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Formulation and *in Vitro* Evaluation of Ibrutinib Extended-Release Matrix Tablets

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Abstract: The present study was aimed at the formulation and in vitro evaluation of Ibrutinib extended-release matrix tablets using different polymers in varying ratios to achieve a controlled and prolonged drug release profile. Extended-release formulations offer several advantages, including reduced dosing frequency, improved patient compliance, and maintenance of therapeutic drug levels over an extended period.

A series of Ibrutinib matrix tablet formulations (F1–F9) were prepared using suitable hydrophilic polymers at different concentrations by direct compression method. The prepared powder blends were evaluated for pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. The compressed tablets were further assessed for post-compression parameters including hardness, thickness, weight variation, friability, and drug content uniformity. All formulations exhibited satisfactory pre-compression and post-compression characteristics and were found to be within the limits specified by the Indian Pharmacopoeia (IP).

The *in vitro* dissolution studies were carried out to evaluate the drug release behaviour of the formulated tablets. The results indicated that the type and concentration of polymers significantly influenced the release pattern of Ibrutinib. Among all the formulations, formulation F6 demonstrated the most desirable extended-release profile and was considered the optimized formulation. F6 showed a cumulative drug release of 99.96% over a period of 12 hours, providing a controlled and sustained release pattern compared to the other formulations.

The findings of the study suggest that the optimized formulation (F6) is a promising extended-release matrix tablet of Ibrutinib with acceptable physicochemical properties and excellent in vitro drug release characteristics. Therefore, the developed formulation has the potential to improve therapeutic efficacy and patient compliance.

Keywords: Ibrutinib extended-release matrix tablets

1. INTRODUCTION

The oral route is the most popular route used for administration of drugs, which is due in part to the ease of administration and to the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes. The terms Sustained release, prolonged release, modified release, extended release or depot formulations are used to identify drug delivery systems that are designed to achieve or

extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. [1,2]

There are several reasons for attractiveness of these dosage forms: provides increased bioavailability of drug product, reduction in the frequency of administration to prolong duration of effective blood levels, reduces the fluctuation of peak trough concentration and side effects and possibly improves the specific distribution of the drug. If one were to develop an ideal drugdelivery system, two pre-requisites would be required: Firstly single dose for the duration of treatment whether for days or weeks as with infection, diabetes orhypertension. Second it should deliver the active entity directly to the site of action minimizing the side effects.

There are certain considerations for the preparation of extended release formulations: If the active compound has a long half-life, it is sustained on its own, If the pharmacological activity of the active is not directly related to its blood levels, If the absorption of the drug involves an active transport and If the active compound has very short half-life then it would require a large amount of drug to maintain a prolonged effective dose. The above factors need serious review prior to design.[3]

Extended release formulations make the drug available over extended time period after oral administration. The extended release product will optimize therapeutic effect and safety of a drug at the same time improving the patient convenience and compliance. By incorporating the dose for 24 hrs into one tablet/capsule from which the drug is released slowly. This formulation helps to avoid the side effects associated with low and high concentrations. The ideal drug delivery system should show a constant zero-order release rate and maintain the constant plasma concentrations.

It is desirable to maintain a therapeutic blood concentration in order to achieve the desirable pharmacological effects. To maintain a narrow range of therapeutic blood concentration it is desirable to have a dosage form that can deliver the drug in a more sustainable or controlled way to achieve the desired results. Extended release tablets and capsules are commonly taken once or twice daily, compared with counterpart conventional forms that may have to be taken three or four times daily to achieve the same therapeutic effect. Typically, extended release products provide an immediate release of drugs that promptly produces the desired therapeutic effect, followed by gradual release of additional amount of drugs to maintain this effect over a predetermined period. The sustained plasma drug levels provided by extended release products often eliminate the need for night dosing, which benefits not only the patient but the patient but the caregiver as well.[4]

Drawbacks of Conventional Dosage Form[5]

- Poor patient compliance, increased chances of missing the dose of a drug with short halflife for which frequent administration is necessary.
- The unavoidable fluctuations of drug concentration may lead to under medication or over medication.
- A typical peak-valley plasma concentration time profile is obtained which makes attainment of steady-state condition difficult.
- The fluctuations in drug levels may lead to precipitation of adverse effects especially of a drug with small Therapeutic Index (TI) whenever over medication occur.

Advantages of Extended Release Delivery System[6]

- The extended release formulations reduce dosing frequency of drugs.
- The extended release formulations may maintain therapeutic concentrations.
- Reduce the toxicity by slowing drug absorption.
- The use of these formulations avoids the high blood concentration.
- Extended release formulations have the potential to improve the patient compliance and convenience.
- Minimize the local and systemic side effects.
- Increase the stability by protecting the drug from hydrolysis or other degradative changes in gastrointestinal tract.
- Improvement in treatment efficacy.
- Minimize drug accumulation with chronic dosing.
- Improve the bioavailability of some drugs.
- Usage of less total drug.
- Improve the ability to provide special effects. For example, Morning relief of arthritis through bed time dosing.

Disadvantages of Extended Release Delivery System[6]

- Extended release formulation contains a higher drug load and thus any loss of integrity of the release characteristics of the dosage form.
- The larger size of extended release products may cause difficulties in ingestion or transit through gut.
- The release rates are affected by various factors such as food and the rate of transit through the gut.
- Some differences in the release rate from one dose to another dose but these have been minimized by modern formulations.
- High cost of preparation.
- Sometimes the target tissue will be exposed to constant amount of drug over extended period results in drug tolerance.

Rationale of Extended Drug Delivery[7]

The main objective to formulate an API in an extended drug delivery system is related to its pharmacokinetics parameters. An appropriate formulation can make the absorption, distribution, metabolism and elimination (ADME) profile of a drug much more favourable. This change of the ADME can have a profound impact on many aspects of the clinical use of the drug from patient compliance and convenience to its very efficacy, tolerance and safety parameters.

Pellets

Palletization is an agglomeration process, that converts fine powder blend of drug(s) and excipients into small, free flowing, spherical units, referred to as pellets. Rationale of extended release pellets Pellets provide the development scientist with a high degree of flexibility during the design and development of oral dosage forms. They can be divided into desired dose strengths without formulation or process changes, and can also be blended to deliver incompatible bioactive agents simultaneously or particles with different release profiles at the same site or at different sites within the gastrointestinal tract.

Advantages of extended release pellets

- Reduce dosing frequency of drugs.
- Maintain therapeutic concentrations.
- Reduce the toxicity by slowing drug absorption.
- The use of pellets avoids the high blood concentration.
- Extended release formulations have the potential to improve the patient compliance and convenience.
- Minimize the local and systemic side effects.
- Increase the stability by protecting the drug from hydrolysis or other degradative changes in gastrointestinal tract.

METHODOLOGY

7.1. Analytical method development:

7.1.1 Determination of Wavelength:

10 mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution - 10µg/ml). The working solution was taken for determining the wavelength.

7.1.2 Determination of Calibration Curve:

10 mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 8.1 and 8.2) and those concentrations absorbance were found out at required wavelength.

7.2. Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by thequality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose:

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$$\tan \theta = h / r \quad \tan \theta = \text{Angle of repose}$$

h = Height of the cone, r = Radius of the cone base

Table 7.1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density:

Density is defined as weight per unit volume. Bulk density, is defined as themass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / V_o$$

Where,M = weight of sample

V_o = apparent volume of powder

Tapped density:

After carrying out the procedure as given in the measurement of bulk densitythe cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

$$\text{Tap} = M / V$$

Where, Tap = Tapped Density

M = Weight of sample

V= Tapped volume of powder

Measures of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticle interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

$$\text{Carr's Index} = [(\text{tap} - \text{b}) / \text{tap}] \times 100$$

Where, b = Bulk Density

Tap = Tapped Density

Table 7.2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

7.3. Formulation development of Tablets:

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 7.3. The tablets were prepared as per the procedure given below and aim is to prolong the release of Ibrutinib. Total weight of the tablet was considered as 200mg.

Procedure:

1. Ibrutinib and all other ingredients were individually passed through sieve no ≠ 60.
2. All the ingredients were mixed thoroughly by triturating up to 15 min.
3. The powder mixture was lubricated with talc.
4. The tablets were prepared by using direct compression method.

Table 7.3: Formulation composition for tablets

INGREDIENTS (MG)	**FORMULATION**								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ibrutinib	40	40	40	40	40	40	40	40	40
Carbopol 71 G	20	40	60	-	-	-	-	-	-
HPMC (K4M)	-	-	-	20	40	60	-	-	-
Eudragit RSPO	-	-	-	-	-	-	20	40	60
PVP K 30	12	12	12	12	12	12	12	12	12
Talc	8	8	8	8	8	8	8	8	8
Magnesium Stearate	6	6	6	6	6	6	6	6	6
MCCph102	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Total weight	200	200	200	200	200	200	200	200	200

All the quantities were in mg

7.4. Evaluation of post compression parameters for prepared Tablets

The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined.The percent deviation was calculated using the following formula.

$$\% \text{ Deviation} = (\text{Individual weight} - \text{Average weight} / \text{Average weight}) \times 100$$

Table 7.4: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability:

It is measured of mechanical strength of tablets. Roche Friabilator was used to determine the friability by following procedure. Pre weighed tablets were placed in the Friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

$$\% \text{ Friability} = [(W1-W2) / W] \times 100$$

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content:

Tablets were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of drug were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with media. The solution was suitably diluted and the absorption was determined by UV–Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* drug release studies**

Dissolution parameters:

Apparatus – USP-II, Paddle Method

Dissolution Medium – 0.1 N HCl, p H 6.8 Phosphate buffer

RPM – 50

Sampling intervals (hrs) – 0.5,1,2,3,4,5,6,7,8,9,10,11,12

Temperature – 37°c ± 0.5°c

Procedure:

900 ml 0f 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablet was placed in the vessel and apparatus was operated for 2 hours and then the media 0.1 N HCl were removed and pH 6.8 phosphate buffer was added process was continued up to 12 hrs at 50 rpm. At definite time intervals withdrawn 5 ml of sample, filtered and again 5ml media was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at required wavelength using UV-spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyse the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data are fitted to the followingequation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rateconstant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$Log (100-F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plottedthen it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k\ t1/2$$

Where, 'k' is the Higuchi constant.
In Higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage ofdrug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t/ M_\infty = K\ t^n$$

Where,M_t/ M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' isthe diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0;while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport),n=1; and for super case II transport, n > 1.In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100-Q_t)^{1/3}= 100^{1/3}– K_{HC}.t$$

Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrixthrough mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

7.5. Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy:

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany(Alpha T).The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 cm^{-1} to 400cm^{-1}.

8 RESULTS AND DISCUSSION

The present study was aimed to developing extended-release tablets of Ibrutinib using various polymers. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

8.1. Analytical Method

Graphs of Ibrutinib were taken in 0.1N HCl and in pH 6.8 phosphate buffer at 260 nm and 263 nm respectively.

Table 8.1: Observations for graph of Ibrutinib in 0.1N HCl (260nm)

Conc. [µg/ml]	Absorbance
0	0
5	0.115
10	0.218
15	0.336
20	0.439
25	0.546

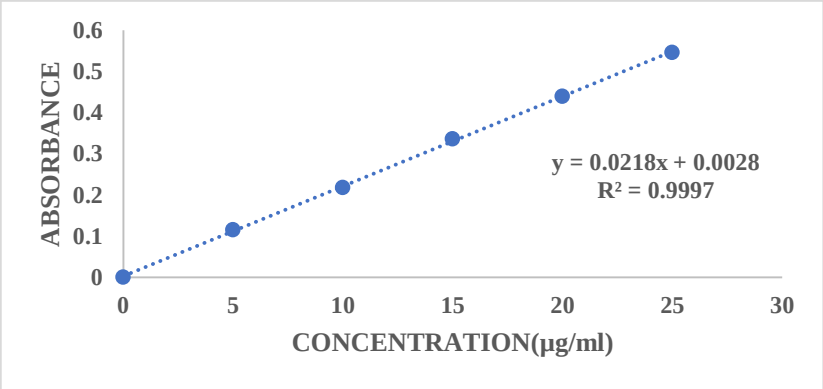

Fig 8.1: Standard graph of Ibrutinib in 0.1N HCl

Table 8.2: Observations for graph of Ibrutinib in pH 6.8 phosphate buffer (263nm)

Concentration [µg/ml]	**Absorbance**
0	0
5	0.131
10	0.265
15	0.388
20	0.518
25	0.653

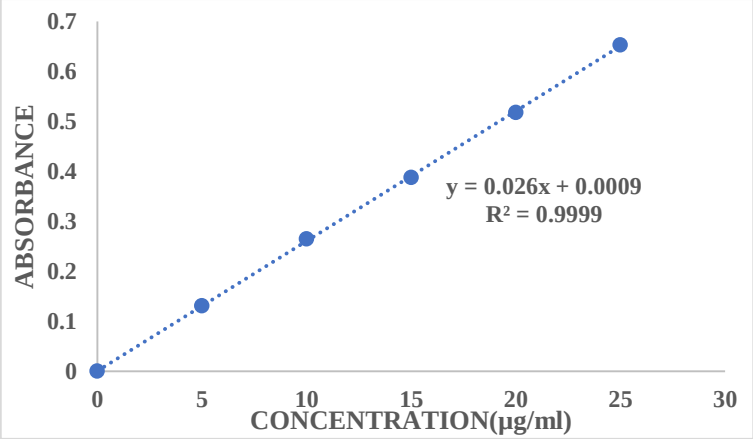

Fig 8.2: Standard graph of Ibrutinib pH 6.8 phosphate buffer (263 nm)

8.3. Preformulation parameters of powder blend

Table 8.3: Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	27.43±0.16	0.58±0.04	0.69±0.02	15.94±0.43	1.18±0.03
F2	24.33±0.12	0.56±0.06	0.66±0.05	15.15±0.14	1.17±0.01
F3	29.56±0.32	0.53±0.05	0.63±0.04	15.87±0.28	1.18±0.11
F4	30.00±0.17	0.65±0.05	0.76±0.03	14.47±0.37	1.16±0.09
F5	28.25±0.11	0.74±0.02	0.82±0.02	9.75±0.59	1.10±0.11
F6	27.97±0.81	0.72±0.06	0.84±0.04	14.28±0.67	1.16±0.02
F7	26.05±0.73	0.52±0.04	0.66±0.03	20.45±0.56	1.26±0.10
F8	25.24±0.71	0.64±0.01	0.75±0.05	16.92±0.67	1.17±0.04
F9	23.00±0.72	0.71±0.01	0.82±0.02	13.14±0.42	1.15±0.01

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 23.00±0.72 to 30.00±0.17 (gm/cm^3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.63±0.04 to 0.84±0.04 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 18 which show that the powder has good flow properties.All the formulations has shown the Hausner ratio below 1.22 indicating the powder has good flow properties.

8.4. Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

Table 8.4: *In-vitro* quality control parameters for tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	199.13	2.85	0.65	1.86	98.12
F2	198.48	2.64	0.45	1.72	99.38
F3	201.63	2.73	0.39	1.79	99.45
F4	199.88	2.88	0.49	1.88	97.37
F5	200.45	2.69	0.61	1.85	99.22
F6	200.37	2.71	0.44	1.82	99.12
F7	201.66	2.75	0.52	1.76	98.08
F8	199.85	2.68	0.59	1.73	97.18
F9	198.72	2.72	0.61	1.81	98.46

Weight variation test:

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 8.4. The average weight of the tablet is approximately in range of 198.48 to 201.63 mg, so the permissible limit is ±7.5% (>200mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

Hardness test:

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 8.4. The results showed that the hardness of the tablets is in range of 2.64 to 2.88kg/cm^2,which was within IP limits.

Thickness:

Thickness of three tablets of each batch was checked by using Micrometer and data shown in Table-8.4. The result showed that thickness of the tablet is raging from 1.72 to 1.88mm.

Friability:

Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 8.4. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Drug content:

Drug content studies were performed for the prepared formulations. From the drug content studies it was concluded that all the formulations were showing the % drug content values within 97.18 -99.45 %.

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

8.5. In-vitro drug release studies

Table 8.5: Dissolution data of Ibrutinib tablets

TIME (H)	CUMULATIVE percent drug dissolved								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	26.43	22.15	19.74	18.28	15.01	12.51	22.67	19.69	12.73
1	36.64	28.67	22.55	26.23	21.56	18.74	28.56	25.31	17.39
2	51.01	36.46	29.63	39.75	27.08	29.66	33.34	29.46	22.16
3	56.81	45.63	33.42	45.31	33.42	35.32	42.65	36.25	27.62
4	62.25	49.86	39.36	52.67	39.93	43.07	51.84	42.86	32.43
5	64.96	54.65	47.89	58.54	45.58	48.22	58.57	45.11	39.17
6	75.08	62.37	52.28	63.12	52.85	57.39	62.23	46.27	43.89
7	82.52	66.16	58.81	71.68	56.16	63.82	66.68	57.86	48.46
8	88.73	72.25	64.38	77.02	59.04	69.45	73.52	62.22	54.73
9	91.28	75.56	72.75	85.52	65.37	72.89	79.09	66.76	59.54
10	93.44	83.68	76.98	89.83	77.56	83.65	86.35	69.45	64.13
11	95.12	87.29	89.21	93.13	82.47	85.23	91.83	78.51	68.21
12	97.68	93.77	98.75	95.25	96.58	99.96	95.25	87.29	72.27

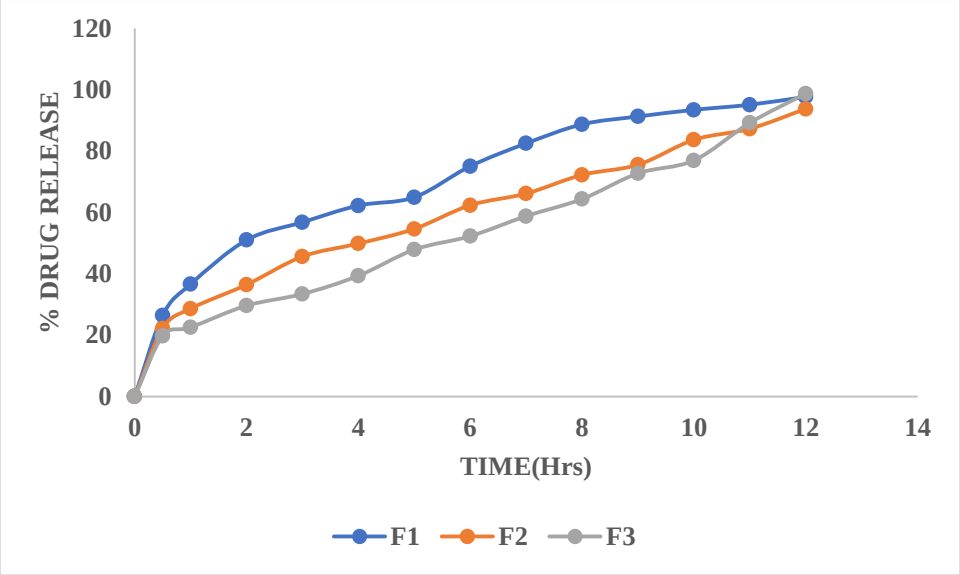

Fig 8.3: Dissolution profile of Ibrutinib (F1, F2, F3 formulations)

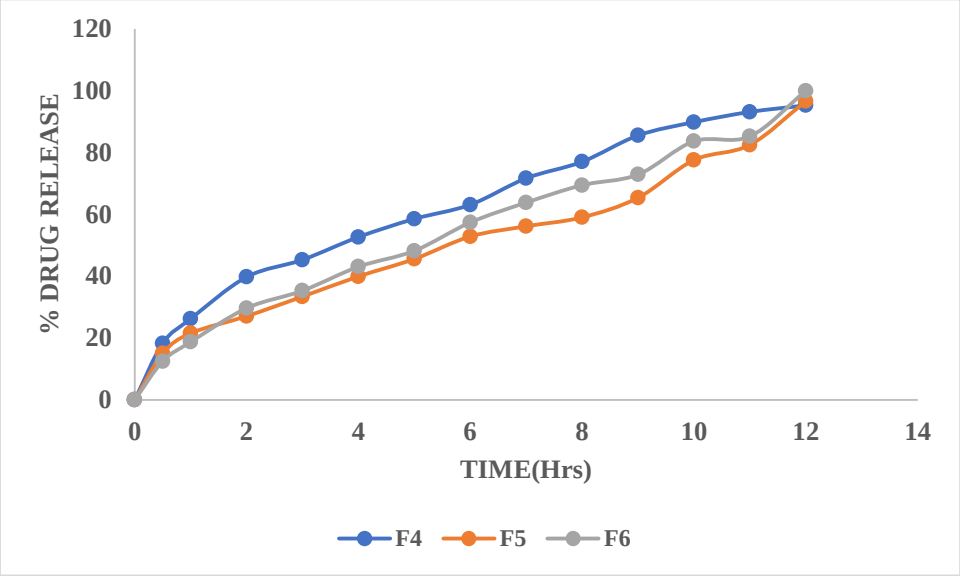

Fig 8.4: Dissolution profile of Ibrutinib (F4, F5, F6 formulations)

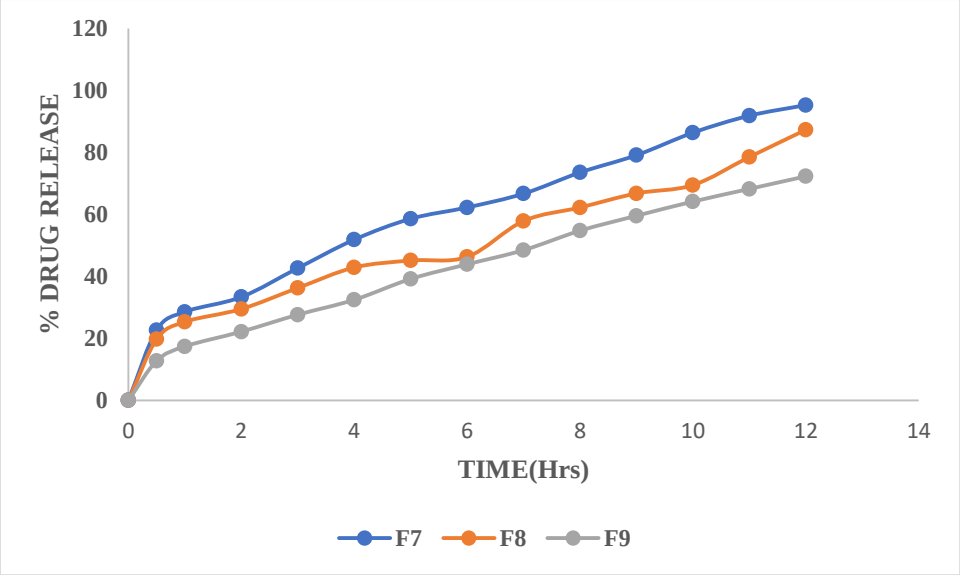

Fig 8.5: Dissolution profile of Ibrutinib (F7, F8, F9 formulations)

Formulations prepared with Carbopol 71 G retarded the drug release in the concentration of 60 mg (F3Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 98.75% in 12 hours with good retardation.

From the dissolution data it was evident that the formulations prepared with different concentrations as20, 40and 60mgpolymer were retard the drug release up to desired time period i.e., 12 hours.

Formulations prepared with HPMC K100M retarded the drug release in the concentration of 60mg (F6 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.96% in 12 hours with good retardation.

From the dissolution data it was evident that the formulations prepared with different concentrations as20, 40 and 60mgpolymer were retard the drug release up to desired time period i.e., 12 hours.

Formulations prepared with Eudragit RSPO retarded the drug release in the concentration of 20 mg (F7Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 95.25% in 12 hours with good retardation.

From the dissolution data it was evident that the formulations prepared with different concentrations as20, 40 and 60mgpolymer were retard the drug release up to desired time period i.e., 12 hours.

From the above results it was evident that the formulation F6is best formulation with desired drug release pattern extended up to 12 hours.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyse the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Table 8.6: Release kinetics data for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	%) REL	LOG (T	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0	0	0	0	0	0	0	0	0	0	0
12.51	0.5	0.707	0.841	0.917	0.958	0.979	0.989	0.995	0.997	0.999	0.999	-0.001
18.74	1	1.000	1.273	0.000	1.910	18.740	0.0534	-0.727	81.26	4.642	4.331	0.310
29.66	2	1.414	1.472	0.301	1.847	14.830	0.0337	-0.528	70.34	4.642	4.128	0.514
35.32	3	1.732	1.548	0.477	1.811	11.773	0.0283	-0.452	64.68	4.642	4.014	0.627
43.07	4	2.000	1.634	0.602	1.755	10.768	0.0232	-0.366	56.93	4.642	3.847	0.795
48.22	5	2.236	1.683	0.699	1.714	9.644	0.0207	-0.317	51.78	4.642	3.727	0.914
57.39	6	2.449	1.759	0.778	0.389	9.565	0.0174	-0.241	42.61	4.642	3.493	1.149
63.82	7	2.646	1.805	0.845	0.423	9.117	0.0157	-0.195	36.18	4.642	3.307	1.334
69.45	8	2.828	1.842	0.903	0.452	8.681	0.0144	-0.158	30.55	4.642	3.126	1.515
72.89	9	3.000	1.863	0.954	0.477	8.099	0.0137	-0.137	27.11	4.642	3.004	1.638
83.65	10	3.162	1.922	1.000	0.500	8.365	0.0120	-0.078	16.35	4.642	2.538	2.104
85.23	11	3.317	1.931	1.041	0.521	7.748	0.0117	-0.069	14.77	4.642	2.454	2.188
99.96	12	3.464	2.000	1.079	0.540	8.330	0.0100	0.000	0.04	4.642	0.342	4.300

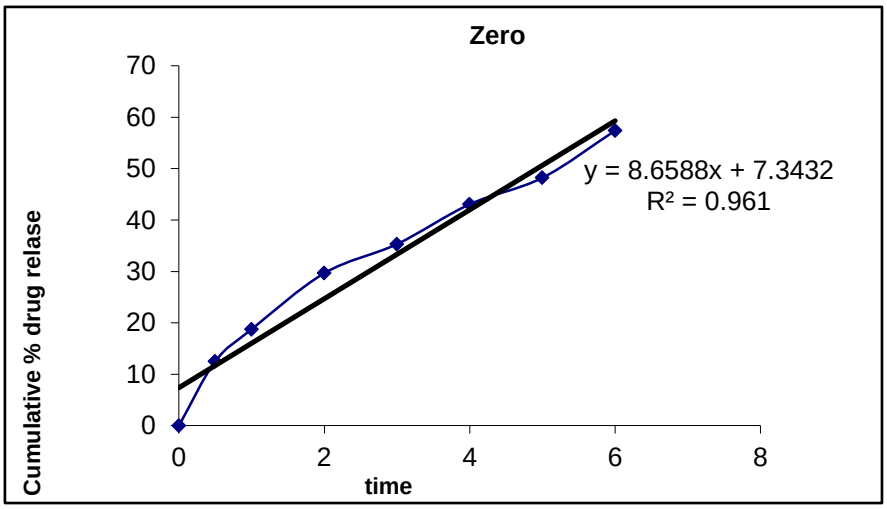

Fig 8.6: Zero order release kinetics graph

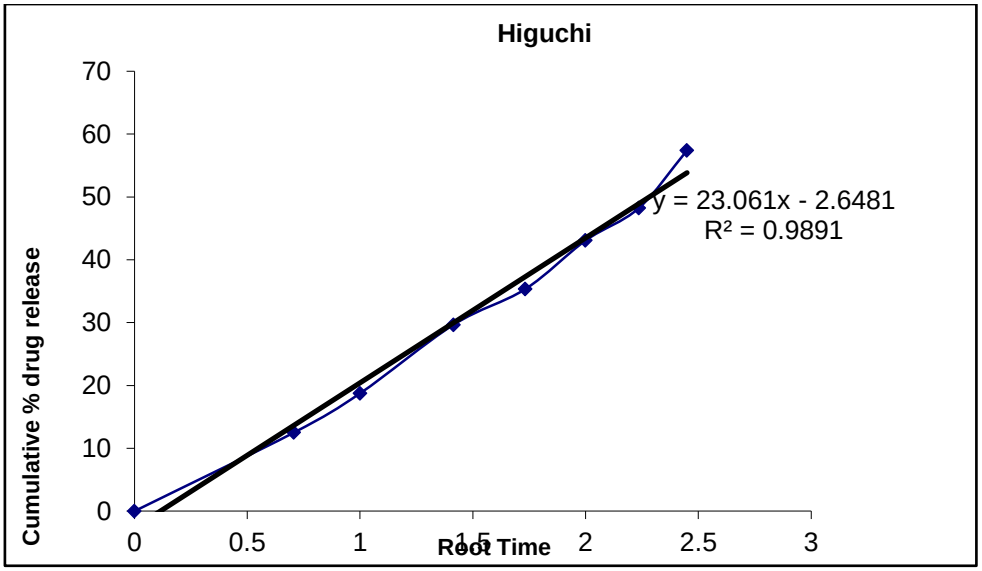

Fig 8.7 : Higuchi release kinetics graph

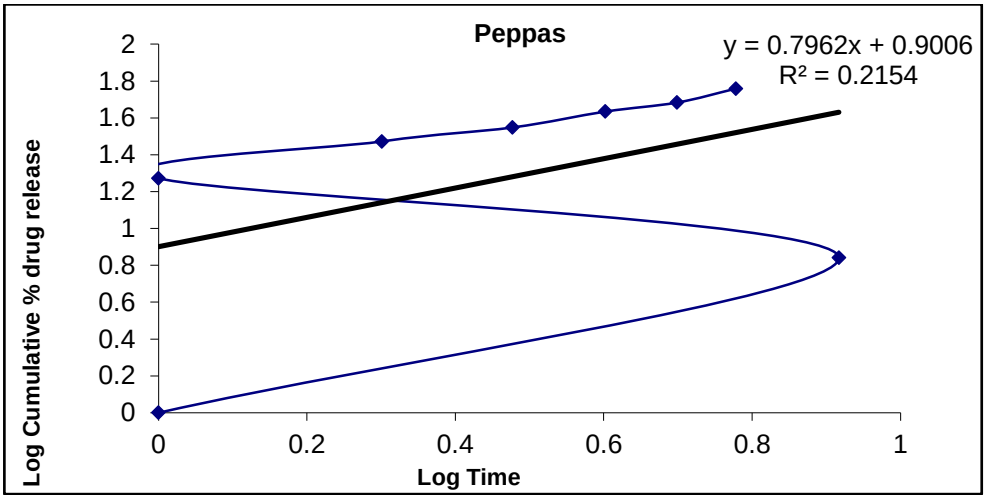

Fig 8.8: Kars mayer Peppas graph

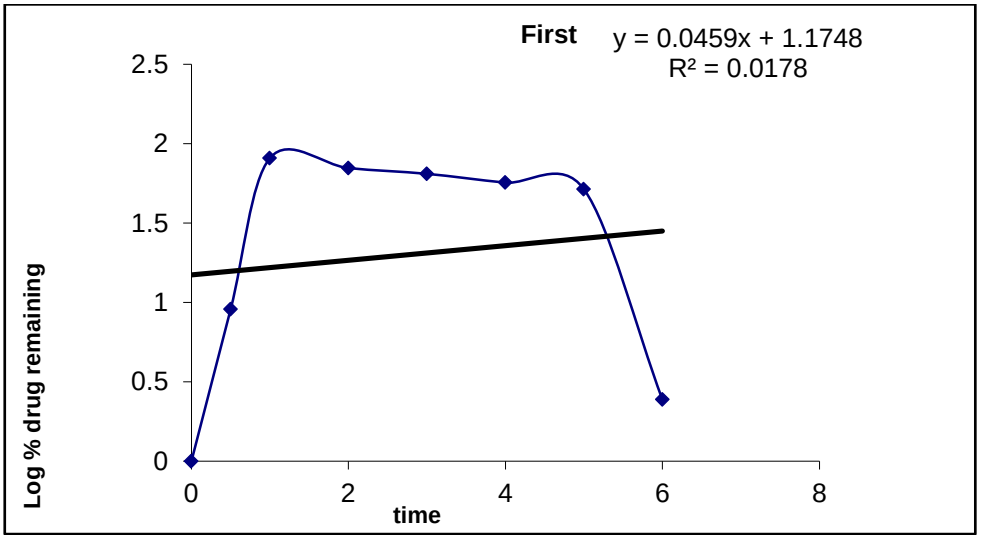

Fig 8.9: First order release kinetics graph

From the above graphs it was evident that the formulationF6 was followed First order release.

Drug – Excipient compatibility studies

Fourier Transform-Infrared Spectroscopy:

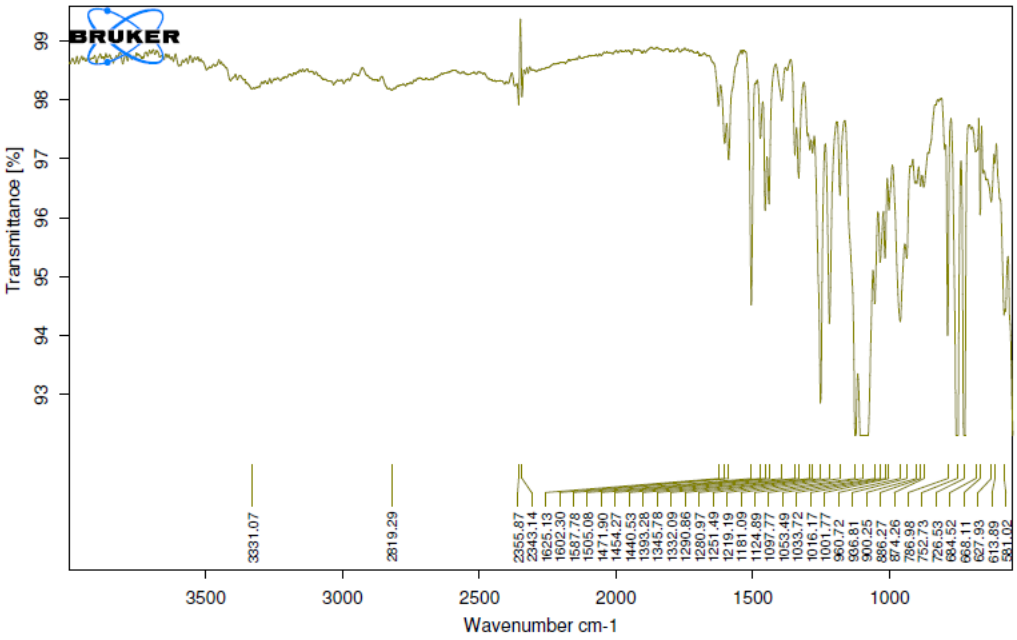

Fig 8.10: FT-IR Spectrum of pure drug

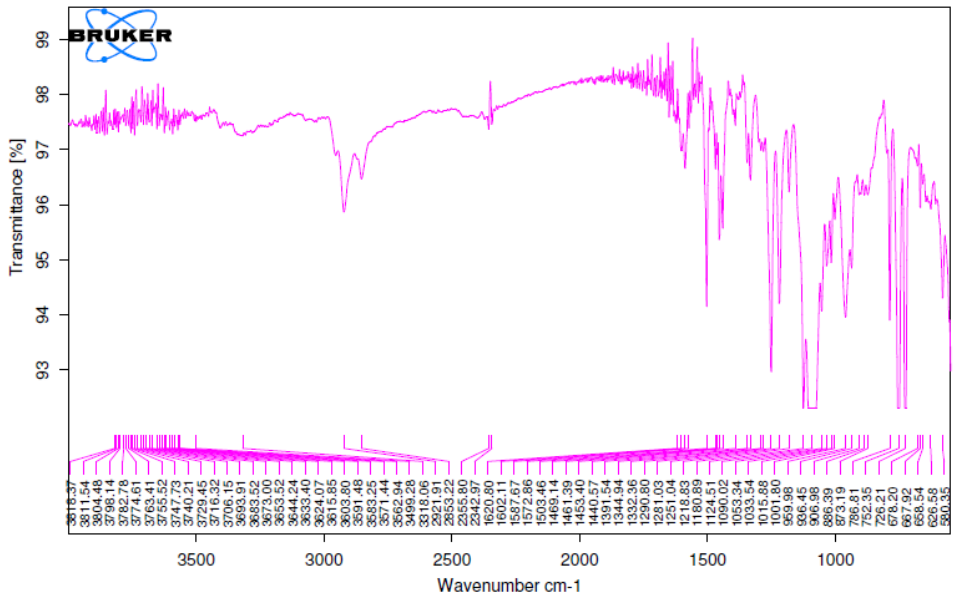

Fig 8.11: FT-IR Spectrum of Optimized Formulation

9. CONCLUSION

The present study successfully formulated and evaluated extended-release matrix tablets of Ibrutinib using different polymers at varying concentrations and ratios. The prepared formulations were subjected to comprehensive pre-compression and post-compression evaluation to assess their pharmaceutical suitability and performance.

The pre-compression parameters, including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio, indicated satisfactory flow properties and compressibility of the powder blends.

The post-compression evaluation revealed that all formulations complied with the Indian Pharmacopoeia (IP) specifications for tablet weight variation, hardness, thickness, friability, and drug content uniformity, confirming the adequacy of the manufacturing process and tablet quality.

The in vitro dissolution studies demonstrated that the type and concentration of polymers significantly influenced the drug release profile. By optimizing the polymer composition and ratio, a controlled and prolonged release of Ibrutinib was achieved over the intended duration. The optimized formulation exhibited a desirable extended-release pattern with consistent drug release, thereby reducing the frequency of administration and potentially improving patient compliance.

Overall, the study concludes that extended-release matrix tablets of Ibrutinib can be effectively developed using suitable polymer combinations. The optimized formulation showed acceptable physicochemical characteristics and satisfactory in vitro drug release behavior, indicating its potential as a promising extended-release oral dosage form for the effective management of diseases treated with Ibrutinib. Further stability studies and in vivo investigations are recommended to establish the long-term performance and therapeutic efficacy of the developed formulation.

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REFERANCES

1. Mr. Samir J. Shah , Dr. Paresh B. Shah Dr. Mukesh S. Patel , Dr. Mukesh R. Patel. A review on extended release drug delivery system And multiparticulate system. Vol 4, Issue 08, 2015.
2. Gupta PK and Robinson JR. Oral controlled release delivery. Treatise on controlled drug delivery., 1992; 93(2): 545-555.
3. Jantzen GM and Robinson JR. Sustained and Controlled-Release Drug Delivery systems. Modern Pharmaceutics., 1995; 121(4): 501-502.
4. Khyati patel , dr. Upendra patel ,bhavinbhimani ,ghanshyampatel, dhirendaslaniya. Extended Release Oral Drug Delivery System. IJPRBS, 2012: Volume1(3): 1-26.
5. Wani MS. Controlled Release System A Review; Pharmaceutical Reviews., 2008; 6(1): 41-46.
6. Hayashi T. Formulation, study and drug release mechanism of a new Theophylline sustained release preparation, Int. J Pharm., 2005; 304: 91-101.
7. Venkatraman S, Davar N and Chester A. An overview of controlled release systems: Edited by Donald L Wise, New York, Marcel Dekker Inc. Handbook of Pharmaceutical controlled release Technology., 2000; 431- 465.
8. Patel P., Pellets: A General Overview, International Journal of Pharma World Research; 2010; 1(2): 1-15.
9. Hamed Barzeh , Bharani S Sogali, Sepideh Shadvar. A Review OnExtended Release Matrix Tablet. Journal of Pharmaceutical Research Vol.15. No.4, Oct. - Dec. 2016 : 148.
10. Brahmankar H A, Jaiswal S B. Bio pharmaceutics and pharmacokinetics. Treatise: Vallabh Prakashan; 2000.
11. Bhargava A, Rathore R P S, Tanwar Y S,Gupta S, Bhaduka G. oral sustained release dosage form an opportunity to prolong the release of drug. Int J Adv Res Pharm Bio Sci. 2013;3(1):7-14.
12. Chauhan M J, Patel S A. Aconcise review on sustained drug delivery system and its opportunities. Am J Pharm Tech Res. 2012;2(2): 227-238.
13. Venkatraman S, Davar N, Chester A. An overview of controlled release systems. Donald L Wise, Marcel Dekker Inc; 2000.p.431- 465.

14. Jantzen GM and Robinson JR. Sustained and controlled release drug delivery systems, in Banker GS, Rhodes CT(Eds.) Modern pharmaceutics. 3rd Ed. Revised and expanded, drugs and the pharmaceutical sciences. Marcel Dekker Inc:New York; 1995.p. 575-609.
15. Brahmankar H A, Jaiswal S B. Bio pharmaceutics and pharmacokinetics.Treatise: Vallabh Prakashan; 2000.p. 337,348-357.
16. Patel KK, Patel MS, Bhatt NM, Patel LD, Pathak NL, Patel KJ. An overview: extendedrelease matrix technology. Int J Pharm Chem Sci 2012;1(2):828.
17. Patel Kundan K , Patel Mehul S , Bhatt Nayana M, Patel LaxmanbhaiD ,PathakNimish L and Patel Kanu J. An Overview: Extended Release Matrix Technology. Vol. 1 (2) Apr – Jun 2012.
18. Venkatraman S, Davar N and Chester A. An overview of controlled release systems: Edited by Donald L Wise, New York, Marcel Dekker Inc. Handbook of Pharmaceutical controlled release Technology, 2000; 431- 465.
19. Jantzen GM., Robinson JR, Sustained and controlled-release drug delivery systems, in Banker GS, Rhodes CT (Eds.) Modern Pharmaceutics, Third Edition, Revised and Expanded, Drugs and the Pharmaceutical Sciences, Marcel Dekker, Inc., New York., 1995; 72: 575-609.
20. BrahmankarHA ., Jaiswal SB. Biopharmaceutics and Pharmacokinetics A Treatise, Vallabh Prakashan., 2000; 337: 348-357.
21. Cox PJ., Khan KA., Munday DL, Development and evaluation of a multiple-unit oral sustained release dosage form for S (+)-ibuprofen: preparation and release kinetics. Int. J. Pharm.; 1999; 193: 73 - 84.
22. Kincl M., Meleh M., Veber M., Vrecer F. Study of physiochemical parameters affecting the release of diclofenac sodium from lipophillic matrix tablets, Acta Chim Slov; 2004; 51: 409-425.
23. Schwartz JB., Simonelli AP., Higuchi WI. Drugs release from wax matrices I : Analysis of data with first order kinetics and with the diffusion controlled model. J Pharm Sci.; 1968; 57: 274-277.
24. Chandra , S., Sharma, V., N., R., & Kumawat, S. (2024). Formulation and Evaluation of Extended-Release Tablets of Ranolazine. International Journal of Health Advancement and Clinical Research (tz), 2(1), 8–14.
25. Liping Yu, Xin Huang, Manhua Jiang, Wentao Guo, Xue Li, Fangfang Huang, Jinsong You, Design and evaluation of oseltamivir phosphate dual-phase extended-release tablets for the treatment of influenza, International Journal of Pharmaceutics, Volume 661, 2024,