Journal of Pharma Research
Available online through
www.jprinfo.com

Research Article
ISSN: 2319-5622

FORMULATION AND EVALUATION PARAMETERS OF EXTENDED-RELEASE TABLETS OF ILAPRAZOLE BY USING NATURAL AND SYNTHETIC POLYMERS

B. Divya [1,3]*, J. Sreekanth [2], D. Satyavati [3]

*[1] Research Scholar, Faculty of Pharmaceutical Sciences, JNTU Hyderabad, Telangana, INDIA.
[2] General Manager, Progenerics Pharma Pvt. Ltd, Hyderabad, Telangana, INDIA.
[3] Principal, Brilliant Group of Institutions (Integrated Campus), Abdullapurmet, Hayathnagar, R.R Dist, Telangana, INDIA.

Received on: 18-11-2016; Revised and Accepted on: 31-12-2016

ABSTRACT

Ilaprazole is a Proton Pump Inhibitor (PPI), an anti-acidic drugused in the treatment of dyspepsia, peptic and duodenal ulcer disease, gastroesophageal reflux disease (GERD).Ilaprazole at oral doses of 10 mg has shown higher suppression of gastric acid secretion and more prolonged plasma half-life, and similar safety compared to 20 mg omeprazole. Elimination half-life for Ilaprazole ranged from 4.7 to 5.3 h, Administration of Ilaprazole in an extended-release dosage form would be more desirable by maintaining the plasma drug concentrations at a prolonged period of time. It will be more beneficial in maintaining nocturnal gastric pH<4. The main objective to formulate and evaluate extended-release matrix tablets of Ilaprazole by wet granulation technique by using natural polymers and synthetic polymers. The granules were evaluated by angle of repose, Bulk and Tapped density, Hausner's ratio, Carr's index. The tablets were subjected to Thickness, Weight variation, Drug content, Hardness, Friability and In-vitro drug release studies. The Physicochemical properties of tablets were found within the limits. In-vitro dissolution study was carried out for first 2 hrs in 0.1N Hcl and remaining 10 hrs in 6.8 PH Phosphate buffer as a dissolution medium. Based on the results F-21 (Drug: Eudragit RSPO ratio 1:2) formulation was chosen as a best among all the formulations in the point of drug release and mechanism. The release mechanisms were explored and explained with Zero order, First order, Higuchi, Peppas.

Keywords: *Ilaprazole, wet granulation technique, Eudragit RSPO, Zero-order Kinetics*

INTRODUCTION

Extended-release dosage forms are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. The objective in formulating an extended-release dosage form is to be able to provide a similar blood level pattern for up to 12 hours after oral administration of the drug. The basic goal of therapy is to achieve a steady-state blood or tissue level that is therapeutically effective and nontoxic. The design of proper dosage regimens is an important element in accomplishing this goal. This is usually accomplished by maximizing drug availability, i.e., by attempting to attain a maximum rate and extent of drug absorption; however, control of drug action through formulation also implies controlling bioavailability to reduce drug absorption rates [1].

***Corresponding author**:

B. Divya,
Research Scholar,
Faculty of Pharmaceutical Sciences,
JNTU Hyderabad, Telangana, INDIA.
Email: divya.balne444@gmail.com

DOI: doi.org/10.5281/zenodo.6413946

Ilaprazole is a substituted benzimidazole prodrug with selective and irreversible proton pump inhibitor activity. A weak base, Ilaprazole accumulates in the acidic environment of the secretory canaliculus of the gastric parietal cell where it is converted to an active sulfenamide form that binds to cysteine sulfhydryl groups on the luminal aspect of the proton pump (H+/K+ATPase), thereby inhibiting the pump's activity and the parietal cell secretion of H+ ions into the gastric lumen, the final step in gastric acid production. Ilaprazole used in the treatment of dyspepsia, peptic ulcer disease (PUD), gastro esophageal reflux disease (GORD/GERD) and duodenal ulcer. It is available in strengths of 5, 10, and 20 mg.

MATERIALS AND METHODS

Ilaprazole was received as a gift sample from Lupin Pharmaceutical Limited, Hyderabad. HPMC Polymers and Carbopol derivatives were purchased from Yarrow Chem products, Mumbai, Eudragit polymers and gums were purchased from S.D Fine Chemicals Ltd, Mumbai.

Methodology:
Preformulation Studies:
Construction of Calibration curve of Ilaprazole:
Standardization of Ilaprazole by UV-Visible Spectrophotometry:

a) In 0.1 N Hcl Solution:

i) Preparation of stock solution: Stock solution 100µg/ml of Ilaprazole was prepared in 0.1N Hcl solution. This solution was approximately diluted with 0.1N Hcl to obtain a concentration of 10µg/ml. The resultant solution was scanned in range of 200-400nm using UV double beam spectrophotometer (Lab India UV-3000+).

ii) Standard calibration of Ilaprazole in 0.1N Hcl: 100mg of Ilaprazole was accurately weighed and dissolved in 100ml of 0.1N Hcl to obtain a concentration of 1000µg/ml. From the above, 10ml was withdrawn and diluted to 100ml to obtain a concentration of 100µg/ml. From this stock solution aliquots of 1ml, 2ml, 3ml, 4ml and 5ml were diluted in 10ml volumetric flask with phosphate buffer to give concentrations in range of 10-50µg/ml respectively, absorbance was measured at 230nm (Table 4; Fig 1).

b) In pH 6.8 Buffer:

i) Preparation of stock solution: Stock solution 100µg/ml of Ilaprazole was prepared in phosphate buffer of pH 6.8. This solution was approximately diluted with phosphate buffer of pH 6.8 to obtain a concentration of 10µg/ml. The resultant solution was scanned in range of 200- 400nm using UV double beam spectrophotometer (Lab India UV-3000+).

ii) Standard calibration of Ilaprazole in phosphate buffer of pH 6.8: 100mg of Ilaprazole was accurately weighed and dissolved in100ml of pH 6.8 phosphate buffer to obtain a concentration of 1000µg/ml. From the above 10ml was withdrawn and diluted to 100ml to obtain a concentration of 100µg/ml. From this stock solution aliquots of 1ml, 2ml, 4ml, 6ml and 8ml were diluted in 10ml volumetric flask with phosphate buffer to give concentrations in range of 10-80µg/ml respectively, absorbance was measured at 232nm (Table 5; Fig 2).

Evaluation of Granules: [2-11]

Pre-compression Parameters: Flow properties:

Angle of Repose: It is performed to determine the flow rate of powder done by the funnel method. The powder was poured into a funnel which is fixed from height of 2cm of the plane surface. Circumference was drawn with a pencil on the graph paper and the radius of base of a pile was measured at 5 different points and average was taken for calculating Angle of repose using following formula:

$$\theta = \tan^{-1} H/R$$

θ=angle of repose; H=height of powder cone; R=radius of powder cone

Angle of Repose less than 30^0 shows the free-flowing property of the material.

Bulk Density: Apparent bulk density was determined by pouring pre-sieved drug excipients blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/mL and is given by,

$$D_b = M / V_0$$

Where, M is the mass of powder and V_0 is the Bulk volume of the powder.

Tapped density: It was determined by placing a graduated cylinder, containing a known mass of drug- excipients blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml

$$D_T = M / V_T$$

Where, M is the mass of powder and V_T is the tapped volume of the powder.

Carr's index: It measures the % Compressibility, higher the compressibility, greater the interparticle interaction, poorer the flowablity of the powder. Percentage Compressibility index was calculated by the formula given below.

$$I = D_t - D_b / D_t \times 100$$

Where, I is the Compressibility index, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Hausner's ratio: The Hausner ratio is a number that is correlated to the flowability of a powder or granular material. The Hausner ratio is calculated by the formula

$$H = D_t / D_b$$

Where, D_t is the tapped density of the powder, D_b is the bulk density of the powder.

Hausner ratio greater than 1.25 is considered to be an indication of poor flowability.

Pre-compression parameters of all Ilaprazole formulations were done and results were tabulated in Table 6 & 7.

Formulation Studies:

Formulation Design and Development of Ilaprazole ER Tablets: [12-27]

Preparation of granules for Ilaprazole: The granules were prepared for Ilaprazoleby wet granulation method. This method involved use of appropriately selected tablet additives which would act as binders for the mixtures of drug and other tablet excipients.

Procedure for the preparation of Ilaprazole tablets by wet granulation method: Ilaprazole, Avicel pH 102, Sodium bicarbonate and extended-release polymer were accurately weighed and sifted through # 40 mesh and were blended in a poly bag for 5 minutes. Then granulated with binder solution (Required quantity of PVP K-30 was added slowly to Isopropyl Alcohol under continuous stirring and stirred well till to get a clear solution) in Rapid Mixer Granulator (RMG) with Impeller at 150 rpm and chopper at 1000 rpm for 5 minutes. Wet mass was passed through #10 mesh and dried at 60^0C until LOD is 1-2% w/w. Dried granules were passed through #20 mesh. Talc, Magnesium stearate was accurately weighed and sifted through #40 mesh and added to sifted dried granules. Then blended together in a poly bag for 2 min and compressed into tablets using Tablet Compression machine with 7 mm Round shaped standard concave punches. In all Formulations, the amount of Ilaprazole is equivalent to 10mg (Table 1-3).

Table No. 1: Compositions of Ilaprazole ER Tablets (F1-F10)

S.no	Ingredients (mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Ilaprazole	10	10	10	10	10	10	10	10	10	10
2	HPMC-K4M	5	10	20	---	---	---	---	---	---	---
3	HPMC-K15 M	---	---	---	5	10	20	---	---	---	---
4	HPMC-K100 M	---	---	---	---	---	---	5	10	20	---
5	Carbopol-934	---	---	---	---	---	---	---	---	---	5
6	Sodium bicarbonate	10	10	10	10	10	10	10	10	10	10
7	Avicel PH 102	156	151	141	156	151	141	156	151	141	156
8	PVP-K 30 (5%)	10	10	10	10	10	10	10	10	10	10
9	IPA	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
10	Talc	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
11	Mg.Stearate	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
	Total Weight (mg)	200	200	200	200	200	200	200	200	200	200

Table No. 2: Compositions of Ilaprazole ER Tablets (F11-F20)

S.no	Ingredients (mg/tab)	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20
1	Ilaprazole	10	10	10	10	10	10	10	10	10	10
2	Carbopol-934	10	20	---	---	---	---	---	---	---	---
3	Eudragit-S100	---	---	5	10	20	---	---	---	---	---
4	Eudragit-L100	---	---	---	---	---	5	10	20	---	---
5	Eudragit-RSPO	---	---	---	---	---	---	---	---	5	10
6	Sodium bicarbonate	10	10	10	10	10	10	10	10	10	10
7	Avicel PH 102	151	141	156	151	141	156	151	141	156	151
8	PVP-K 30 (5%)	10	10	10	10	10	10	10	10	10	10
9	IsoPropyl Alcohol	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
10	Talc	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
11	Mg.Stearate	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
	Total Weight (mg)	200	200	200	200	200	200	200	200	200	200

Table No. 3: Compositions of Ilaprazole ER Tablets (F21-F30)

S.no	Ingredients (mg/tab)	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
1	Ilaprazole	10	10	10	10	10	10	10	10	10	10
2	Eudragit- RSPO	20	---	---	---	---	---	---	---	---	---
3	Sodium CMC	---	5	10	20	---	---	---	---	---	---
4	Xanthan gum	---	---	---	---	5	10	20	---	---	---
5	Guar gum	---	---	---	---	---	---	---	5	10	20
6	Sodium bicarbonate	10	10	10	10	10	10	10	10	10	10
7	Avicel PH 102	141	156	151	141	156	151	141	156	151	141
8	PVP-K 30 (5%)	10	10	10	10	10	10	10	10	10	10
9	Iso Propyl Alcohol	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
10	Talc	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
11	Mg.Stearate	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
	Total Weight (mg)	200	200	200	200	200	200	200	200	200	200

Evaluation of Extended-Release Matrix tablets:

Post-Compression parameters:[28-50]

The prepared tablets were evaluated Physical appearance, thickness, hardness, weight variation, friability and uniformity of weight and the results were tabulated in Table 8 and 9.

Physical appearance:

The tablets were inspected for smoothness, absence of cracks, chips and other undesirable characteristics. If they are colored, it includes examination for mottling and other evidence of non-uniform color distribution except where they are used intentionally.

Weight variation:

20 tablets were randomly selected from each formulation and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight.

Hardness:

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2.

Dimension (Thickness and Diameter):

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Callipers in kg/cm^2.

Friability test:

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche friabilator (Lab India, FT 1020). It is expressed in percentage (%). Ten tablets were initially weighed [$W_{(initial)}$] and transferred into friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again [$W_{(final)}$]. The percentage friability was then calculated by,

$$\mathbf{F} = \frac{[\mathbf{W(initial)} - \mathbf{W(final)}]}{\mathbf{W(initial)}} \times \mathbf{100}$$

Drug content:

All the Extended-release matrix tablets prepared were tested for assay. A precisely weighed amount of each composition was dissolved in small volume of methanol and moreover diluted with methanol. The content of Ilaprazole as well as Tenatoprazole sodium was tested spectrophotometrically at their λ max with UV-visible spectrophotometer.

$$\textbf{Drug content } \% = \frac{\textbf{practical yield}}{\textbf{therotical yield}} \times \mathbf{100}$$

***In-Vitro* Dissolution studies of Ilaprazole ER tablets:** [51-54]

The *in-vitro* dissolution was carried out using USP type II dissolution apparatus was determined using USP Dissolution testing apparatus type-II (Paddle method; Lab India DS 8000+), Temperature is 37±0.5ºC and RPM is 50. Dissolution medium was maintained at 0.1N Hydrochloric acid for first 2 hours and then pH 6.8 phosphate buffer for next 10 hours.

The tablets were placed in the dissolution medium and the apparatus was run. At intervals of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 hours 5 ml aliquots were withdrawn and replacement was done each time with equal amounts of fresh dissolution medium maintained at same temperature. Each 5 ml aliquot was filtered through Whatman filter paper (No.41). 5 ml of sample was diluted to 10 ml 0.1N Hydrochloric acid for first 2 hours and then with pH 6.8 phosphate buffer for next 10 hours and absorbance of these solutions was measured by using a UV spectrophotometer. Drug concentrations in the sample were determined from standard calibration curve. The release data were calculated. The results were shown in the Table 10-13 and Fig: 3-8.

Release Kinetics: [55, 56]

To study the release kinetics of *in-vitro* drug release, data was applied to kinetic models such as Zero order, First order, Higuchi and Korsmeyer-Peppas and the results were shown in Table 14 and Fig: 9-12.

Data Analysis (Curve Fitting Analysis):

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were graphed as:

- Cumulative percentage drug dissolved Vs Time (Zero order plots)
- Log cumulative percentage drug remaining Vs Time (First order plots)
- Cumulative percentage drug dissolved Vs Square root of time (Higuchi's plots)
- Log percentage drug released Vs Log time (Peppas plots)

Zero order:

$$\boldsymbol{C = K_0 t}$$

Where; K_0 is the zero-order rate constant expressed in units of concentration/time; t -is the time in hrs

First order:

$$\boldsymbol{LogC = LogC_0 - Kt / 2.303}$$

Where; C_0 - is the initial concentration of drug, K - is the first order constant, t - is the time in hrs.

Higuchi:

$$\boldsymbol{Qt = Kt^{1/2}}$$

Where; Q_t - is the amount of the release drug in time t, K- is the kinetic constant and t- is time in hrs

Korsmeyer Peppas:

$$\boldsymbol{Mt/ M_\infty = Kt\ n}$$

Where; M_t - represents amount of the released drug at time t, M_∞- is the overall amount of the drug (whole dose) released after 12 hrs, K- is the diffusional characteristic of drug/ polymer system constant, n- is a diffusional exponent that characterizes the mechanism of release of drug.

The value of n indicates the drug release mechanism related to the geometrical shape of the delivery system, if the exponent n = 0.5, then the drug release mechanism is Fickian diffusion. If n < 0.5 the mechanism is quasi-Fickian diffusion, and 0.5 < n < 1.0, then it is non-Fickian or anomalous diffusion and when n = 1.0 mechanism is non Fickian case II diffusion, n> 1.0 mechanism is non Fickian super case II.

RESULTS AND DISCUSSION

Construction of calibration curve of Ilaprazole:

In this study at 230nm and 232nm, simulated gastric fluid (0.1N HCl) and phosphate buffer pH 6.8 respectively had good reproducibility in the concentration between the range of 10-50µg/ml and 10-80µg/ml respectively. Correlation between

concentration and absorbance was closer to 1 indicating that the method obeyed Beer Lamberts law (Table 4 & 5; Fig. 1 & 2).

Pre-compression Parameters: Flow properties:

Bulk Density of the formulation blend plays an important role in the compression of the powder. The bulk density of the composition was commenced to be in the range of 0.38 ± 0.64to 0.59 ± 0.41 g/cm3. Tapped density also plays a considerable role in knowing the compressibility of the formulation blend. It was in the range of 0.47 ± 0.63 to 0.64 ± 0.16 g/cm3. It was noted that the Tapped density of all the compositions were greater than their respective bulk density thus indicating that all the powder formulation had a good compressibility. The Hausner ratio for all the formulations were ranged from 1.01 ± 0.14 to 1.25 ± 0.15. Hausner ratio greater than 1.25 is considered to be an indication of poor flowability. The Carr's index for all the formulations were ranged from 7.99 ± 0.89 to 14.38 ± 0.14. It gives the % Compressibility, higher the compressibility, greater the interaparticle interaction, poorer the flowablity of the powder. But here with respect to Ilaprazole formulations, the % Compressibility was found to be less, so have a good flowability. 5-15 range of Carr's index indicates excellent flowability of powder blend. The flow properties of granules were analyzed by determining the angle of repose. They were ranged to be 25°.11 ± 0.85 to 30°.73 ± 0.85. Angle of Repose less than 30^0 shows the free-flowing property of the material (Table 6 & 7).

Post-Compression parameters:

The tablets were observed visually and did not show any imperfections such as capping, molting, chipping and lamination. The physical characteristic of Ilaprazole ER tablets (F-1 to F-30) such as thickness, diameter, hardness, friability, weight variation and drug content were determined and values of the formulations (F-1 to F-30) were found to be within the official limits. Excessive variation in the tablet thickness and diameter can result in problems with packaging. The sizes (diameter) of the tablets of all formulations were embark on to be 7.0 ± 0.0 mm and thickness ranged between 3.19 ± 0.18to 4.58 ± 0.62. The Hardness or Tablet crushing strength (fc) of tablets was in the range of 4.01 ± 0.14 to 5.39 ± 0.39 kg/cm2. This indicates good tablet strength. A tablet is formulated to hold a concrete amount of drug. When the average mass of the tablet is 200 mg the Pharmacopeial limit for percentage deviation is ± 7.5 %. The entitlement deviation from average tablet weight for all the tablet was found to be within the precise limits and therefore all formulations comply with the test for weight variation according to the Pharmacopeial specifications. They ranged from 198 ± 0.22 to 200 ± 0.85. Percentage friability of all the formulations was found to be in between 0.54 ± 0.04 to 0.78 ± 0.94 %. This indicated good handling property of the prepared Extended-release tablet. The content of active ingredient i.e., Drug in the formulation were ranged between 98.28 ± 0.98to 101.66 ± 0.25w/w, which is within the specified limit as per IP 2007 (i.e., 90-110 % w/w) (Table 8 & 9).

In-vitro dissolution studies of Ilaprazole:

The Ilaprazole tablets were evaluated for in-vitro dissolution studies in acid buffer (pH-1.2) for 2 hours followed by pH 6.8 buffer for 10 hours. The results of cumulative % drug dissolved revealed that the Ilaprazole was released in an extended manner from all the formulations, whereas formulation F-21 showed maximum cumulative % drug dissolved i.e. 99.73 ± 0.19% at the end of 12^{th} hour which was the intention of the finalized formulation (to prolong the drug dissolution up to 12 hrs) while others not being reached to the time point of maximum release are still extending the release of the drug Ilaprazole (Table 10 - 13; Fig. 3 - 8).

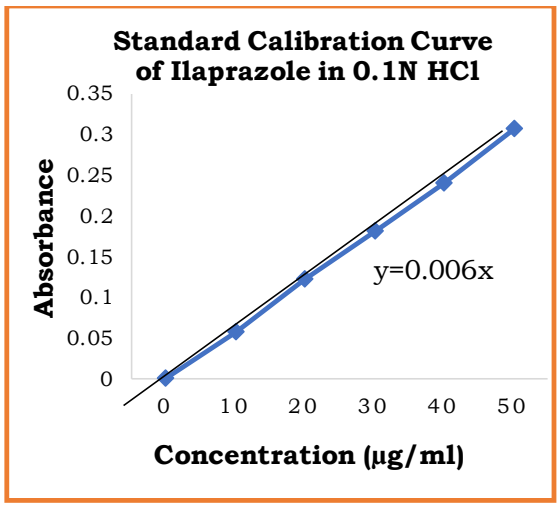
In-vitro dissolution kinetics of optimized formulation of Ilaprazole Extended-release tablets was calculated. It was examined that the drug dissolution kinetics from the formulation followed zero order as the R^2 value of zero order was found to be 0.9928 and the mechanism of drug release was found to be following non-Fickian super case-II diffusion as the n value of Korsmeyer-Peppas was found to be 1.443 (Table 14; Fig. 9 - 12).

Table No. 4: Absorbances of Ilaprazole in 0.1N HCl (230nm)

S.No	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.058
3	20	0.122
4	30	0.181
5	40	0.239
6	50	0.306

Table No. 5: Absorbances of Ilaprazole in 6.8 pH Phosphate buffer (232nm)

S.No	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.071
3	20	0.129
4	40	0.261
5	60	0.385
6	80	0.499



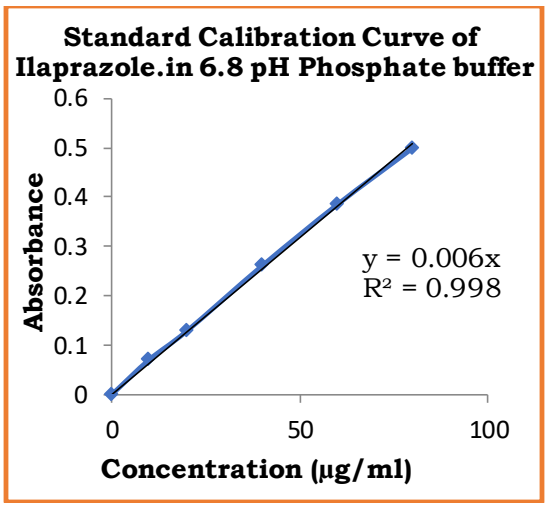


Fig. 1 & 2: Standard Calibration curve of Ilaprazole in 0.1N HCl at 230nm and in 6.8 pH Phosphate buffer at 232 nm.

Table No. 6: Flow properties of powder blend for Ilaprazole (F1-F14)

Formulation Code	Bulk density (gm/cm3)*	Tapped density (gm/cm3)*	Hausner ratio (HR)*	Carr's index (IC)*	Angle of repose (θ)*
F1	0.49±0.63	0.59±0.83	1.08±0.05	10.05±0.41	27°.84±0.46
F2	0.41±0.35	0.58±0.54	1.01±0.14	8.36±0.91	29°.36±0.86
F3	0.59±0.41	0.61±0.35	1.10±0.09	11.73±0.87	26°.29±0.74
F4	0.42±0.13	0.57±0.09	1.16±0.03	9.42±0.91	29°.18±0.71
F5	0.45±0.25	0.58±0.14	1.18±0.21	10.09±0.42	26°.36±0.09
F6	0.44±0.72	0.51±0.17	1.16±0.33	12.36±0.27	28°.04±0.05
F7	0.51±0.86	0.61±0.05	1.14±0.08	10.36±0.15	30°.07±0.03
F8	0.41±0.29	0.54±0.19	1.22±0.01	13.01±0.18	26°.75±0.36
F9	0.48±0.65	0.62±0.13	1.09±0.64	7.99±0.89	25°.11±0.85
F10	0.46±0.11	0.59±0.73	1.01±0.86	12.71±0.65	27°.55±0.07
F11	0.47±0.35	0.55±0.83	1.25±0.15	10.37±0.28	29°.27±0.83
F12	0.49±0.27	0.54±0.37	1.11±0.27	8.98±0.79	28°.16±0.35
F13	0.54±0.84	0.59±0.44	1.17±0.16	14.24±0.29	27°.34±0.53
F14	0.49±0.29	0.54±0.75	1.12±0.09	11.12±0.15	29°.17±0.16

Table No. 7: Flow properties of powder blend for Ilaprazole (F15-F30)

Formulation Code	Bulk density (gm/cm3)*	Tapped density (gm/cm3)*	Hausner ratio (HR)*	Carr's index (IC)*	Angle of repose (θ)*
F15	0.46±0.09	0.57±0.35	1.16±0.35	10.26±0.97	29°.05±0.08
F16	0.52±0.83	0.61±0.83	1.18±0.13	8.87±0.95	30°.73±0.85
F17	0.49±0.27	0.54±0.53	1.14±0.19	11.13±0.17	28°.16±0.01
F18	0.46±0.15	0.58±0.35	1.18±0.44	12.36±0.03	29°.36±0.37
F19	0.45±0.44	0.52±0.62	1.09±0.05	14.38±0.14	26°.28±0.29
F20	0.39±0.65	0.48±0.09	1.16±0.09	9.98±0.27	30°.26±0.47
F21	0.48±0.36	0.58±0.03	1.03±0.08	10.07±0.73	27°.28±0.15
F22	0.52±0.94	0.59±0.79	1.15±0.01	9.71±0.19	28°.56±0.29
F23	0.43±0.52	0.54±0.18	1.04±0.04	8.27±0.36	25°.15±0.32
F24	0.46±0.09	0.55±0.05	1.03±0.21	9.46±0.36	29°.74±0.14
F25	0.57±0.01	0.64±0.16	1.16±0.42	12.34±0.02	27°.46±0.98
F26	0.44±0.63	0.53±0.35	1.18±0.05	10.35±0.36	29°.32±0.64
F27	0.49±0.72	0.57±0.71	1.17±0.41	11.36±0.73	30°.36±0.24
F28	0.38±0.64	0.47±0.63	1.04±0.03	8.71±0.45	27°.14±0.75
F29	0.49±0.42	0.56±0.37	1.11±0.07	9.27±0.72	25°.56±0.24
F30	0.54±0.83	0.61±0.76	1.09±0.09	10.46±0.23	28°.72±0.29

All the values are expressed as mean± SE, n=3

Table No. 8: Post Compression characteristicsof Ilaprazole ER Tablets (F1-F14)

Formulation Code	Thickness (mm)*	Hardness (Kg/cm²) *	Weight variation test (%)	Friability (%) *	Drug content (%) *
F1	3.19±0.18	4.47±0.28	200±0.36	0.59±0.71	99.26±0.36
F2	3.47±0.53	4.08±0.36	199±0.47	0.67±0.63	99.71±0.98
F3	3.68±0.69	4.47±0.59	200±0.35	0.63±0.26	101.66±0.25
F4	3.52±0.37	4.28±0.48	198±1.26	0.59±0.16	100.35±0.83
F5	3.98±0.29	4.46±0.18	200±0.37	0.62±0.73	99.78±0.38
F6	4.57±0.36	4.49±0.47	199±0.29	0.78±0.94	98.36±0.98
F7	3.99±0.48	5.01±0.03	200±0.73	0.54±0.04	99.14±0.62
F8	3.47±0.59	4.28±0.17	199±0.24	0.55±0.13	101.35±0.56
F9	3.78±0.37	5.39±0.39	200±0.15	0.69±0.91	99.37±0.35
F10	4.02±0.49	4.13±0.21	199±0.28	0.63±0.94	98.98±0.78
F11	3.96±0.14	4.28±0.48	198±0.37	0.57±0.65	99.34±0.06
F12	3.98±0.18	4.01±0.14	200±0.18	0.59±0.14	99.28±0.47
F13	3.77±0.97	4.55±0.37	198±0.35	0.55±0.35	100.54±0.29
F14	3.79±0.74	4.83±0.16	200±0.28	0.64±0.47	98.37±0.74

All the values are expressed as mean± SE, n=3

Table No. 9: Post Compression characteristics of Ilaprazole ER Tablets (F15-F30)

Formulation Code	Thickness (mm)*	Hardness (kg/cm²)*	Weight variation test (%)	Friability (%)*	Drug content (%)*
F15	3.68±0.27	4.38±0.28	200±0.85	0.64±0.42	99.68±0.35
F16	4.01±0.36	4.32±0.49	198±1.49	0.55±0.53	98.59±0.73
F17	3.68±0.19	4.86±0.26	199±0.87	0.73±0.64	100.42±0.24
F18	3.89±0.27	4.38±0.13	197±1.75	0.56±0.31	99.34±0.76
F19	3.77±0.14	4.37±0.58	200±0.73	0.61±0.26	98.28±0.98
F20	3.86±0.46	4.05±0.97	198±0.22	0.72±0.67	100.04±0.48
F21	4.07±0.47	4.85±0.29	200±0.15	0.61±0.28	99.96±0.64
F22	3.79±0.59	4.46±0.14	199±0.89	0.59±0.32	101.37±0.47
F23	3.59±0.03	4.19±0.22	200±0.75	0.64±0.18	99.85±0.57
F24	4.09±0.02	4.38±0.47	198±0.36	0.57±0.24	100.47±0.59
F25	3.99±0.55	5.09±0.01	200±0.82	0.63±0.31	98.98±0.71
F26	4.08±0.31	4.85±0.08	199±0.27	0.69±0.42	100.05±0.36
F27	3.38±0.37	4.48±0.36	200±0.18	0.72±0.29	99.87±0.69
F28	4.58±0.62	4.14±0.49	199±0.75	0.66±0.35	99.85±0.57
F29	3.49±0.44	5.02±0.08	200±0.57	0.54±0.19	100.47±0.59
F30	3.43±0.52	4.78±0.39	199±0.37	0.67±0.25	98.98±0.71

All the values are expressed as mean± SE, n=3

Table No. 10: *In-Vitro* dissolution studies of Ilaprazole ER Tablets (F1-F7)

Time (hrs)	CUMULATIVE % DRUG RELEASE						
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
0	0	0	0	0	0	0	0
1	3.47±0.28	4.28±0.91	6.46±0.76	2.98±0.27	3.63±0.82	4.13±0.73	3.26±0.15
2	7.39±0.16	6.46±0.56	7.37±0.19	6.14±0.39	5.19±0.37	6.19±0.92	5.28±0.37
3	14.28±0.49	13.56±0.29	16.45±0.35	11.37±0.73	12.47±0.41	12.42±0.31	12.44±0.18
4	21.47±0.73	25.75±0.48	19.79±0.72	23.21±0.15	21.38±0.29	18.21±0.74	20.37±0.83
5	32.21±0.35	36.38±0.19	24.47±0.11	31.63±0.74	33.82±0.82	27.36±0.27	32.63±0.46
6	43.57±0.19	47.14±0.53	29.82±0.32	42.72±0.43	42.18±0.75	35.44±0.14	45.38±0.13
7	54.25±0.37	55.31±0.74	37.26±0.92	51.41±0.82	53.39±0.54	44.53±0.53	53.41±0.29
8	58.98±0.71	64.53±0.22	46.74±0.67	61.77±0.28	61.37±0.36	57.64±0.75	62.39±0.17
9	66.63±0.13	71.34±0.73	58.36±0.53	70.22±0.39	74.16±0.93	63.13±0.53	71.28±0.19
10	74.31±0.39	79.42±0.14	72.72±0.16	78.38±0.72	78.83±0.61	75.87±0.31	79.38±0.37
11	81.76±0.97	84.26±0.31	84.28±0.37	85.99±0.45	85.76±0.92	83.24±0.89	82.19±0.49
12	89.62±0.39	91.49±0.87	93.17±0.46	88.43±0.14	90.27±0.54	92.15±0.64	86.43±0.36

Each value represents the mean ± SD. (n = 3)

Table No. 11: *In-Vitro* dissolution studies of Ilaprazole ER Tablets (F8-F14)

Time (hrs)	CUMULATIVE % DRUG RELEASE						
	F8	F9	F10	F11	F12	F13	F14
0	0	0	0	0	0	0	0
1	3.18±0.31	4.17±0.47	2.73±0.63	3.72±0.29	4.24±0.31	2.42±0.42	3.82±0.26
2	4.39±0.17	5.29±0.28	4.82±0.73	6.21±0.63	5.87±0.82	3.74±0.86	6.73±0.14
3	14.18±0.39	15.23±0.17	10.27±0.57	10.13±0.18	21.92±0.47	9.86±0.35	14.65±0.75
4	22.29±0.53	21.73±0.48	22.46±0.93	21.74±0.15	32.46±0.24	19.64±0.26	26.93±0.53
5	34.48±0.48	36.49±0.34	33.28±0.26	32.82±0.28	44.47±0.82	30.35±0.75	37.54±0.24
6	43.14±0.83	41.53±0.62	45.47±0.74	44.65±0.36	53.82±0.92	41.97±0.24	45.88±0.97
7	52.83±0.29	57.16±0.48	51.29±0.93	52.38±0.68	69.22±0.53	54.44±0.76	59.64±0.46
8	61.59±0.18	64.73±0.82	58.56±0.46	61.82±0.34	77.65±0.17	65.71±0.24	67.42±0.35
9	74.17±0.11	71.36±0.63	62.83±0.62	74.41±0.12	79.76±0.69	69.52±0.86	74.12±0.29
10	78.15±0.27	80.22±0.89	70.45±0.47	78.39±0.37	81.46±0.29	73.85±0.33	80.96±0.14
11	85.26±0.35	85.65±0.53	82.69±0.39	82.48±0.58	86.51±0.82	80.16±0.63	85.73±0.53
12	90.49±0.68	89.28±0.26	88.28±0.57	90.18±0.74	93.13±0.54	86.28±0.72	93.82±0.92

Each value represents the mean ± SD. (n = 3)

Table No. 12: *In-Vitro* dissolution studies of Ilaprazole ER Tablets (F15-F22)

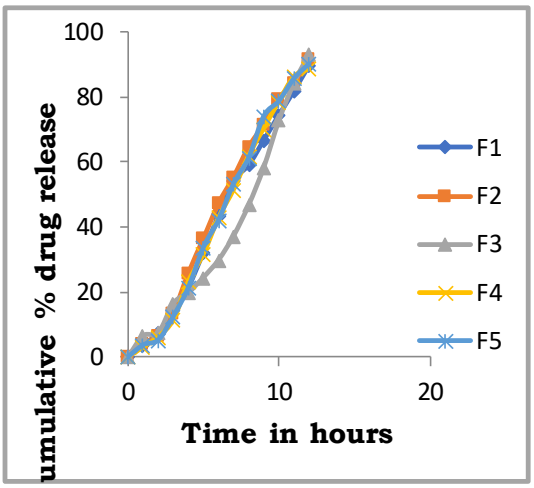
Time (hrs)	CUMULATIVE % DRUG RELEASE							
	F15	F16	F17	F18	F19	F20	F21	F22
0	0	0	0	0	0	0	0	0
1	4.14±0.14	2.92±0.46	3.14±0.53	5.25±0.63	3.65±0.82	4.14±0.64	4.24±0.62	2.18±0.53
2	5.74±0.93	5.46±0.87	4.53±0.14	7.37±0.77	5.87±0.76	5.25±0.86	6.65±0.16	3.52±0.14
3	14.36±0.24	10.28±0.59	11.76±0.65	17.45±0.26	11.59±0.56	10.43±0.35	18.86±0.74	11.63±0.13
4	20.24±0.62	19.53±0.45	21.24±0.75	22.79±0.84	23.83±0.97	22.15±0.24	29.35±0.37	20.25±0.75
5	26.75±0.26	29.83±0.24	33.47±0.24	30.47±0.35	30.28±0.49	34.63±0.96	36.84±0.86	33.72±0.68
6	30.13±0.31	33.37±0.75	46.13±0.35	42.82±0.89	41.34±0.14	43.76±0.24	47.29±0.13	47.63±0.53
7	41.22±0.95	44.64±0.48	59.42±0.87	51.26±0.13	49.18±0.83	55.13±0.68	59.14±0.42	59.14±0.17
8	49.97±0.64	53.49±0.63	67.86±0.54	60.74±0.24	55.76±0.45	66.64±0.87	68.97±0.64	61.53±0.34
9	60.14±0.86	61.82±0.37	74.42±0.29	73.36±0.53	67.41±0.28	70.35±0.43	77.25±0.16	68.15±0.75
10	71.42±0.86	70.74±0.82	80.86±0.13	79.72±0.97	73.38±0.76	81.24±0.26	85.53±0.75	79.73±0.41
11	84.16±0.41	78.12±0.58	86.25±0.64	86.28±0.54	80.16±0.35	89.61±0.84	91.14±0.36	82.85±0.67
12	94.18±0.86	85.96±0.92	89.86±0.78	92.17±0.13	87.35±0.76	92.15±0.31	99.73±0.19	85.31±0.14

Each value represents the mean ± SD. (n = 3)

Table No. 13: *In-Vitro* dissolution studies of Ilaprazole ER Tablet (F23-F30)

Time (hrs)	CUMULATIVE % DRUG RELEASE							
	F23	F24	F25	F26	F27	F28	F29	F30
0	0	0	0	0	0	0	0	0
1	4.31±0.61	5.15±0.35	3.53±0.23	2.13±0.85	2.14±0.65	1.35±0.14	2.35±0.13	4.14±0.17
2	6.53±0.14	7.64±0.73	4.74±0.46	4.45±0.42	4.53±0.14	3.73±0.86	7.12±0.35	8.53±0.14
3	10.15±0.85	17.35±0.74	13.13±0.75	12.74±0.14	14.85±0.85	10.21±0.35	17.64±0.85	18.67±0.85
4	22.74±0.22	24.14±0.12	19.85±0.24	21.21±0.53	21.64±0.33	22.57±0.63	26.25±0.29	27.35±0.22
5	34.17±0.74	33.34±0.63	30.36±0.97	32.74±0.64	36.21±0.18	34.75±0.82	38.86±0.21	35.13±0.64
6	45.85±0.97	48.12±0.34	44.74±0.25	43.13±0.78	44.67±0.36	45.85±0.21	47.25±0.35	47.16±0.75
7	57.31±0.14	57.71±0.82	51.42±0.53	51.84±0.31	51.35±0.25	50.23±0.95	55.99±0.74	55.57±0.24
8	65.14±0.53	64.86±0.34	59.86±0.24	64.52±0.45	57.95±0.96	63.47±0.54	66.12±0.25	66.45±0.76
9	74.35±0.76	75.41±0.17	62.32±0.75	70.74±0.77	62.24±0.27	72.62±0.31	79.52±0.96	72.33±0.37
10	78.82±0.13	83.86±0.37	75.97±0.14	76.13±0.34	70.41±0.74	79.88±0.85	85.33±0.25	80.19±0.14
11	83.24±0.87	87.52±0.64	80.53±0.46	85.74±0.13	85.62±0.22	84.39±0.36	90.64±0.21	85.71±0.66
12	88.51±0.42	91.13±0.52	84.42±0.13	92.61±0.75	88.74±0.76	90.53±0.83	92.72±0.13	93.24±0.85

Each value represents the mean ± SD. (n = 3)



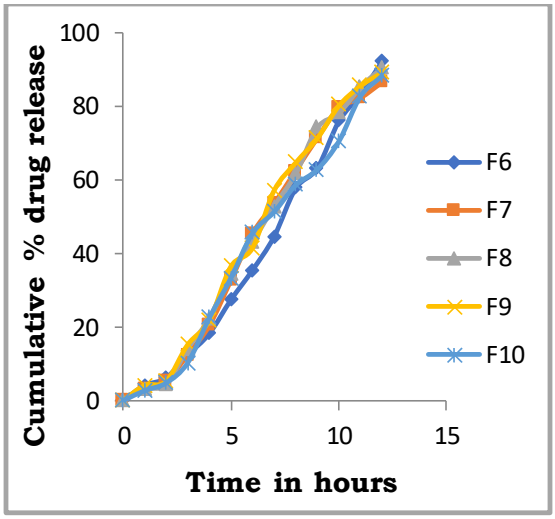
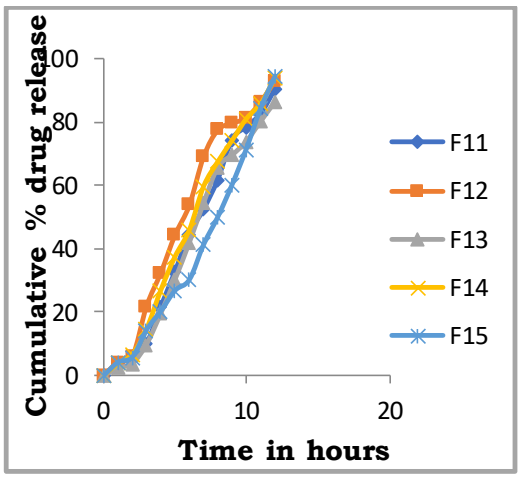


Fig. 3 & 4: *In-Vitro* dissolution studies of Ilaprazole formulations F1 to F5 and F6 to F10



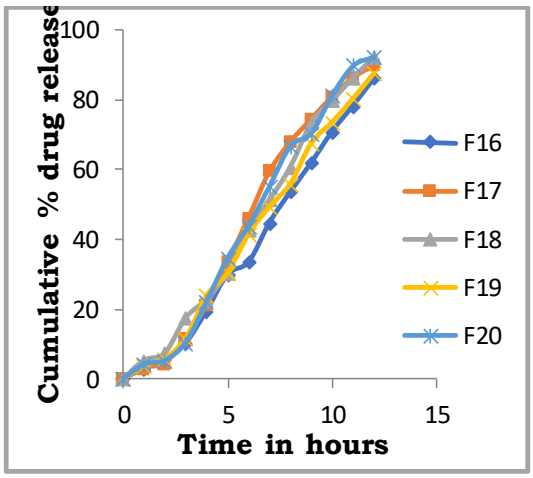
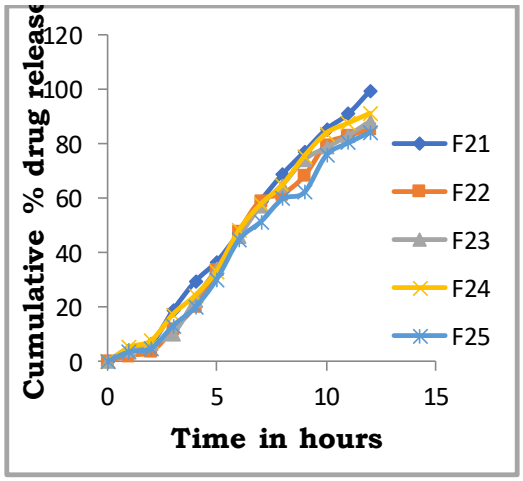


Fig. 5 & 6: *In-Vitro* dissolution studies of Ilaprazole formulations F11 to F15 and F16 to F20



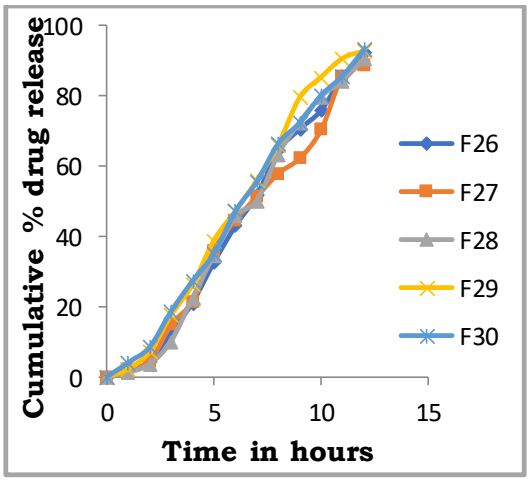
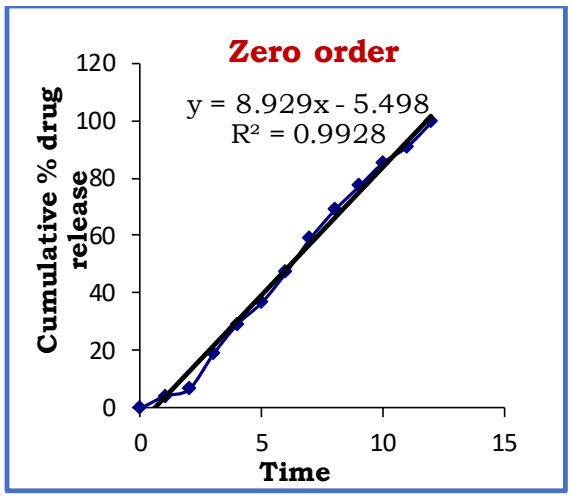


Fig. 7 & 8: *In-Vitro* dissolution studies of Ilaprazole formulations F21 to F25 and F26 to F30

Table No. 14: Ilaprazole Release Kinetic Parameters for Optimized Formulation

F.Code	Zero Order	First Order	Higuchi	Best fit	Korsmeyer-Peppas		Release Mechanism
	R^2	R^2	R^2		R^2	n-value	
F21	0.9928	0.6526	0.8915	Zero order	0.9771	1.443	Non-Fickian super case II



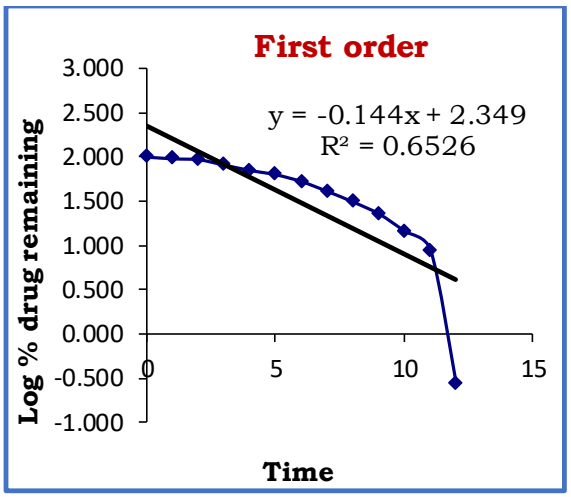
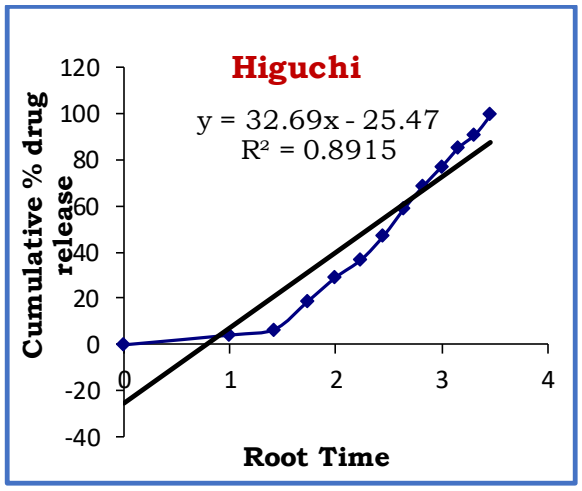


Fig. 9 & 10: Zero order release kinetics and First order release kinetics of Ilaprazole optimized Formulation (F-21)



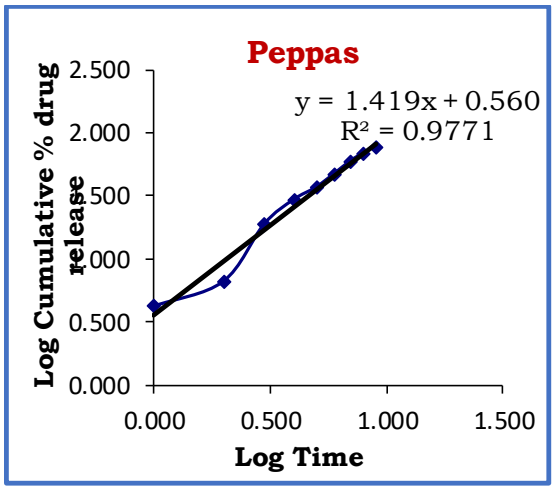


Fig. 11 & 12: Higuchi model kinetics and Korsmeyer-Peppas model kinetics of Ilaprazole optimized Formulation (F-21)

CONCLUSION

Ilaprazole Extended-release tablets were formulated by wet granulation method by using different Polymers such as HPMC K4M, K15M, K100M, Carbopol 934, Eudragit-S100, Eudragit -L100, Eudragit-RSPO and Natural Polymers such as Sodium CMC, Xanthan gum, Guar gum and Talc is used as a glidant, magnesium stearate is lubricant, PVP-K30 as binder, IPA as solvent, Sodium bicarbonate as acid neutralizing agent and Avicel PH 102 was used as diluent. Ilaprazole formulated tablet blend and tablets were subjected to their pre and post formulation characteristics like flow properties and weight variation, hardness, friability, drug content. Results of all these parameters were within the pharmacopoeial limits. Prepared formulations were subjected for *in-vitro* dissolution and release kinetic studies. The results of cumulative % drug dissolved revealed that the Ilaprazole was released in an extended manner from all the formulations whereas formulation F-21 showed maximum cumulative % drug dissolved i.e., 99.73 ± 0.19% at the end of 12th hour which was the intention of the finalized formulation (to prolong the drug dissolution up to 12 hrs) while others not being reached to the time point of maximum release are still extending the release of the drug Ilaprazole.

ACKNOWLEDGEMENTS

The authors are very thankful to Progenerics Pharma Pvt. Ltd, Hyderabadand also thankful to Brilliant Group of Institutions (Integrated Campus), Abdullapurmet, Hayathnagar, R.R Dist, Telangana, India for providing necessary facilities to carry out this work.

REFERENCES:

1. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed., Varghese Publishing House, Mumbai: **1987**; p. 430-432.
2. Aulton ME. Pharmaceutics- The Design and Manufacture of Medicines, 3rd edn. Philadelphia: Churchill living stone; **2007**: 355-357.
3. Bhavani B, Kamala Kumari P.V, Chowdary K.P.R Formulation and evaluation of glipizide sustained release tablets. Int J Pharm Biomed Res, **2012**; 3(1): 44-48.
4. Gupta Bijank, Debnath Rabindra, Ghosh Soumyadeep, Chakraborty Manas, Biswas Amitava. Formulation development studies of bilayer tablet glipizide: a novel and evolutionary approach in the treatment of diabetes. Asian J Pharm Clin Res, **2013**; 6(4): 131-137.

5. Kamalakkannan V, Sivaprakash R, Venkatraman P, Sambath kumar R, Arul kumaran K.S.G. Design and Development of Sustained Release Matrix Tablets of Tramadol Hydrochloride are using Gum kondagogu as a Natural polymer. Sch Acad J Pharm, **2015**; 4(3): 199-207.
6. Murali Krishna K, Arunkumar S. Effect of Geometrical Proportionality on Losartan Potassium SR Matrix Tablets: A Comparative Evaluation of Wet Granulation & Direct Compression. Res J Pharm Biol& Chem Sci, **2012**; 3(4): 1146-1158.
7. Perves Khan Md, Syed Abdul Azeez Basha, Hamid Mudabbir M.A. Formulation and evaluation of bilayer matrix tablets for controlled delivery of metformin hcl & vildagliptin. Int J Pharm Tech, **2014**; 6(2): 6739-6756.
8. Anil kumar A, Sujatha kumari M, Surekha K, Prasad ChSS, Suresh S. Formulation and evaluation of sustained release valsartan matrix tablets by using natural polymers. Int JPharmChemBiol Sci, **2012**; 2(2): 146-150.
9. Afrasim Moin, Shiva kumar HG. Formulation of Sustained-Release Diltiazem Matrix Tablets Using Hydrophilic Gum Blends. Tropi J Pharm Res, **2010**; 9(3): 283-291.
10. Bharathi A, Sushma CH, Silpika K, Deepthi K.N.V, Bhagya Lakshmi S. Formulation development and evaluation of sustained release matrix tablets of quetiapine fumarate. J Chem Pharm Res, **2014**; 6(4): 628-632.
11. Gourishyam Pasa, Uma Shankar Mishra, Niraj Kanti Tripathy, Kishanta Kumar Pradhan, Ghanshyam Panigrahi, Amar Kant Goudo. Preparation and in-vitro evaluation of sustained-release matrix tablets of diclofenac sodium using natural retarding polymers by model dependent approaches. Int J Adv in Pharm Res, **2011**; 2(11): 602-606.
12. Utpal Das, Shimul Halder, Abul Kalam Lutful Kabir, Harun-Or-Rashid, Abu Shara Shamsur Rouf. Development and *in-vitro* Evaluation of Sustained Release Matrix Tablets of Indapamide from Methocel K15 MCR and K100 LVCR. Dhaka Univ. J Pharm Sci, **2011**; 10(2): 87-92.
13. Rahman Mofizur Md, Sayeed Hasan, Ashiqul Alam Md, Sumon Roy, Mithilesh Kumar Jha, Qamrul Ahsan Md, Habibur Rahman Md. Formulation and evaluation of Ranolazine sustained release matrix tablets using Eudragit and HPMC. Int J Pharm Biomed Res, **2011**; 2(1): 7-12.
14. Kumar V, Soni GC, Prajapati SK. Sustained Release Hydrophilic Matrix Tablet of Ibuprofen: Influence of Polymers on In-Vitro Release and Bioavailability. Int Jfor Pharm Res Sch, **2012**; 1(4): 68-83.
15. Asim Kumar Biswal, Sanjay kumar Panda, Kirti Ranjan Parida, Harekrishna Roy. Design and In-Vitro Evaluation of Sustained Release Matrix Tablet of Complexed Nicardipine Hydrochloride. Int JPharm Chem Sci, **2013**; 2(3): 1266-1272.
16. Jarkko Ketolainen, Seppo Pohja, Eero Suihko, Mika Vidgren, Petteri Paronen. Starch acetate as a tablet matrix for sustained drug release. J Cont Rel, **2004**; 94: 293-302.
17. Asif Khan Md, Saeed Md, Amir Badshah, Naveed Md, Jahangir Khan, Farhat Ali Khan, Haroon Khan, Shafiq ur Rahman. Design, formulation, optimization and evaluation of sustained release tablets of domperidone. AfrJ Pharm Pharmacol, **2011**; 5(16): 1882-1887.
18. Jannatun Tazri, Mizanur Rahman Moghal Md, Syed Masudur Rahman Dewan, Wahiduzzaman Noor, Nor Mohammad. Formulation and Quality Determination of Indapamide Matrix Tablet: A Thiazide Type Antihypertensive Drug. Adv Pharm Bullet, **2014**; 4(2): 191-195.
19. Barot N, Darshan M, Dr. Praful D. Formulation, Development and Evaluation of Sustained Release Matrix Tablets of Repaglinide. Int J Pharm Res Bio Sci, **2014**; 3(2): 370-396.
20. Sumit M. Deshmukh, Hemlata M. Nimje, Rajesh J. Oswal, Rishikesh V. Antre, Calibration Curve Method Development For Analysis Of Tenatoprazole. IJCRR, **2011**; 3(5): 73-77.
21. Hindustan Abdul Ahad, Anand Babu U, Nagesh K, Sai Kiran D, Bindu Madhavi K. Fabrication of glimepiride *datura stramonium* leaves mucilage and poly vinyl pyrrolidone sustained release matrix tablets: *in-vitro* evaluation. Kathmandu Uni J Sci Eng Tech, **2012**; 8(1): 63-72.
22. Prajapati B.G, Patel K.R. Once-Daily Sustained-Release Matrix Tablets of Losartan potassium: Formulation and *in-vitro* Evaluation. Int J Med Clin Res, **2010**; 1(1): 01-07.
23. Sajid Khan Sadozai, Kamran Ahmad Chishti, Rooh Ullah, Zahid Hussain, Majid Khan Sadozai, Shafiq Ur Rahman, Farhad Ullah. Comparative Study of Domperidone Sustained Release Matrix Tablets Prepared by Wet Granulation and Solvent Evaporation Techniques Using Xanthan Gum. Middle-East J Scient Res, **2013**; 15(9): 1206-1215.
24. Shanmuganathan Seetharaman, Harika Balya, Hindustan Abdul Ahad. Formulation and Evaluation of Sustained Release Matrix Tablets of Ciprofloxacin HCL Using Gum Kondagogu and Chitosan as Matrix Forming Polymers. Int J Pharm Sci Rev Res, **2014**; 24(1): 115-119.
25. Phoke S. V, Sakarkar D. M, Mitkare S. S.Formulation and Characterization of Sustain Release Matrix tablet of Venlafaxine Hydrochloride by using Natural Polymers. Int J Pharm Frontier Res, **2012**; 2(4): 14-26.
26. Deshmukh V.N, Singh S.P, Sakarkar D.M. Formulation and Evaluation of Sustained Release Metoprolol Succinate Tablet using Hydrophilic gums as Release modifiers. Int J PharmTech Res, **2009**; 1(2): 159-163.
27. Dinanath Gaikwad, Jadhav RT, Amol Limkar, Sangeeta S, Kisan Bobe, Manoj Patil,Trushali Khade, Bhaskar Gavitre, Vivek Kulkarni, Uday Gaikwad. Formulation and Evaluation of Sustained Release Tablet ofAceclofenac by Film Coating. IntJ Res in Pharm Biomed Sci, **2011**; 2(1): 310-318.
28. Bagyalakshmi J, Phani Krishna Y, Ravi T, K. bilayer tablet formulation of metformin hydrochloride and glipizide: a novel approach in the treatment of diabetes.Int J Pharm Sci Rev Res, **2011**; 8(2): 209-215.
29. Yie W. Chien. Novel Drug Delivery Systems, 2nd edition. Marcel Dekker Inc; New York, **2007**: 139-196.
30. Loyd V. Allen, Howard C. Ansel. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 10th edition. Wolters Kluwer; **2014**: 263-298.
31. Sarika P, Ashutosh B, Deepak Sharma. Sustained release matrix technology and recent advance in matrix drug delivery system: A Review. Int J Drug Res Tech, **2013**; 3(1): 12-20.
32. Tarun P, Soniya, Vishal Singh, Gaurav Singh, Satyanand T, Chirag Patel, Anil Gupta. Novel oral sustained release

technology: A concise review. Int J Res Develop in Pharm Life Sci, **2013**; 2(2): 262-269.
33. Leon Lachman, Herbert A. Lieberman, Joseph L. Kanig. The Theory and Practice of Industrial Pharmacy, CBS publications; **2009**: 430-456.
34. Jain N.K. Controlled and Novel Drug Delivery, 1st edition. New Delhi, CBS; **1997**: 1-26.
35. Aulton ME. Pharmaceutics The Design and Manufacture of Medicines, 3rd edition. Philadelphia: Churchill living stone; **2007**: 483-499.
36. Gilbert S. Banker. "Sustained - and Controlled-release drug-delivery systems", In Modern Pharmaceutics, 4th Edition. Marcel Dekker, New York; **2002**: 501, 505-514.
37. Ratnaparkhi M.P, Gupta Jyoti P. Sustained Release Oral Drug Delivery System - An Overview. Int J Pharm Res Rev, **2013**; 2(3): 11-21.
38. Piyush Mandhar, Gayitri Joshi. Development of Sustained Release Drug Delivery System: A Review. Asian Pacif J Health Sci, **2015**; 2(1): 179-185.
39. Abhijeet U. Bankar, Vidyadhar H. Bankar, Preeti D. Gaikwad, Sunil P.Pawar. Formulation Design and Optimization of Sustained Release Tablet of Ambroxol hydrochloride. Int J Drug Deliv, **2012**; 4(3): 375-385.
40. Darphade SM, Shejul AA, Tathe PR, Biyani KR. Formulation and characterization of sustained release matrixTablet of Metoprolol Succinate by using combination of naturaland synthetic polymer. Int J Resin Pharm Biomed Sci, **2013**; 4(3): 901-906.
41. Joseph Robinson, Vincent H. L. Lee. "Controlled drug delivery Fundamentals and applications", 2nd edition. New York, Inc; Marcel Dekker; **1987**: 3-59.
42. Abdul S. Althaf, Seshadri.T, Sivakranth M, Umal S. Khair. Design and Study of Lamivudine Oral Sustained Release Tablets. Der Pharmacia Sinica, **2010**; 1(2): 61-76.
43. Neetu K, Ajay B, Mahesh K, Gupta Ankit. Patented pharmaceutical oral controlled release matrix system. J Biol Scient Opin, **2013**; 1(3): 263-270.
44. Madhusmruti Khandai, Santanu Chakraborty, Anuradha Sharma, Debashisha Panda, Nazia Khanam, Santosh Kumar Panda. Development of propranolol hydrochloride matrix tablets: an investigation on effects of combination of hydrophilic and hydrophobic matrix formers using multiple comparison analysis. Int J Pharm Sci Rev Res, **2010**; 1(2): 1-7.
45. Manivannan Rangasamy, Venkata Krishna Reddy P, Lakshmi Narayana Rao B. Formulation development and evaluation of Voriconazole sustained release tablets. Int Curr Pharm J, **2013**; 2(10): 165-169.
46. Vikrant Saluja, Chandan Garg. Once-daily sustained-release matrix tablets of metformin hydrochloride based on an enteric polymerand chitosan. J Pharm Educ Res, **2013**; 4(1): 92-97.
47. Sethuraman S, Shrinivas gopal hukeri, Jayachandran.D.L, Jeganath.S, Praveen Kumar.T, Vinay Kumar.D, Arunachalam A. Preparation and evaluation of diltiazem sutained release tablets by using wet granulation technique. J Glob Trends in Pharm Sci, **2011**; 2(2): 187-195.
48. Swathi Kalepu, chaitanya M, Narayan raju P. Formulation and Evaluation of Sustained Release Matrix Tablets of Zidovudine. Int J Pharm Res Health Sci, **2015**; 3(3): 754-762.
49. Basavaraj, Someswara Rao B, S.V Kulkarni, Pramod Patil, Chetan Surpur. Design and Characterization of Sustained Release Aceclofenac Matrix Tablets Containing Tamarind Seed Polysaccharide. Asian J Pharm Tech, **2011**; 1(1): 17-21.
50. Hosseinali Tabandeh, Seyed Alireza Mortazavi, Tina Bassir Guilani. Preparation of Sustained-Release Matrix Tablets of Aspirin with Ethylcellulose, Eudragit RS100 and Eudragit S100 and Studying the Release Profiles and their Sensitivity to Tablet Hardness. Iran J Pharm Res, **2003**; 2: 201-206.
51. Dinesh mohan S, Roja G, Harika Y, Harika R, Gupta. V. R. M. Effect of hydrophilic and hydrophobic polymer combinations in vildagliptin sustained release tablets: fabrication and *in-vitro* characterization. Asian J Pharm, **2015**; 9(4): 298-306.
52. Prakash pawan, Kumar Nitin. Design and development of Sustained Release Matrix Tablet of Diclofenac sodium using natural polymer. Int Res JPharm, **2013**; 4(1): 169-176.
53. Sunitha Reddy M, Shoeb Ahmed Md. Formulation and evaluation of sustained release vildagliptin matrix tablets by using pectin natural polymers as release retardant. World J Pharm Pharm Sci, **2015**; 4(10): 1451-1464.
54. Prakash Rao R.B, Vijay K, Narendra C, Jitendra. Development of Isosorbide-5-mononitrate sustained release matrix tablet by statistical optimization technique. Int J Pharm Drug Anal, **2014**; 2(9): 710-718.
55. Shubhasis Dan, Hira Choudhury, Pradipta Sarkar, Bapi Gorain, Anwesha Barik, Balaram Ghosh, Tapan Kumar Pal., (2014) A randomized two-way crossover comparative pharmacokinetic study of two different tablet formulations containing Ilaprazole in healthy human Indian volunteers, Arch Med Health Sci, **2014**; 2(2): 160-164.
56. Madhusmruti Khandai , Santanu Chakraborty, Anuradha Sharma, Debashisha Panda, Nazia Khanam, Santosh Kumar Panda. Development of propranolol hydrochloride matrix tablets: an investigation on effects of combination of hydrophilic and hydrophobic matrix formers using multiple comparison analysis. Int J Pharm Sci Rev Res, **2010**; 1(2): 1-7.

How to cite this article:

B. Divya, et al., Formulation and Evaluation Parameters of Extended-Release Tablets of Ilaprazole by using Natural and Synthetic Polymers. J Pharm Res **2016**; 5(12): 256-267. **DOI: doi.org/10.5281/zenodo.6413946**

Conflict of interest: The authors have declared that no conflict of interest exists.
Source of support: Nil

