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FORMULATION AND EVALUATION OF MOUTH DISSOLVING LANSOPRAZOLE TABLET

Uma Shankar Mishra*, Prof.Dr.S.K.Prajapati, Dr.P.Bhardwa

Institute of Pharmacy Bundelkhand University Jhansi.

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***Correspondence for Author**
Uma Shankar Mishra
Institute of Pharmacy
Bundelkhand University
Jhansi.

ABSTRACT

In the present investigation of research is oriented through increasing safety and efficacy of existing drug molecule through novel concept of oral drug delivery Lansoprazole is a synthetic steroid that has an Anti-Ulcer Agents, Enzyme Inhibitors ,Proton-pump Inhibitors effect. It is used to decrease in Anti-Ulcer Agents various different diseases and conditions. Lansoprazole works by acting within cells to prevent the release of certain chemicals that are important in the immune system. These chemicals are normally involved in producing immune and allergic responses; resulting in Anti-Ulcer Agents .By decreasing the release of these chemicals in a particular area, Anti-Ulcer Agents is reduced. This can help control a wide number of disease states characterized by excessive. Anti-Ulcer Agents. These include severe allergic reactions, Anti-Ulcer Agents of the stomach. Mouth dissolving tablets of Lansoprazole were prepared by Superdisintegrant addition method using Kyron T 314, PolyKoVidone XL, SSG, and Croscarmellose sodium as superdisintegrants at 5-10% w/w, showed minimum time to disintegrate the tablet.(20) The prepared 12 batches were evaluated for organoleptic properties, hardness, friability, weight variation, in vitro dispersion time, wetting time, in vitro drug release studies, in vivo and stability studies. The drug-excipients interaction was checked and found negative through IR. Finally it was concluded that Mouth dissolving tablets oflansoprazole can be successfully formulated by Superdisintegrant addition methods with improved patient compliance.

KEY WORDS: Mouth dissolving tablets, Lansoprazol, Kyron T-314, and PolyKoVidone XL, Direct compression method.

INTRODUCTION[1,5]

Mouth dissolving tablets are solid dosage forms containing drugs that disintegrate in the oral cavity within less than one minute leaving. The convenience of administration and improved patient compliance are important in the design of oral drug delivery system which remains the preferred route of drug delivery inspite of various disadvantages. One such problem can be solved in the novel drug delivery system by formulating "mouth dissolving tablets" (MDTs) which disintegrates or dissolves rapidly without water with in few seconds in the mouth due to the action of superdisintegrant or maximizing pore structure in the formulation To overcome the problems associated with other dosage form which are commonly used to enhance patient compliance like effervescent tablets, dry syrup require intake of water and in the case of chewable tablets patients may experience bitter taste or unpleasant taste of drug. Injections generally are not favored by the patients due to invasiveness. So, the development of an appropriate dosage form is most desirable. One such approach is mouth dissolving tablets. The concept of mouth dissolving drug delivery system emerged from the desire to provide patient with more conventional means of taking their medication. Lansoprazole .2-({[3-methyl-4- (2 ,2, 2-trifluoroethoxy) pyridin-2-yl] methane} sulfinyl)- 1H-1,3 benzodiazole Bioavailability 90% Half-life1.5 (± 1.0) hours The basic aim of the present investigation is to formulate and evaluate mouth dissolving tablets of Lansoprazole which expected to provide the best remedy for patients suffering from hypersensivity reaction and dysphagia especially Anaphylactic Reaction and adjuvant to Adrenaline to stabilize the patients and also to enhance the bioavailability of drug.The present investigation is to prepare fast dissolving tablets of Lansoprazole using Superdisintegrants (Croscarmellose sodium, PolyKoVidone XL, sodium starch Glycolate, Kyron T-314) and study the performance of fast dissolving tablets of Lansoprazole.

MATERIALS AND METHOD[2,3]

Materials[3]

Lansoprazole was obtained as a gift sample from cipla solan Pvt. India Ltd. Microcrystalline cellulose, Sodium Starch Glycolate, Talc was obtained from CDH, New Delhi, India.Croscarmellose Sodium was obtained as a gift sample from Maple biotech Pune. PolyKoVidoneTM was obtained as a gift sample from Gangwal Chemicals Pvt. Ltd. Malad, Mumbai and Kyron T-314, Acryflow-L, Kyron T-114, was obtained as a gift sample from Corel Pharma Chem. Ahmedabad.

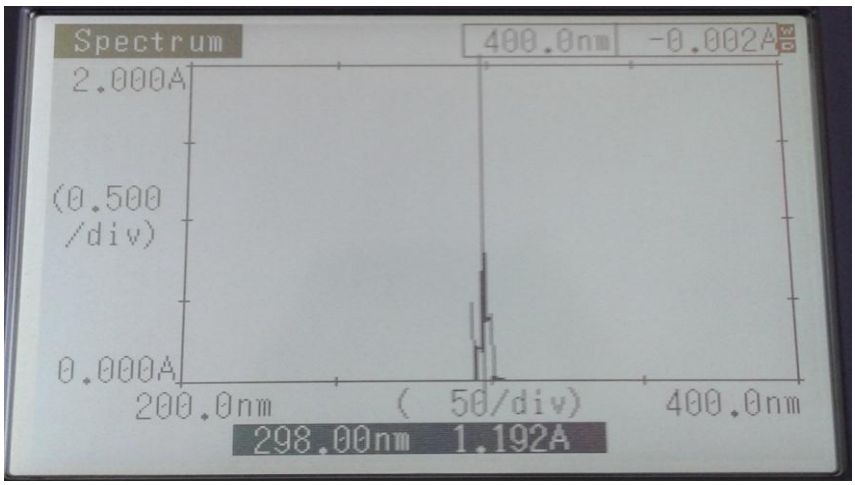
Method of preparation mouth dissolving tablet of Lansoprazole[4]

Lansoprazole tablets were prepared by direct compression method. All the ingredients were accurately weighed and shifted through sieve No. #100. The blend was mixed uniformly for 10 min after that Acryflow L, talc and kyron T-114 were added and mixed properly. Then tablets were compressed on 9 mm standard concave punch, single punch tableting machine. Prepared tablets were evaluated for different parameter like thickness, weight variation, crushing strength, friability and disintegrating time etc.

PREFORMULATION STUDIES OF DRUG[5]

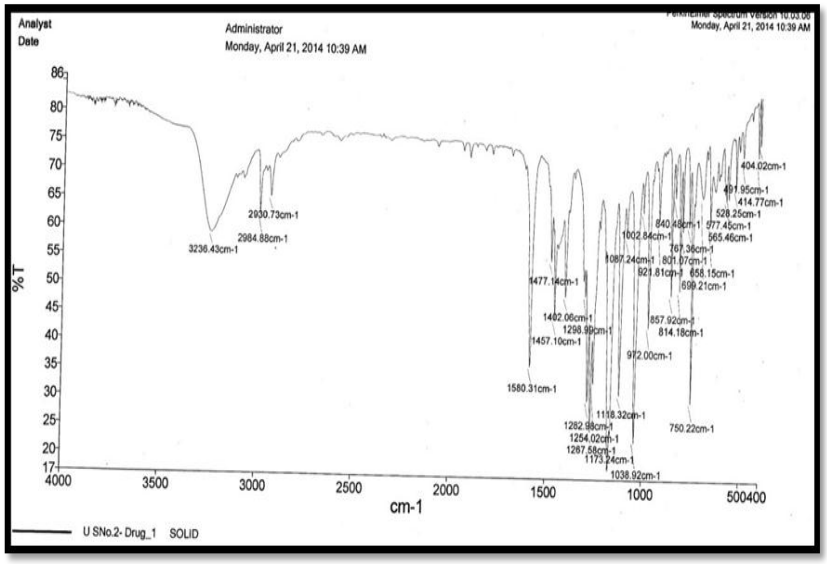
Uv spectral studies (λ_{max}) of Lansoprazole

The UV spectrophotometry has been used for structural validation of drug in the identification studies. Molecules with structural unsaturation are able to absorb light within specific frequency range. The degree of unsaturation coupled with the presence of chromospheres will influence the extent of absorption and whether UV (400-200nm) or visible (800-400nm) light will absorb. The drug was dissolved in methanol to produce 10 µg/ml solutions. This 10 µg/ml drug solution was scanned between 200-400 nm using the UV spectrophotometer (Shimadzu-1800, Japan). The spectrum of the drug is shown in Fig and the value of $\lambda_{max}$is 298 nm.



2 Fourier transform infrared (FTIR) spectral studies of lansoprazole[7]

FTIR spectrum of Lansoprazole was obtained by means of a FTIR spectrophotometer. The potassium bromide dispersion pellet of the given sample of Lansoprazole was prepared and scanning was done by Bruker FTIR spectrophotometer, IIT Kanpur(Measurements were attempted with the accumulation of 8 scans and a resolution of 4 cm^{-1} over the range of 400 to 4000 cm^{-1}). The spectrum is shown in Fig and characteristic peaks are given in Table.



FTIR spectrum of Lansoprazole

Characteristic peaks of FTIR Spectrum of Lansoprazole

Peak cm^{-1}	Groups
767 & 750	Aromatic meta Di-substitution
2984	Aromatic
2930	$-CH_3$
3236.43	NH_2
1347	S=O

EVALUATION OF MOUTH DISSOLVING TABLETS

1 Evaluation of Blend[6]

The quality of tablet, once formulated, is generally dictated by the quality of physicochemical properties of blend. There are many formulation and process variables involved in mixing step and all these can affect the characteristics of blends produced.

2 Angle of Repose (θ)[8,9]

The frictional forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder. It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane. Angle of repose was determined by using funnel method. Powder was poured from funnel, which can be raised vertically until a maximum cone height.

$$\theta = \tan^{-1}\frac{h}{r}$$

Whereas;

θ is angle of repose h is height of pile and r is the radius of the base pile.

3 Bulk Density (Db)[10,11]

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve #20) into a measuring cylinder and the initial volume was noted. From this, the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by.

$$Db = \frac{M}{Vb}$$

Where, M is the mass of powder.

Vb is the bulk volume of the powder.

4 Tapped Density (Dt)[12]

It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 100 times. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by.

$$Dt = \frac{M}{Vt}$$

Where, M is the mass of powder,Vt is the tapped volume of the powder.

5 Compressibility Index (Carr's Consolidation Index)[12,13]

One of the ways of measurement of free flowing powder is compressibility as computed from density of a powder. It was calculated by using the formula.

$$\%\ \textbf{Compressibility} = \left(\frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density}\right) \times 100$$

6 Hausner Ratio

Hausner ratio is an indirect index of ease of powder flow. If the Hausner ratio of powder is near to 1.25, indicates better powder flow. It is calculated by the formula

$$Hausner\ Ratio = \frac{Dt}{Db}$$

Where,

Db = Bulk density of the powder.

Dt = Tapped density of the powder.

Evaluation of mouth dissolving tablets

1 Appearance[14,15]

The uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

Dimension

Thickness and diameter were measured using a calibrated barmier calliper. Six tablets of each formulation were picked randomly and dimensions determined.

2 Hardness test[16]

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Six tablets were randomly picked and analysed for hardness. The mean and standard deviation values were also calculated.

3 Friability test[17,18]

Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This in process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. Permitted friability limit is 1.0 %. Roche friabilator was used to measure the friability of the tablets. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets were exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. It was rotated at a rate of 25 rpm. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively. The percent friability was determined using the following formula.

$$Friability = \left[\frac{W1 - W2}{W1}\right] \times 100$$

Where,

W1 = weight of the tablet before test, *W2* = weight of the tablets after test.

Weight Variation Test[20]

Twenty tablets were weighed individually and all together. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average

weight. The percentage difference in the weight variation should be within the permissible limits (±7.5%). The percent deviation was calculated using the following formula.

$$\text{Percentage Diviation} = \left(\frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}}\right) \times 100$$

Drug Content Estimation

Twenty tablets were weighed and powdered, 20 mg of equivalent of lansoprazole was weighed and dissolved in 100 ml of pH 6.8 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 298nm using UV- spectrophotometer (UV 1800 Shimadzu, Japan).

Wetting time[22,43]

Wetting time of dosage form is related with the contact angle. Wetting time of the mouth dissolving tablets is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. The wetting time of the tablet can be measured using a simple procedure.

A piece of tissue paper folded twice was placed in a small petridish containing 10 ml of PB pH 6.8. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using equation.

$$R = \left(\frac{Wa - Wb}{Wb}\right) \times 100$$

Where,

Wa = weight of tablet after absorption Wb = weight of tablet before absorption

Six tablets from each formulation were analysed performed and standard deviation was also determined.

In vitro dispersion time[23,21]

In vitro dispersion time of prepared tablet was done by dropping the tablet in 10 ml measuring cylinder containing 6 ml of simulated salivary fluid (pH 6.8). Time required for complete dispersion of tablet was measured.

In vitro disintegration time[19]

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined by using modified disintegrating test.

Disintegration test[25]

Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 (simulated saliva fluid) maintained at $37^0 \pm 2^0$C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at $37^0 \pm 2^0$C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

In vitro dissolution studies[41,42]

In vitro drug release of lansoprazole mouth dissolving tablet was determined using USP Dissolution Apparatus II (Paddle type) (Electrolab TDT-08L, India). The dissolution test was performed using 900 ml of Phosphate buffer SSF pH 6.8 at 37 ± 0.5^0C. The speed of rotation of paddle was set at 50 rpm. 2 ml sample were withdrawn at time points of 2, 4, 6, 8, and 10 min and same volume was replaced with fresh media. The samples were filtered and from the filtrate 1ml was taken and diluted to 10ml with pH 6.8 Phosphate buffer. Absorbance of solution was checked by using UV- spectrophotometer (UV 1800 Shimadzu, Japan) at a wavelength of 298 nm and drug release was determined from standard curve.

Comparison of formulation and marketed preparation of lansoprazole[27]

The prepared formulation of mouth dissolving tablets of Lansoprazole (FP3) was compared with the plain drug of lansoprazole.

***In-vivo* studies (in vivo bioavailability studies in rabbits)**[28,29]

The in vivo bioavailability studies in rabbits were performed as per the method reported by Charde et al. The optimized formulation FP3 had shown good disintegration hence was finally selected for in vivo study.The *in-vivo* study was performed as per the guidelines approved by the committee for the purpose of control and supervision of experiments on animals (CPCSEA), ministry of social justice empowerment, and government of India.

The central animal facilities of Institute of Pharmacy, Bundelkhand University provided six young and healthy male albino rabbits with mean weight of 2.5 ± 0.5 kg. The study was conducted with the approval of (**Protocol Approval Number: BU/Pharm/IAEC/13/09**) and

as per guidelines prescribed by Institutional Animal Ethics committee, Bundelkhand University, under the supervision of registered veterinarian.

***Preparation of calibration curves in blood plasma*[30,24]**

The calibration curve of Lansoprazole was prepared in blood plasma by preparing 1 to 10 µg/ml dilutions. The aliquots of 1, 2, 3, 4, 5, 6…….10 ml of stock solution (10 µg/ml) were transferred quantitatively into a series of 10 ml volumetric flasks and volume was made up to10 ml with blood plasma to produce solutions of concentration ranging 1to 10 µg/ml. the absorbance of these solution was determined at λmax (302 nm) against blank (blood plasma). The data were linearity regressed curve.

Experimental design

Rabbits, weighing 2.00-2.50 kg were divided into two groups, each consisting of three animals. Rabbits were kept on fasting 12 hrs before drug administration and until 24 hrs post dosing. Water *ad-libitum* was given throughout the study. The dose selected of lansoprazole was 1.75mg/kg. The first group received oral administration (Plain drug preparation) of 200 mg tablet in blood plasma. The second group received oral mouth dissolving tablet in blood plasma.

***Collection of blood sample*[31]**

For the collection of blood samples, the rabbit artery was dilated by topical application of an alcohol swab. Blood sample were collected by means of a 1 ml syringe fitted with a 25 gauge needle. The needle, with the level in the upright position, was inserted at 25º to 30º angle into the skin and aimed directly into the artery. The needle was lowered until it was almost flush with the skin and aimed directly into the artery. Blood samples of 1.5 ml were collected in the specific time intervals. The blood samples were collected in clean 2 ml centrifuges tubes without anticoagulants. The blood was separated by placing the tubes in a centrifuge 15 minutes at 2000 rpm. Separated serum samples were taken by micro pipette and diluted up to suitable required dilution with phosphate buffer pH 6.8.The plasma drug concentration of lansoprazole was analyzed by UV spectrophotometer at 298.0 nm

Stability Studies[34,40]

Stability is defined as the ability of a particular drug or dosage form in a specific container to remain within its physical, chemical, therapeutic, and toxicological specifications. Drug decomposition or degradation occurs during stability, because of chemical alteration of the

active ingredients or due to product instability, lowering the concentration of the drug in the dosage form

Stability studies as per ICH Guidelines[37]

A systemic approach has been adopted for the presentation and evaluation of the stability information for physical, chemical and biological quality characteristics, including particular properties of the dosage form (dissolution rate for oral solid dosage forms). The guidelines were provided by the European Agency for the Evaluation of Medical Product (Human Medicine Evaluation unit, CPMP/ICH/380/95) (ICH Harmonized Tripartite guidelines, 2003).

Accelerated stability testing[38,39]

The products were also subjected for temperature dependent accelerated studies. The deterioration of active ingredients in the pharmaceutical dosage forms may take place by hydrolysis, oxidation, reduction, recemerization, ring cleavage, decarboxylation, photolysis and pyrolysis. Prediction was based on Arrhenius explanation, which could be applied to enumerate the effect of temperature on degradation.

The degradation rate constant (K) at various elevated temperatures are obtained by plotting some function for residual drug concentration against time. From the slope of the plot, the degradation rate at that particular temperature is obtained. The effect of temperature is given by an equation proposed by Arrhenius.

$$K = Ae^{-Ea/RT}$$

Where,

K is specific rate, A is constant known as a frequency factor, Ea is energy of activation, R is gas constant and T is the absolute temperature.

Accelerated Stability studies[37,32]

The lansoprazole mouth dissolving tablets were subjected for accelerated stability testing at room temperature and 45^0C for 45 days. The Sample were withdrawn after 15, 30 and 45 days and sample were analysed for drug content, disintegration time, crushing strength and time required for complete release of drug. The initial drug concentration was taken as 100%. The dissolution profile of formulation was determined at various time intervals.

RESULT AND DISCUSSION

In the present study, Lansoprazole mouth dissolving tablets were prepared by using synthetic superdisintegrants namely SSG, Croscarmellose, Kyron T-314, and PolyKoVidone XL at 5-10% concentrations.[33,34]

Formulation Chart

INGRIDIENTS	FS1	FS2	FS3	FC1	FC2	FC3	FP1	FP2	FP3	FK1	FK2	FK3
Lansoprazole	20	20	20	20	20	20	20	20	20	20	20	20
Kyron 314	10	15	20	---	---	---	---	---	---	---	---	---
PolyKoVidoneXL	---	---	---	10	15	20	---	---	---	---	---	---
Croscarmellose	---	---	---	---	---	---	10	15	20	---	---	---
SSG	---	---	---	---	---	---	---	---	---	10	15	20
Acryflow L	2	2	2	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3	3	3	3
Kyron 114	3	3	3	3	3	3	3	3	3	3	3	3
Micro-crystalline cellulose up to	200	200	200	200	200	200	200	200	200	200	200	200

Evaluation of Powder (Blend)

Batch Code	Angle of Repose*	Bulk Density*	Tapped Density*	% Compressibility*	Hausner ratio*
FS1	34.16±1.09	0.48±0.01	0.67±0.02	27.16±1.35	1.37±0.01
FS2	33.87±1.54	0.50±0.01	0.71±0.01	26.86±2.46	1.35±0.03
FS3	33.34±2.47	0.53±0.01	0.73±0.02	25.28±2.66	1.31±0.02
FC1	31.62±1.10	0.51±0.01	0.68±0.04	22.06±2.36	1.30±0.03
FC2	32.52±1.62	0.52±0.02	0.65±0.03	20.48±4.10	1.26±0.05
FC3	31.99±0.80	0.54±0.01	0.66±0.02	18.98±1.63	1.24±0.02
FP1	33.31±0.72	0.53±0.03	0.64±0.02	16.65±3.38	1.20±0.05
FP2	31.34±0.74	0.55±0.01	0.65±0.05	14.85±5.65	1.18±0.09
FP3	33.26±0.80	0.56±0.02	0.64±0.03	13.01±2.15	1.17±0.02
FK1	33.74±1.12	0.52±0.02	0.65±0.03	16.97±3.85	1.21±0.03
FK2	34.76±2.87	0.53±0.01	0.64±0.03	15.23±1.74	1.18±0.01
FK3	32.12±0.76	0.54±0.01	0.66±0.02	14.75±2.58	1.17±0.03

The blend of all the batches were evaluated for parameter like angle of repose. The angle of repose was found to be between 31.34±0.74 to 34.76±2.87, this indicates satisfactory flowability. Bulk density was found to be between 0.48±0.01 to 0.56±0.02 g/cm^3 and tapped density between 0.64±0.02 to 0.73±0.02 g/cm^3.

Hausner's ratio was found to be between 1.17±0.02 to 1.37±0.01, lower Hausner's ratio (<1.25) indicate better flow properties than higher one (>1.25) and Compressibility index was

found to be between 13.01±2.15 to 26.86±2.46 , Compressibility index (<15%) show better flow properties than (>25%). All the formulations showed good blend properties for direct compression and hence tablets were prepared by direct compression technology.

Hardness of mouth dissolving tablets varied with various ratios and type of polymers. The hardness of the tablet containing Sodium starch glycolate was lower (5.28±0.64 kg/cm^3) and increased by increase in amount of microcrystalline cellulose and the hardness of PolyKoVidone XL was more(6.78±0.74 kg/cm^3) than other formulation and is also increased by increasing the amount of microcrystalline cellulose.. Friability test of the matrix tablets was performed by using Roche friabilator. The loss in total weight of the tablets due to the friability was in the range of 0.56±0.04 to 0.93±0.06 % and was found to be within the limits of conventional oral tablets stated in the Indian pharmacopoeia (1996).

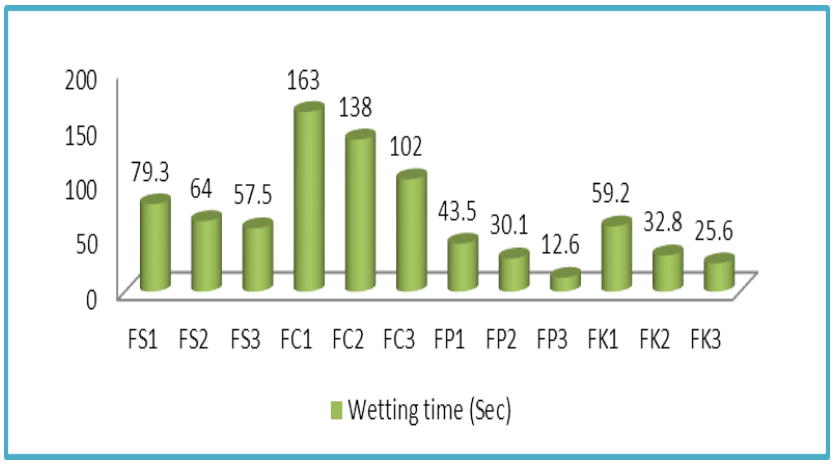
Batch code	Uniformity of Weight #	Drug content uniformity (%)	Friability*	Hardness* (kg/cm^2)	Thickness* (mm)
FS1	201.15±7.24	96.10±2.30	0.76±0.03	5.34±1.15	3.13±0.10
FS2	199.65±7.52	96.57±2.15	0.61±0.04	5.74±1.06	3.28±0.20
FS3	200.15±7.30	97.36±1.89	0.60±.0.03	5.56±1.31	3.32±0.10
FC1	198.35±7.37	95.10±2.26	0.91±0.06	5.28±0.64	3.22±0.09
FC2	198.65±8.42	96.56±2.25	0.78±0.03	5.65±1.87	3.30±0.15
FC3	200.20±7.72	96.69±2.98	0.68±0.04	6.54±0.50	3.19±0.12
FP1	201.50±7.25	97.68±1.80	0.93±0.06	6.78±0.74	3.30±0.11
FP2	198.75±8.72	97.15±2.15	0.87±0.08	6.36±0.65	3.26±0.18
FP3	200.65±8.92	97.68±2.71	0.56±0.04	6.58±0.75	3.32±0.15
FK1	200.35±8.20	97.62±2.20	0.87±0.03	5.72±1.15	3.20±0.12
FK2	201.45±7.42	97.15±1.82	0.73±0.07	6.10±1.30	3.28±0.06
FK3	201.60±8.83	97.22±2.35	0.62±0.06	6.29±0.68	3.12±0.09

In the present study disintegration time of all formulations were found in the range of 22.68±1.88 to 201.61±2.28 sec fulfilling the official requirements (3 min) for mouthdissolving tablets.

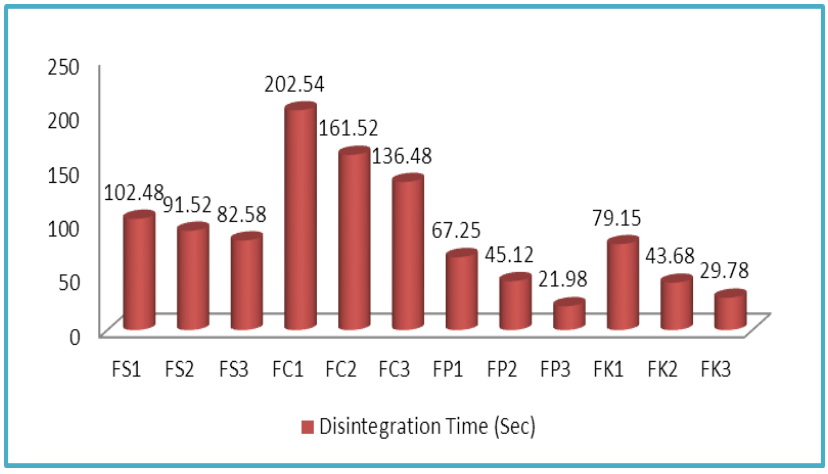
This rapid disintegration of the mouth dissolving tablets were due to penetration of saliva into the pores of tablets, which leads to the swelling of superdisintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablets.

Formulation FP3 was selected as optimized formulation containing PolyKoVidone XL in 10 % concentration.

Batch code	Wetting Time* (Sec)	Disintegration Time*(Sec)	In vitro Dispersion Time*(Sec)	Water absorption ratio*
FS1	79.1±1.29	101.34±2.56	41.52±2.25	220.33±13.89
FS2	65.2±1.51	92.49±3.08	35.66±1.20	241.34±11.21
FS3	56.4±1.24	82.95±4.47	30.56±2.85	263.35±12.64
FC1	75.6±3.89	201.61±2.28	82.38±3.58	180.13±13.43
FC2	29.8±2.84	163.16±4.69	60.58±3.65	201.19±12.67
FC3	40.6±1.90	138.56±1.02	48.11±4.25	217.38±21.36
FP1	43.5±1.16	68.19±3.48	26.45±2.10	160.32±15.32
FP2	30.6±1.16	45.06±2.69	17.58±1.54	186.12±12.38
FP3	11.4±1.32	22.68±1.88	12.21±2.85	191.38±25.68
FK1	62.1±1.42	79.35±1.70	33.12±1.05	165.35±10.08
FK2	31.6±1.85	45.19±3.59	27.25±2.19	181.21±15.55
FK3	25.8±1.35	31.86±1.19	18.38±1.45	195.70±12.26



Wetting time (Sec) of formulations



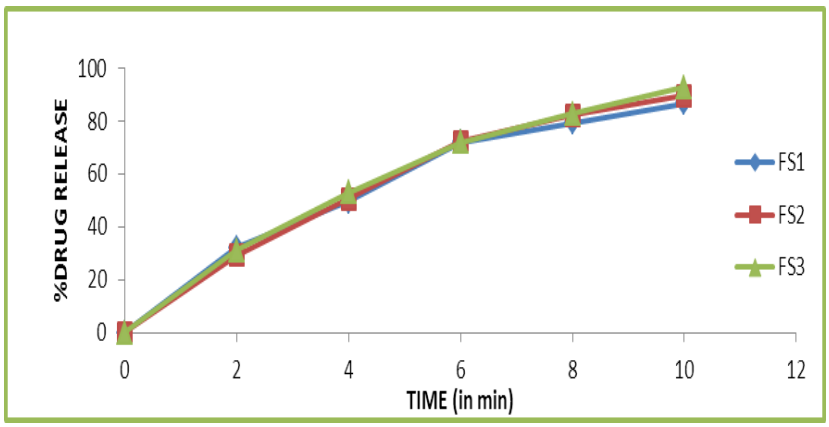
Disintegration time (Sec) of formulations

The disintegration time of optimized formulation was compared with plain drug formulation, the result show that formulated tablet disintegrated in 20 sec as compared to about 60 min for

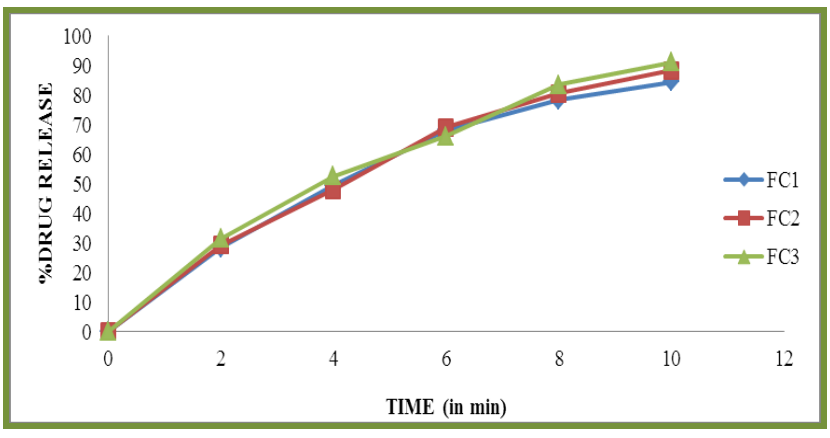
plain drug formulation so FP3 was found to be the best, as this formulation showed less disintegration time.

***In-vitro* drug release studies of the formulations**

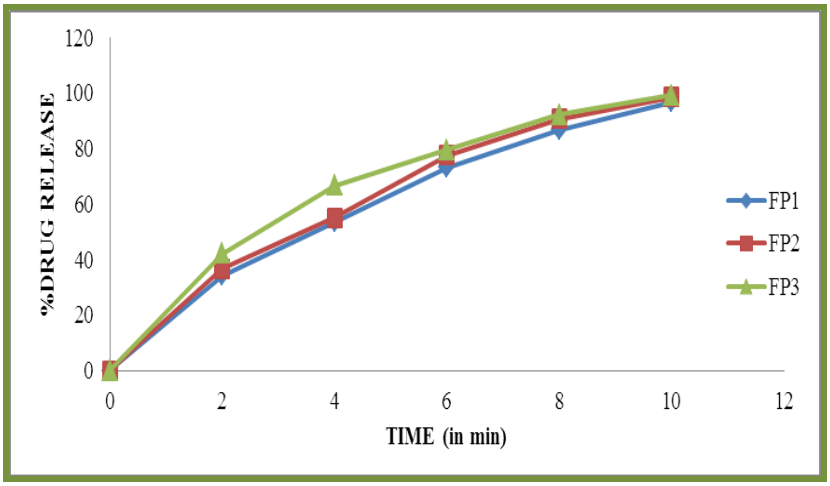
Formulation Code	Cumulative % drug release					
Time (Sec) →	0	2	4	6	8	10
FS1	0	32.05	49.54	72.28	80.48	86.51
FS2	0	31.05	50.55	73.16	83.50	91.53
FS3	0	32.57	52.26	72.66	85.73	93.25
FC1	0	26.24	46.84	67.45	76.53	82.59
FC2	0	27.05	45.73	69.54	78.48	86.43
FC3	0	29.56	50.55	65.51	81.25	89.12
FP1	0	32.26	53.27	72.75	86.51	94.83
FP2	0	35.28	54.86	77.26	90.52	96.45
FP3	0	40.55	65.81	76.98	90.73	98.56
FK1	0	32.86	59.98	74.65	85.35	93.43
FK2	0	37.58	61.19	72.54	86.71	94.54
FK3	0	40.36	64.61	77.76	88.61	96.75



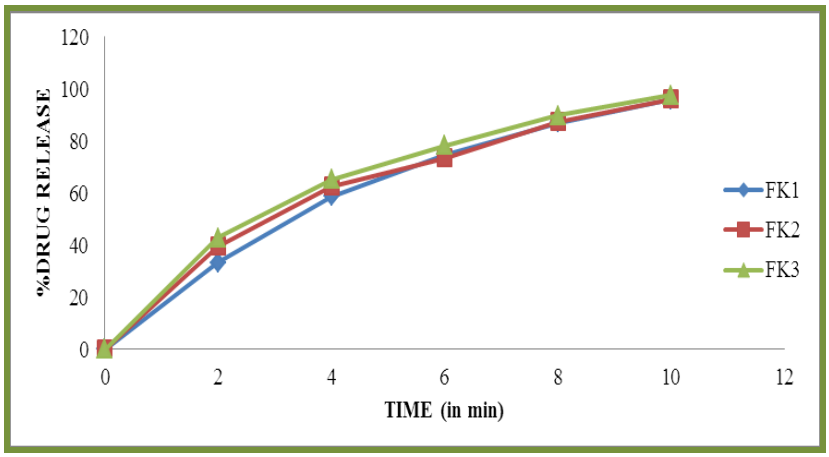
Cumulative % drug release profile of FS1, FS2, FS3



Cumulative % drug release profile of FC1, FC2, FC3



Cumulative % drug release profile of FP1, FP2, FP3



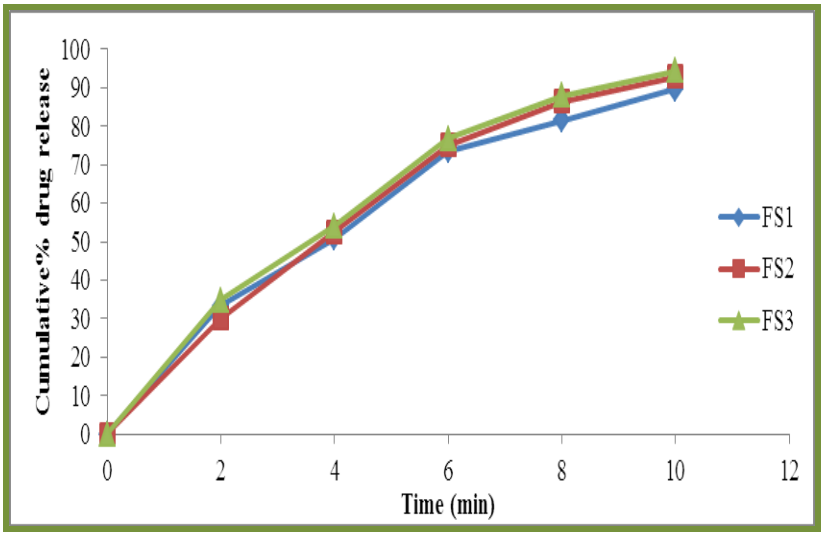
Cumulative % drug release profile of FK1, FK2, FK3

KINETIC DATA TREATMENT OF IN VITRO DRUG RELEASE

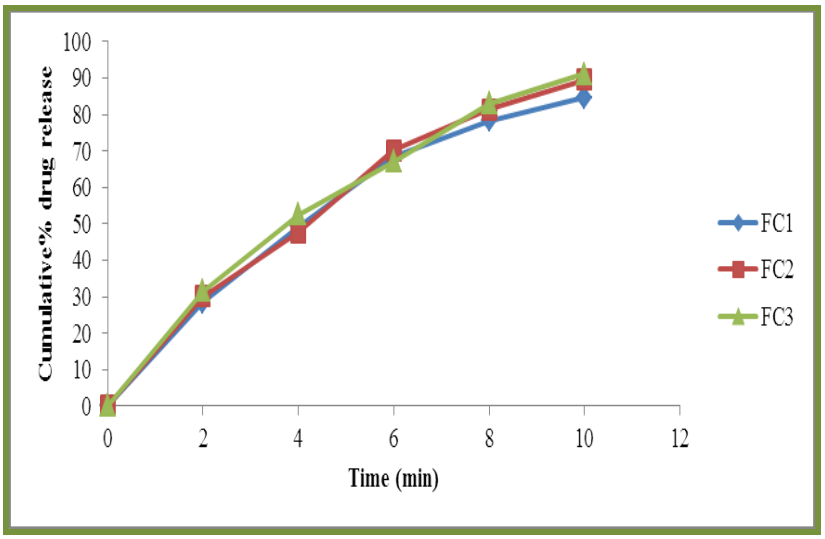
Zero-Order kinetic treatment of mouth dissolving tablet of Lansoprazole

Zero-Order kinetic treatment of dissolution data

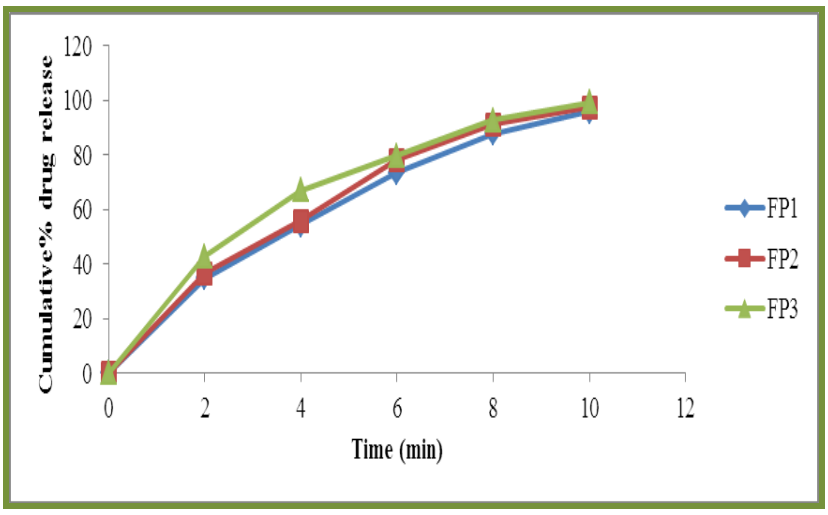
Formulation code	Equation of line	Correlation coefficient
FS1	y = 8.6718x + 10.756	R^2 = 0.9293
FS2	y = 9.2559x + 9.2368	R^2 = 0.9496
FS3	y = 9.2219x + 11.236	R^2 = 0.9513
FC1	y = 8.3506x + 9.106	R^2 = 0.9353
FC2	y = 8.8186x + 8.4714	R^2 = 0.9493
FC3	y = 8.8186x + 9.5412	R^2 = 0.9483
FP1	y = 9.3045x + 10.614	R^2 = 0.9439
FP2	y = 9.5147x + 11.619	R^2 = 0.9332
FP3	y = 9.3018x + 15.167	R^2 = 0.9863
FK1	y = 9.3411x + 10.886	R^2 = 0.9255
FK2	y = 9.2492x + 12.952	R^2 = 0.9147
FK3	y = 9.1181x + 14.818	R^2 = 0.9866



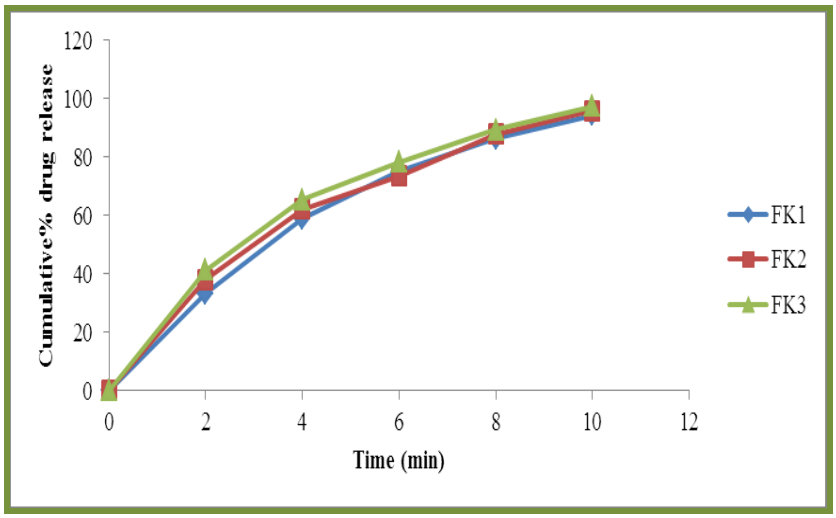
Zero order kinetic treatment of FS1, FS2 and FS3.



Zero order kinetic treatment of FC1, FC2 and FC3.



Zero order kinetic treatment of FP1, FP2 and FP3.

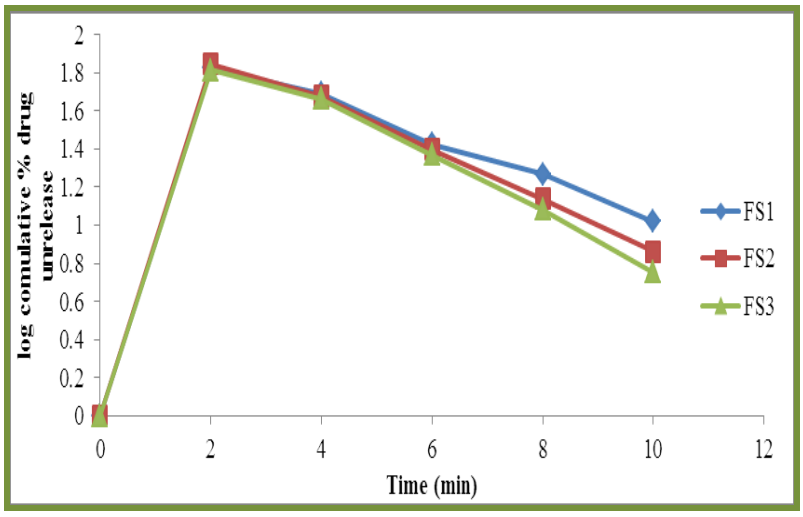


Zero order kinetic treatment of FK1, FK2 and FK3.

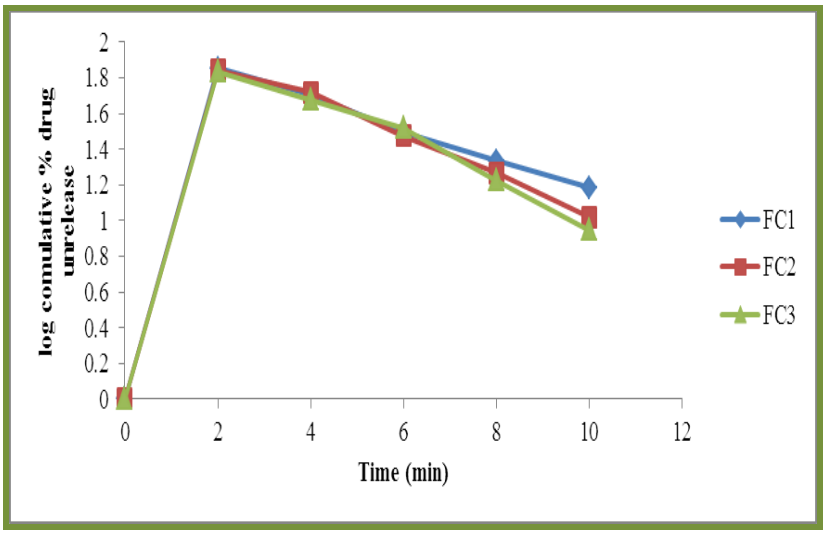
First-Order kinetic treatment of mouth dissolving tablet of Lansoprazole

First-Order kinetic treatment of dissolution data.

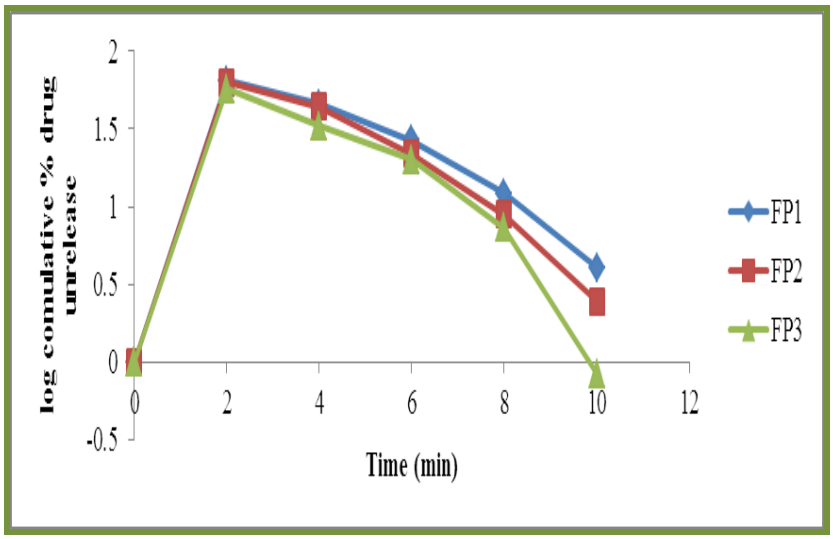
Formulation code	Equation of line	Correlation coefficient
FS1	y = 0.0432x + 0.9684	R^2 = 0.0653
FS2	y = 0.0262x + 1.0267	R^2 = 0.0242
FS3	y = 0.0162x + 1.0118	R^2 = 0.0103
FC1	y = 0.0585x + 0.9556	R^2 = 0.1122
FC2	y = 0.0437x + 0.9875	R^2 = 0.0629
FC3	y = 0.0385x + 1.0025	R^2 = 0.0479
FP1	y = 0.0076x + 1.0448	R^2 = 0.0026
FP2	y = -0.0122x + 1.0768	R^2 = 0.0046
FP3	y = -0.0456x + 1.1183	R^2 = 0.0504
FK1	y = 0.0224x + 1.0135	R^2 = 0.0142
FK2	y = 0.0106x + 1.0165	R^2 = 0.0034
FK3	y = -0.0062x + 1.0349	R^2 = 0.0014



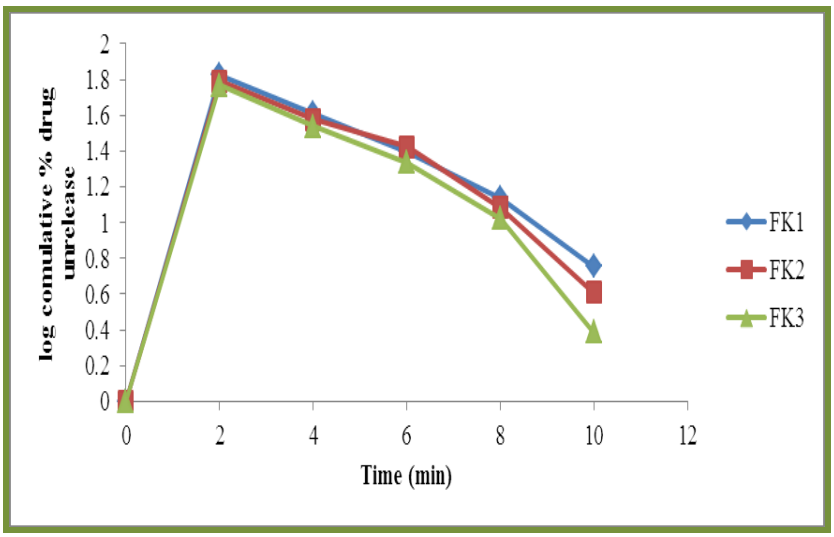
First order kinetic treatment of FS1, FS2 and FS3.



First order kinetic treatment of FC1, FC2 and FC3



First order kinetic treatment of FP1, FP2 and FP3.

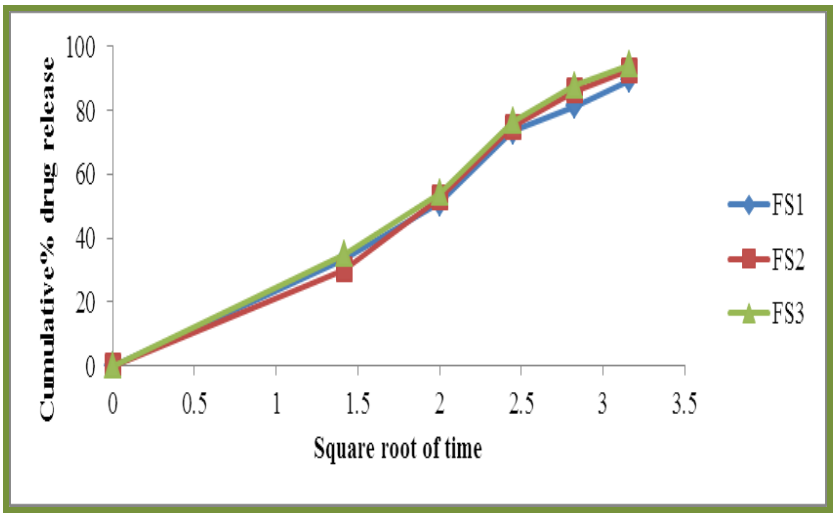


First order kinetic treatment of FK1, FK2 and FK3.

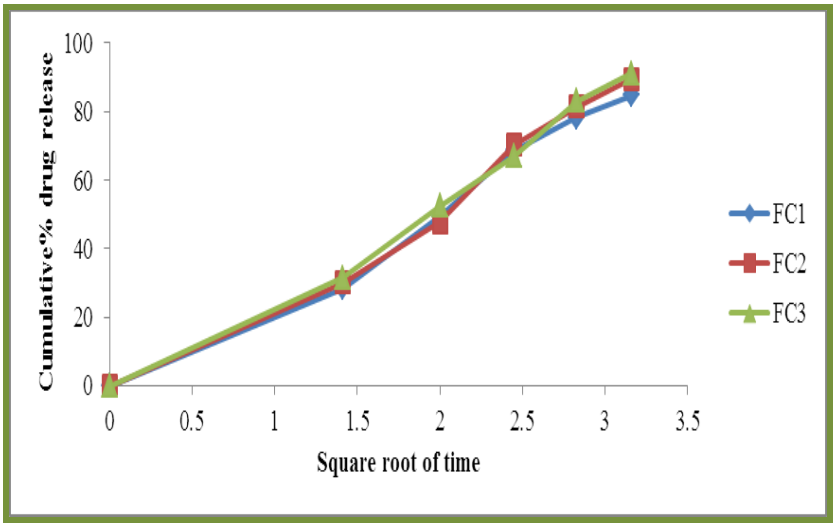
Higuchi's Square Root kinetic treatment of mouth dissolving tablet of Lansoprazole

Higuchi's Square Root kinetic treatment of dissolution data

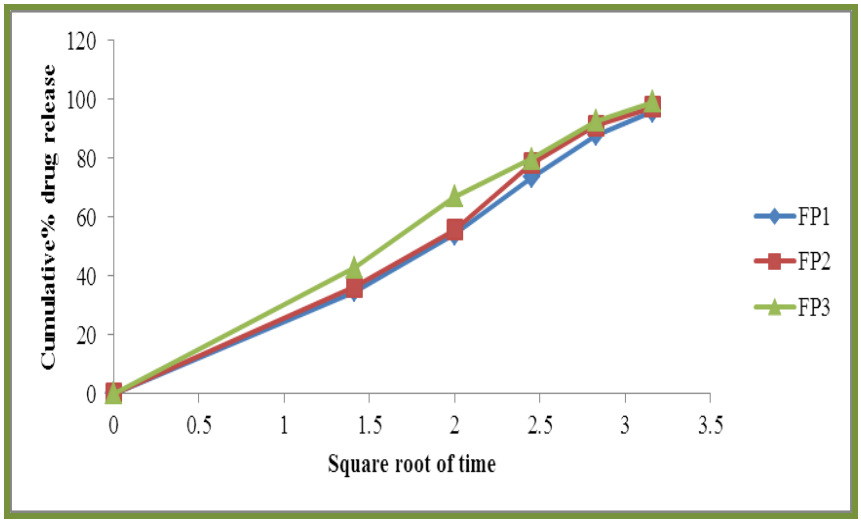
Formulation code	Equation of line	Correlation coefficient
FS1	y = 28.324x - 3.1885	R^2 = 0.9357
FS2	y = 31.934x - 5.0317	R^2 = 0.9163
FS3	y = 30.163x - 3.4583	R^2 = 0.9457
FC1	y = 27.136x - 3.9542	R^2 = 0.9411
FC2	y = 28.255x - 4.7670	R^2 = 0.9678
FC3	y = 28.622x - 4.0766	R^2 = 0.9567
FP1	y = 30.101x - 3.8415	R^2 = 0.9380
FP2	y = 31.213x - 3.5211	R^2 = 0.9268
FP3	y = 31.241x - 0.0719	R^2 = 0.9025
FK1	y = 30.744x - 3.1242	R^2 = 0.9384
FK2	y = 31.896x - 1.4830	R^2 = 0.9656
FK3	y = 30.528x - 0.3199	R^2 = 0.9035



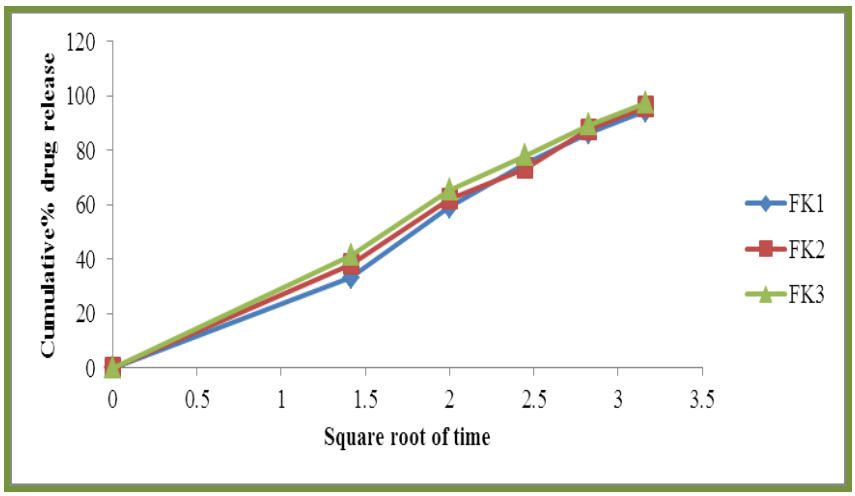
Higuchi's square root kinetic of FS1, FS2 and FS3.



Higuchi's square root kinetic of FC1, FC2 and FC3.



Higuchi's square root kinetic of FP1, FP2 and FP3.

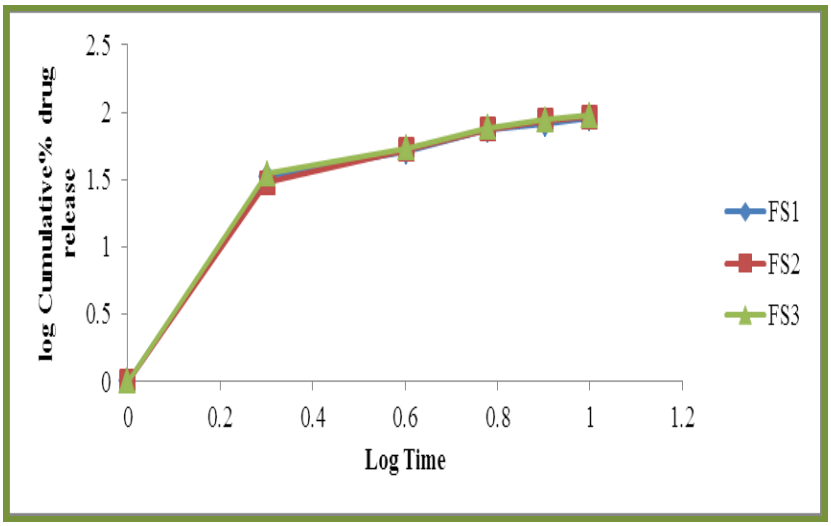


Higuchi's square root kinetic of FK1, FK2 and FK3.

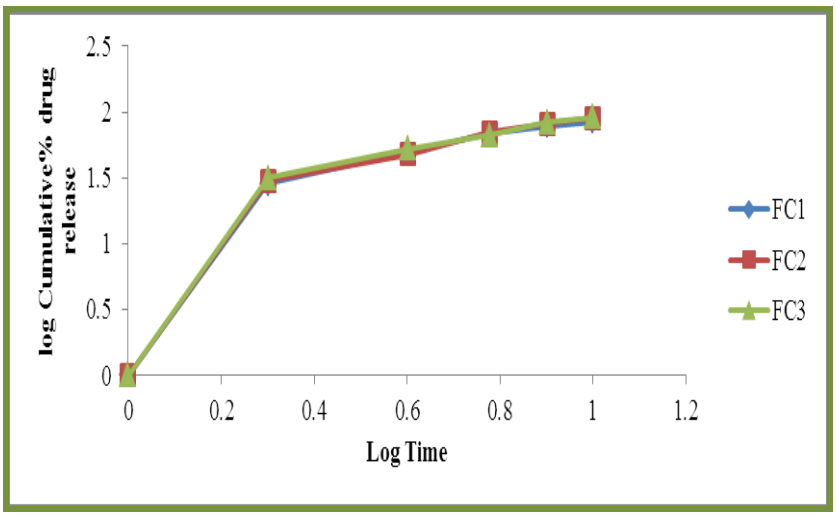
Korsmeyer's Equation kinetic treatment of mouth dissolving tablet of Lansoprazole

Korsmeyer's Equation Root kinetic treatment of dissolution data

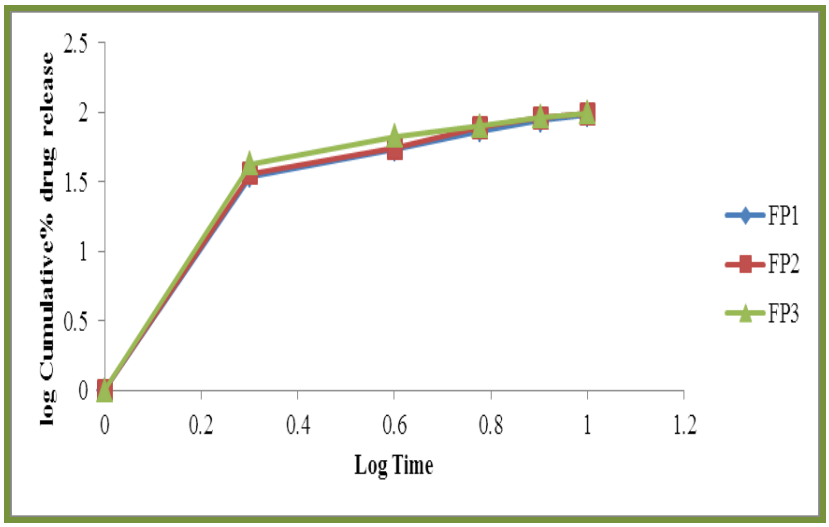
Formulation code	Equation of line	Correlation coefficient
FS1	y = 1.7148x + 0.4535	R^2 = 0.7769
FS2	y = 1.754x + 0.4313	R^2 = 0.8012
FS3	y = 1.7355x + 0.4569	R^2 = 0.7675
FC1	y = 1.7348x + 0.4276	R^2 = 0.7872
FC2	y = 1.7378x + 0.4354	R^2 = 0.7883
FC3	y = 1.7317x + 0.4455	R^2 = 0.7974
FP1	y = 1.7471x + 0.4566	R^2 = 0.7798
FP2	y = 1.7566x + 0.4648	R^2 = 0.7655
FP3	y = 1.7378x + 0.415	R^2 = 0.7420
FK1	y = 1.7512x + 0.4684	R^2 = 0.7702
FK2	y = 1.723x + 0.4847	R^2 = 0.7468
FK3	y = 1.712x + 0.5087	R^2 = 0.7345



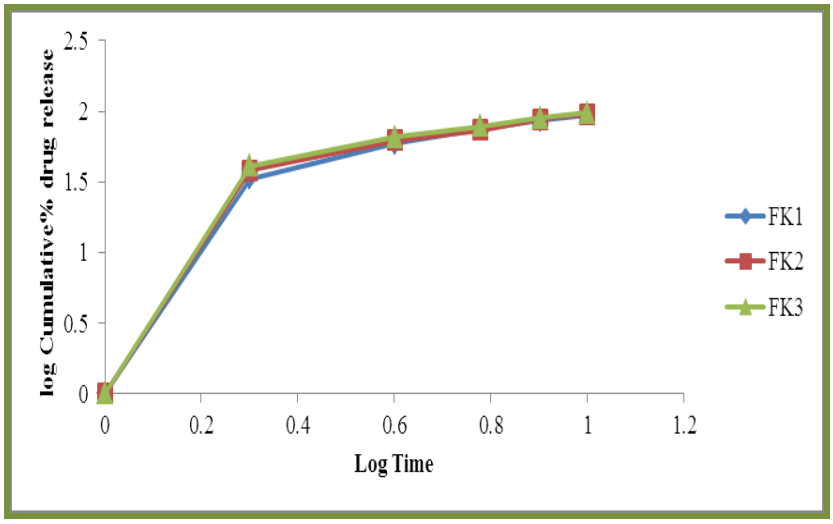
Korsmeyer's kinetic treatment of FS1, FS2 and FS3.



Korsmeyer's kinetic treatment of FC1, FC2 and FC3.



Korsmeyer's kinetic treatment of FP1, FP2 and FP3.



Korsmeyer's kinetic treatment of FK1, FK2 and FK3.

Kinetic models treatment of *in vitro* drug release

FC	Zero order r^2	First order r^2	Higuchi r^2	Korsmeyer's r^2	Best fit model
FS1	0.9293	0.0653	0.9357	0.7769	**Higuchi**
FS2	0.9496	0.0242	0.9163	0.8012	**Zero order**
FS3	0.9513	0.0103	0.9457	0.7675	**Zero order**
FC1	0.9353	0.1122	0.9411	0.7872	**Higuchi**
FC2	0.9493	0.0629	0.9678	0.7883	**Higuchi**
FC3	0.9483	0.0479	0.9567	0.7974	**Higuchi**
FP1	0.9439	0.0026	0.9380	0.7798	**Zero order**
FP2	0.9332	0.0046	0.9268	0.7655	**Zero order**
FP3	0.9863	0.0504	0.9025	0.7420	**Zero order**
FK1	0.9255	0.0142	0.9384	0.7702	**Higuchi**
FK2	0.9147	0.0034	0.9656	0.7468	**Higuchi**
FK3	0.9866	0.0014	0.9035	0.7345	**Zero order**

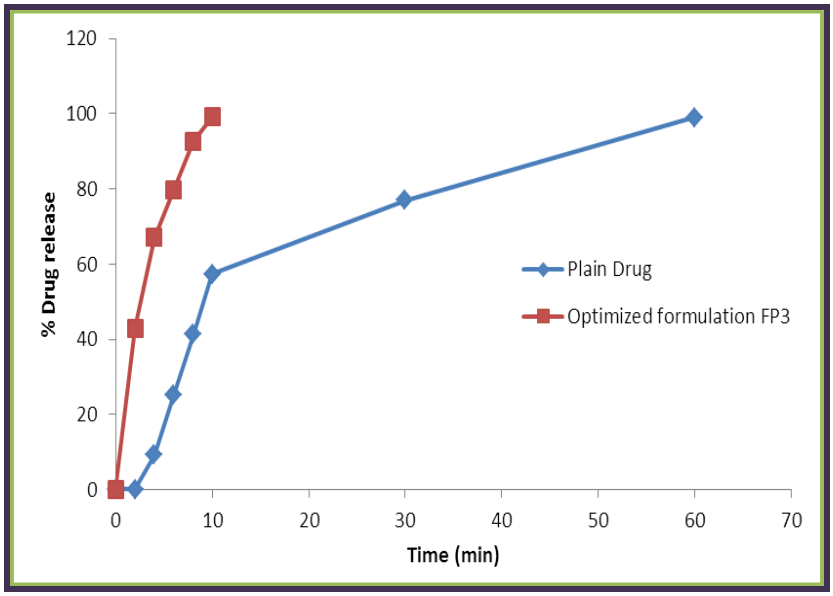
Comparative study of formulation FP3 and plain drug preparation of Lansoprazole

Comparison of formulation FP3 and plain drug preparation of Lansoprazole

Evaluation parameter	Optimized formulation FP3	Plain Drug Lansoprazole
Appearance	white, smooth concave surface	White with smooth surface
Avg wt.	200 mg	200 mg
Disintegration time	23 sec	More than 2 hrs

Dissolution data of prepared and plain drug formulation of Lansoprazole

S. no.	Time (min)	% drug release	
		Plain Drug Lansoprazole	Optimized formulation FP3
1	2	0	41.810
2	4	9.1506	67.017
3	6	24.125	78.764
4	8	40.202	91.621
5	10	56.265	98.216
6	30	75.872	....
7	60	97.842	....

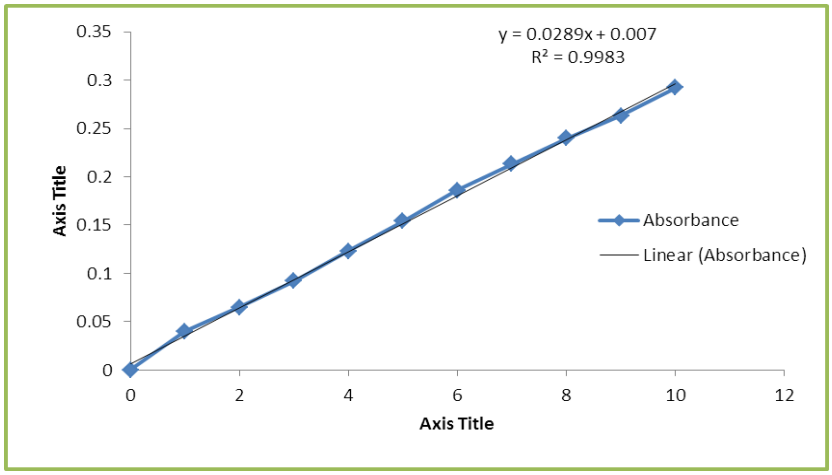


Comparison between Dissolution data of prepared and plain drug formulation of Lansoprazole In vivo studies (In-vivo Bioavailability studies in rabbit).

Standard curve of Lansoprazole in blood plasma.

Standard curve values of Lansoprazole in blood plasma.

S. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	1	0.040
3.	2	0.065
4.	3	0.092
5.	4	0.123
6.	5	0.154
7.	6	0.186
8.	7	0.213
9.	8	0.240
10.	9	0.263
11.	10	0.292

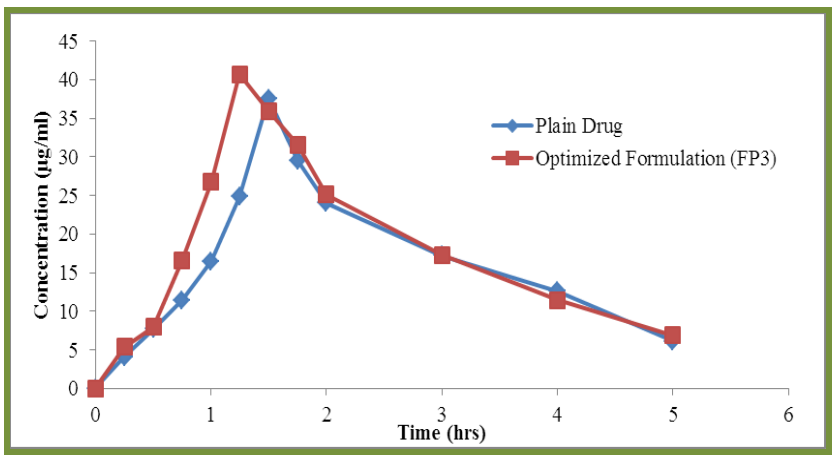


Standard curve of Lansoprazole in blood plasma.

Plasma drug concentration studies of FP3 Lansoprazole formulation

Plasma drug concentration studies of FP3 formulation and Plain drug (Lansoprazole)

S. No.	Time (hrs)	Plasma concentration (µm/ml)	
		Lansoprazole (Plain drug)	Optimized formulation (FP3)
1	0	0	0
2	0.25	4.07	5.26
3	0.50	7.63	7.87
4	0.75	11.23	15.53
5	1	16.45	25.64
6	1.25	23.76	40.37
7	1.50	36.45	34.82
8	1.75	28.42	30.56
9	2	23.06	24.12
10	3	16.27	16.30
11	4	11.61	10.43
12	5	5.11	5.89



Plasma concentration time profile curve of plain drug (Lansoprazole) and formulation FP3.

Pharmacokinetic parameter of plain drug (Lansoprazole) and formulation FP3

S. No.	Formulation	C_{max} (µm/ml)	T_{max} (hrs.)	AUC_{0-5} (µm/ml*h)
1.	Lansoprazole (Control)	37.35	1.50	80.65
2.	Optimized formulation FP3	40.60	1.25	89.25

Stability studies of Optimized formulation FP3

Accelerated Stability studies of Lansoprazole mouth dissolving tablets stored at Room Temperature (RT)

Evaluation parameters	Time (in days)			
	0	15	30	45
Crushing strength	6.5±0.89	6.6±0.80	6.4±0.89	6.5±0.75
Disintegration time	23.58	23.78	23.30	23.00
Time required for complete drug release (Sec)	10	10	10	10
Drug content (%)	98.68	98.89	97.98	97.59

Accelerated Stability studies of Lansoprazole mouth dissolving tablets stored at 45^0C Temperature

Evaluation parameters	Time (in days)			
	0	15	30	45
Crushing strength	6.6±0.60	6.6±0.66	6.4±0.87	6.5±0.75
Disintegration time	23.04	22.98	22.56	22.84
Time required for complete drug release (Sec)	10	10	10	10
Drug content (%)	98.94	98.80	98.5	97.86

Dissolution data of Lansoprazole mouth dissolving tablets stored at Room Temperature (RT)

Time interval (Days)	% drug dissolved				
	2	4	6	8	10
0	41.81	66.21	78.97	93.83	99.86
15	40.97	65.17	78.73	92.27	99.42
30	41.55	64.51	76.82	90.80	99.21
45	42.13	64.16	75.97	91.18	98.63

Dissolution data of Lansoprazole mouth dissolving tablets stored at 45^0C Temperature

Time interval (Days)	% drug dissolved				
	2	4	6	8	10
0	41.80	66.20	78.80	92.89	99.21
15	40.90	64.40	78.13	92.67	97.72
30	42.30	66.50	76.50	89.54	98.78
45	42.12	65.10	76.27	89.40	98.53

CONCLUSION

The mouth dissolving tablets of Lansoprazole were prepared by direct compression method using four superdisintegrants, viz., Sodium starch glycolate, Croscarmellose sodium, Kyron T-314, and PolyKoVidone XL at 5-10% concentrations with microcrystalline cellulose. Among these formulations tablets containing 10% PolyKoVidone XL formulation FP3 were optimized due to its fast *in vitro* dispersion and disintegration when compare to other formulations and drug release with in 10 min. From the above data, it can be concluded that PolyKoVidone XL is having better disintegrant property than other disintegrants namely, Kyron T-314, Croscarmellose sodium and Sodium starch glycolate due to its excellent swelling characteristics after the absorption of moisture and thus drug release without need of water with in sec so that mouth dissolving tablet will surely increased the bioavailability, rapid on set of action, low side effect, good stability and most important patient compliance by prevent the difficulty in swallowing or chewing of solid dosage forms and injections generally are not favored by the patients due to invasiveness.

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