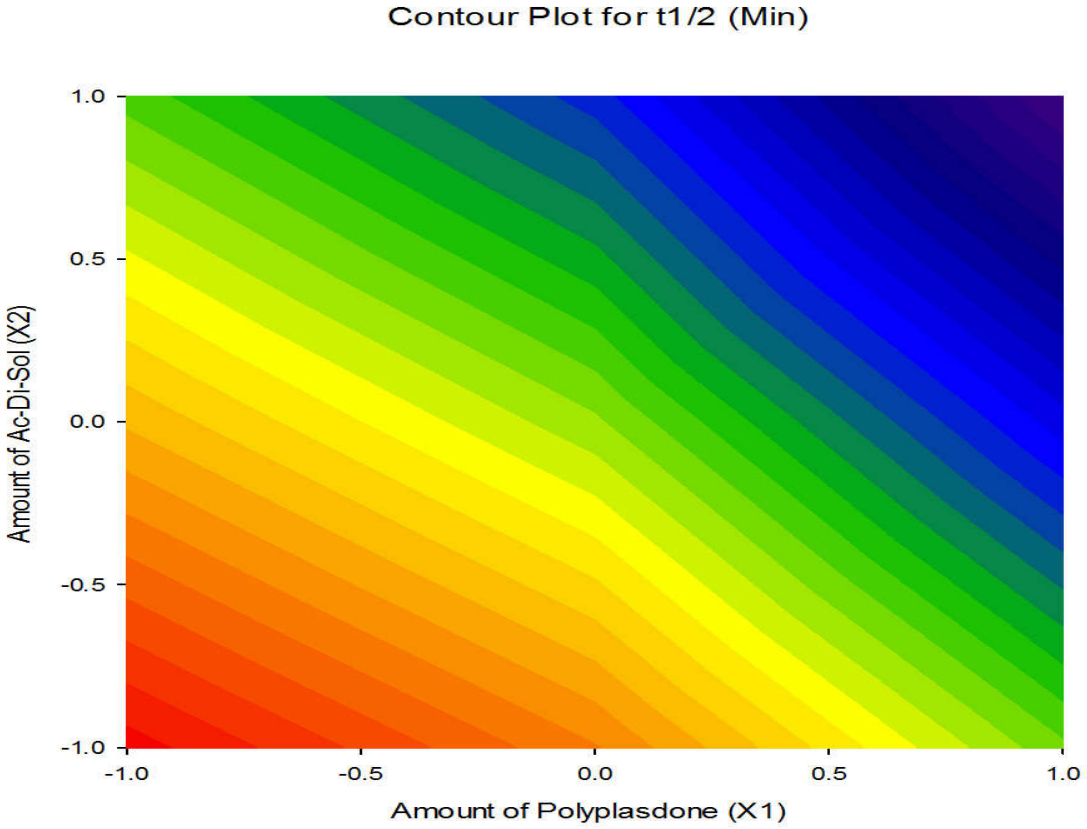

Fig.8 Contour Plot For $t_{50\%}$

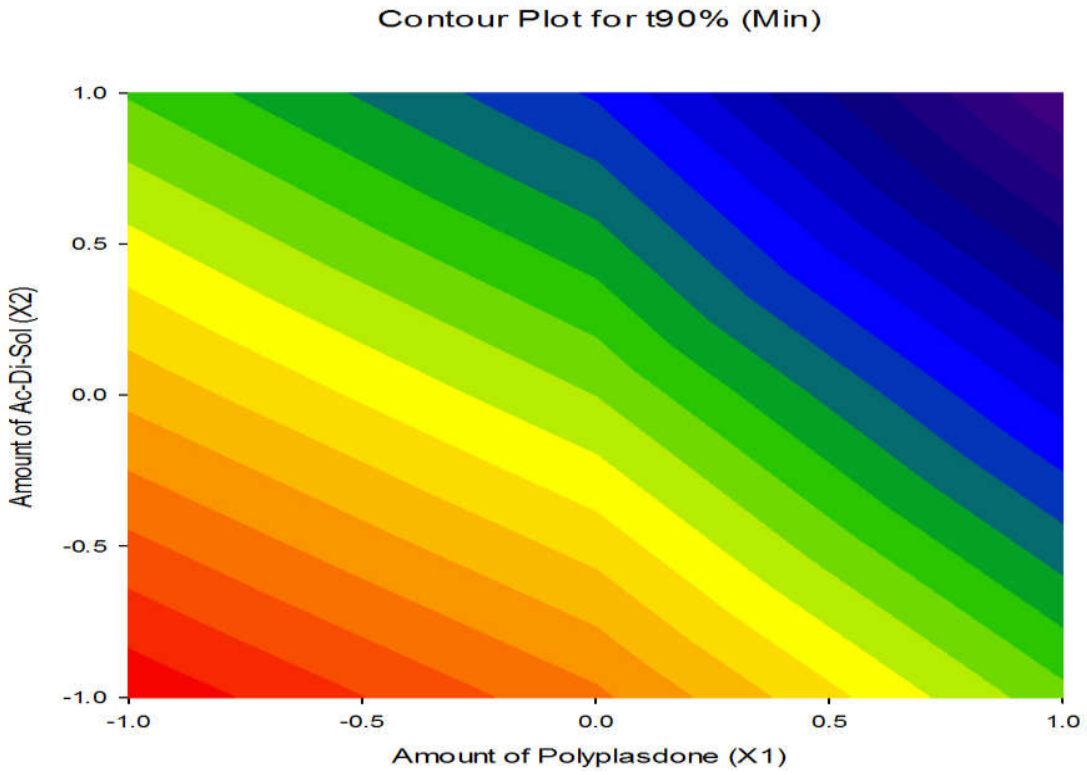

Fig.9 Contour Plot For $t_{90\%}$

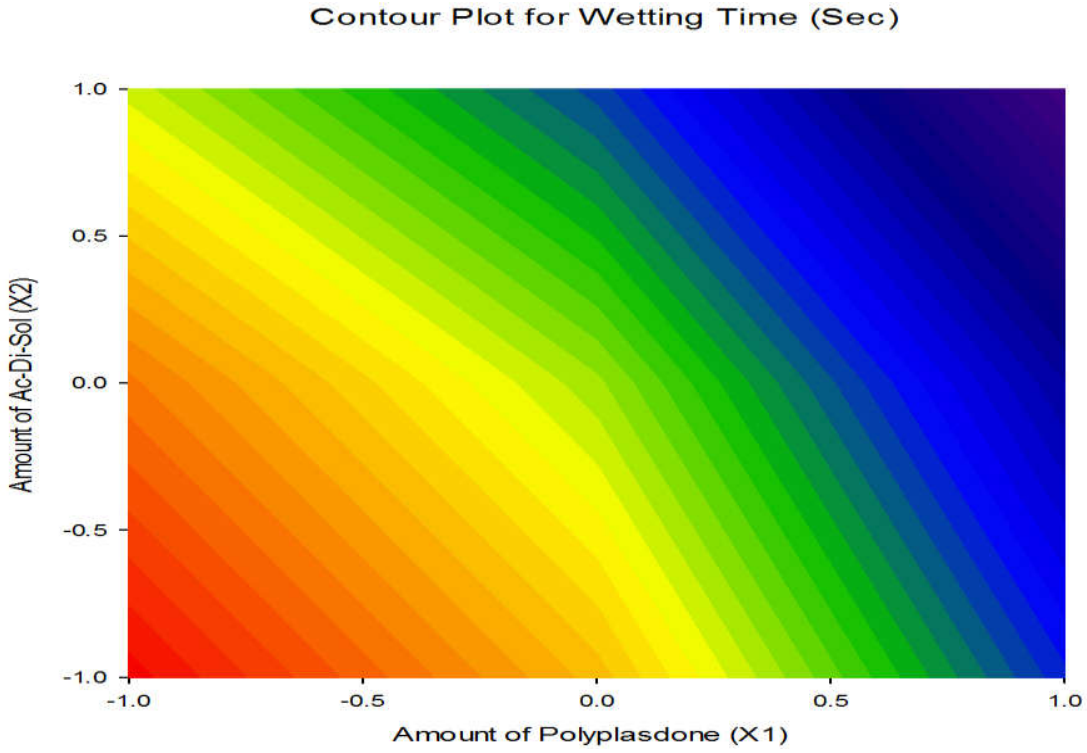

Fig.10 Contour Plot for Wetting Time

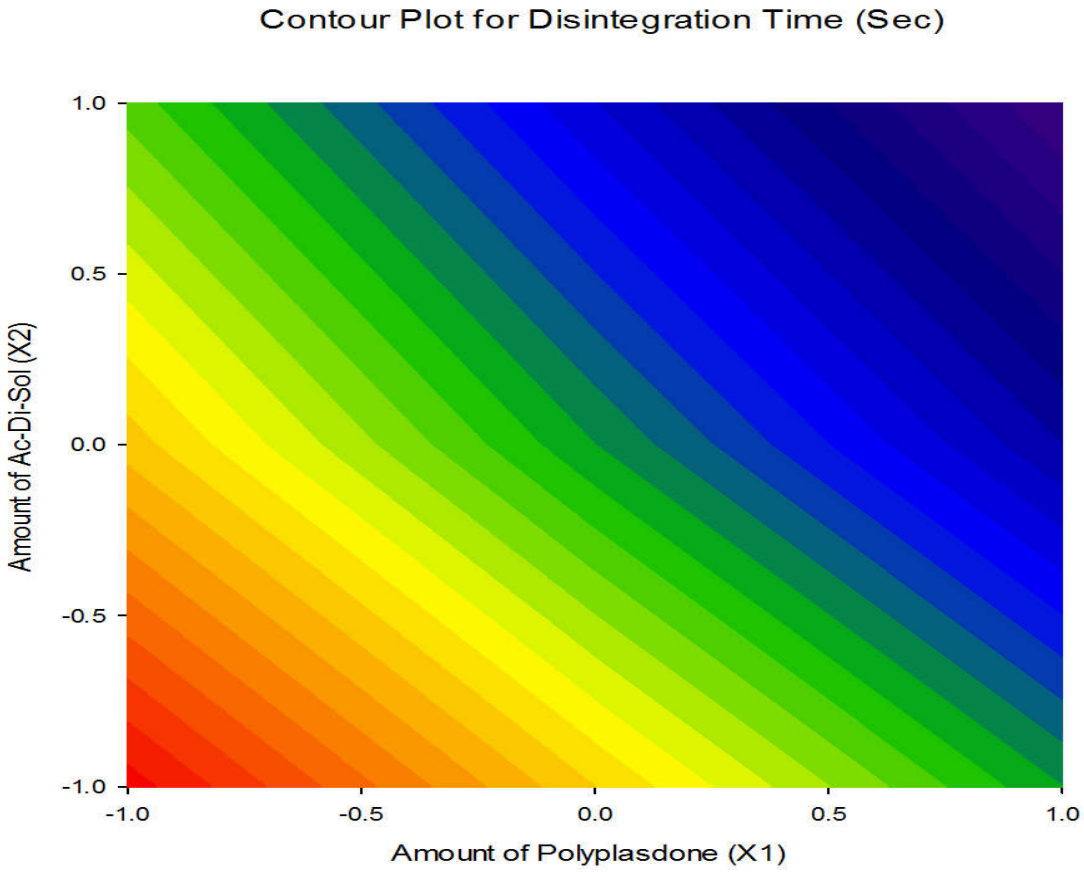

Fig.11 Contour Plot for Disintegration Time

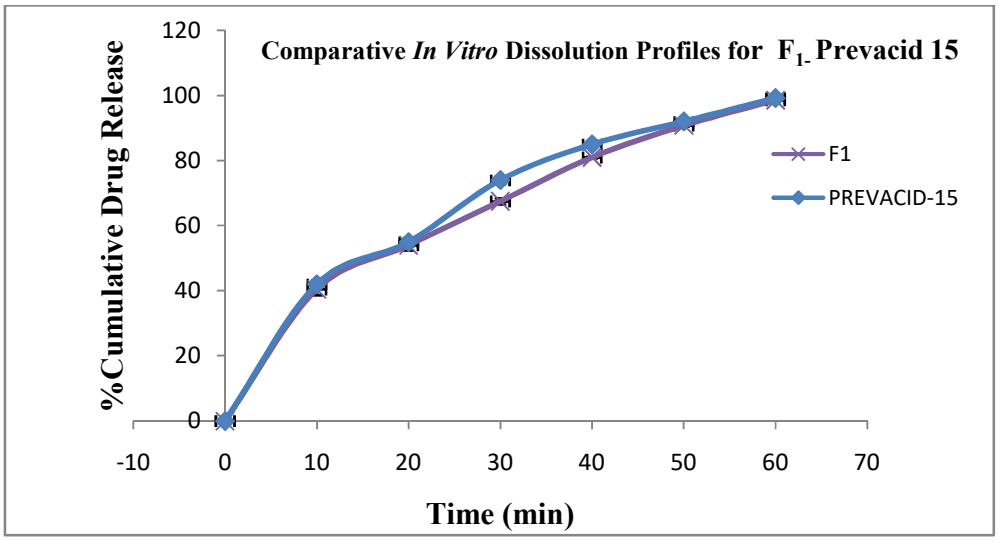

Fig.11 Comparative *In-vitro* Dissolution Profiles for F_1, Prevacid-15