



FORMULATION AND IN VITRO EVALUATION OF EPROSARTAN CONTROLLED RELEASE TABLETS

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ABSTRACT

Eprosartan has a short biological half-life of 5-9 hours and having less bioavailability which necessitates multiple daily dosing. Hence the present study was aimed to develop a controlled release formulation of Eprosartan to reduce the dose related side effects and to reduce the dosage regimen. The present research project aimed to develop a Control release oral formulation of hypertension drug Eprosartan, the present research comprising Eprosartan used for the symptomatic relief of pulmonary arterial hypertension. Polymers like HPMC K15 M, Carbopol 940, Pectin and Gellan Gum were used for controlling the drug release, and the polymers are mixed in a predetermined ratio. Totally 12 formulations were prepared and evaluated for pre-compression and post-compression parameters, and all the results were found to be within the limits. From the drug and excipients compatibility studies (FTIR) it was confirmed that the drug and excipients used weren't have any interactions. The in vitro dissolution studies revealed that the F9 formulation containing 250mg of Pectin controls the drug release up to 12 hours. So Pectin containing F9 formulation was considered to be suitable for the formulation of Eprosartan controlled release tablet and the drug release kinetics revealed that the F9 formulation shows zero order kinetics with super case- II transport mechanism.

Keywords: Eprosartan, Pectin, Angiotensin II Receptor Antagonist, FT-IR.

INTRODUCTION

Due in part to its simplicity of use and the greater design flexibility provided by gastrointestinal physiology compared to most other routes, the oral route is the most widely utilized method for drug delivery. Drug delivery systems that are intended to attain or prolong therapeutic effect by continuously releasing medication over an extended period of time following administration of a single dose are referred to as sustained release, prolonged release, modified release, extended release, or depot formulations.^{1,2} These dosage forms are appealing for a number of reasons: they increase the drug product's bioavailability, decrease the frequency of administration to extend the duration of effective blood levels, lessen side effects and fluctuations in peak trough concentration, and may even enhance the drug's specific distribution. Two prerequisites must be met in order to create the perfect medication delivery system: As with infections, diabetes, or hypertension, the first dose is given once over the course of therapy, whether it be for days or weeks. Second, it should minimize adverse effects by delivering the active ingredient straight to the site of action. When creating formulations for prolonged release, there are a few things to keep in mind: If the active ingredient is sustained on its own and has a lengthy half-life, If the active ingredient's blood levels are not closely correlated with its pharmacological effectiveness, It would take a lot of medication to sustain a long-lasting effective dosage if the drug's absorption requires active transport and the active ingredient has a relatively short half-life. Before designing, the aforementioned elements need to be carefully reviewed.³

Numerous preclinical and clinical investigations have shown that AT1 receptor-mediated activity is functionally antagonistic, and that different physiological outcomes linked to angiotensin II are competitively inhibited. Eprosartan boosted renal plasma flow and salt excretion while decreasing blood pressure and plasma aldosterone levels in healthy volunteers with an active RAS or those on exogenous angiotensin II. With no

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discernible change from baseline in coronary flow reserve and unclear effects on left ventricular mass, mean plasma renin activity and angiotensin II levels were markedly elevated in hypertensive individuals receiving therapeutic doses of eprosartan. Additionally, in hypertension patients using eprosartan at therapeutic doses, undesired changes in platelet function were normalized, fibrinolytic capacity was enhanced, and hemostatic indicators were favorably adjusted.

The main effector peptide of the renin-angiotensin system (RAS), angiotensin II, is selectively inhibited by eprosartan, a nonbiphenyl, nontetrazole antagonist. The well-known actions of angiotensin II are mediated by the angiotensin II type 1 (AT1) receptor subtype, which eprosartan demonstrated a strong affinity for in in vitro experiments.⁴

MATERIALS

Eprosartan were procured from A. R. Life Sciences, Hyderabad, HPMC K15 M, Carbopol 940 were procure from Strides arcolab, Bangalore, Pectin were procured from Himedia laboratory. Mumbai, Gellan Gum, MCC, Lactose, PVP K 30, Magnesium Stearate, Talc were procured from Loba chemie pvt.ltd, Mumbai.

METHODOLOGY

Pre formulation studies⁵⁻⁶

Pre formulation testing is an investigation of physical and chemical properties of drug substances alone and when combined with pharmaceutical excipients. It is the first step in the ratio development of dosage form.

Determination of melting point

Melting point of Eprosartan was determined by capillary method. Fine powder of Eprosartan was filled in glass capillary tube (previously sealed on one end). The capillary tube is tied to thermometer and placed in oil bath (light paraffin oil bath), The temperature at which it starts to melt was noted.

Solubility

Solubility of Eprosartan was determined in pH 1.2 and pH 7.4 and 6.8 phosphate buffers. Solubility studies were performed by taking excess amount of Eprosartan in beakers containing the solvents. The mixtures were shaken for 24hrs at regular intervals. The solutions were filtered by using whattmann's filter paper grade no. 41. The filtered solutions are analyzed by spectrophotometrically.

Compatibility Studies

Compatibility study with excipients was carried out by FTIR. The pure drug and its formulations along with excipients were subjected to FTIR studies. In the present study, the potassium bromide disc (pellet) method was employed.

Identification of Eprosartan⁷

PREPARATION OF BUFFERS

0.1 N HCL

Dilute 8.50 ml of HCL with distilled water to make up the volume to 1000 ml

6.8 pH Phosphate buffer

Dissolve 13.872 g of potassium dihydrogen phosphate and 35.084 g of disodium hydrogen phosphate in sufficient water to produce 1000 ml.

7.4 pH Phosphate buffer

Dissolve 0.6 g of potassium dihydrogen phosphate and 6.4 g of disodium hydrogen phosphate and 5.85 g of sodium chloride in distilled water and dilute upto 1000.0 ml .

Determination of UV spectrum of Eprosartan:

10 mg of Eprosartan was dissolved in 10 ml of buffer. so as to get a stock solution of 1000 µg/ml concentration. From the above stock solution pipette out 1ml of the solution and makeup the volume to 10ml using buffer to get the concentration of 100 µg/ml concentration. From this stock solution pipette out 1ml of the solution and makeup the volume to 10ml using buffer to get the concentration of 10 µg/ml concentration, this solution was scanned under **UV Spectroscopy using 200-400nm.**

Preparation of Standard Calibration Curve of Eprosartan in pH 1.2:

A. Preparation of Stock Solution

10mg of Eprosartan was dissolved in 10ml of pH 1.2 buffers so as to get a stock solution of 1000 µg/ml concentration.

B. preparation Standard Solution

1ml of stock solution was diluted to 10ml with pH 1.2 buffer in 10ml volumetric flask this gives a concentration of 10µg/ml. Aliquot of standard drug solutions were prepared by withdrawing 0.2, 0.4, 0.6, 0.8,1.0 and 1.2ml and transferred in to 10ml volumetric flask and were diluted up to the mark with pH 1.2 buffer. This gives the final concentration of 2, 4, 6, 8, 10 and 12µg/ml of Eprosartan respectively. The absorbances of the solution were measured against pH 1.2 as blank at 233 nm using UV visible spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Preparation of Standard Calibration Curve of Eprosartan in pH 6.8:**A. Preparation of Stock Solution**

10mg of Eprosartan was dissolved in 10ml of pH 6.8 phosphate buffer so as to get a stock solution of 1000µg/ml concentration.

B. preparation Standard Solution

1ml of stock solution was diluted to 10ml with pH 6.8 buffer in 10ml volumetric flask this gives a concentration of 10µg/ml. Aliquot of standard drug solutions were prepared by withdrawing 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2ml and transferred in to 10ml volumetric flask and were diluted up to the mark with pH 6.8 buffer. This gives the final concentration of 2, 4, 6, 8, 10 and 12µg/ml of Eprosartan respectively. The absorbances of the solution were measured against pH 6.8 as blank at 233 nm using UV visible spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

6.6 Preparation of Eprosartan Controlled Release Tablets:⁸⁻¹²

Controlled release tablets of Eprosartan were prepared by Direct compression method using variable concentrations of different polymers like Xanthan Gum, Carbopol 940, Guar Gum. Direct compression method is widely employed method for production of compressed tablets.

Direct Compression:

In this process the tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly in to the die cavity and forms a firm compact.

Brief manufacturing procedure for the preparation of tablets:

Step 1- Weighed all the ingredients separately.

Step 2- The 1 drug and the other excipients were passed through 40# sieve together and blended for 10 minutes.

Step 3- The magnesium stearate was passed through 60# sieve and added to the blend of step 2 and blended for 5 minutes.

Step 4- Compressed the blend of step 3 in to tablets by using 8.5mm, round punches.

Table.1 Tablet composition of different formulations of Eprosartan Controlled Release tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Eprosartan	400	400	400	400	400	400	400	400	400	400	400	400
MCC	186	136	86	186	136	86	186	136	86	186	136	86
HPMC K15 M	150	200	250	-	-	-	-	-	-	-	-	-
Carbopol 940	-	-	-	150	200	250	-	-	-	-	-	-
Pectin	-	-	-	-	-	-	150	200	250	-	-	-
Gellan Gum	-	-	-	-	-	-	-	-	-	150	200	250
Lactose	40	40	40	40	40	40	40	40	40	40	40	40
PVP K30	20	20	20	20	20	20	20	20	20	20	20	20
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg. stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total (mg)	800	800	800	800	800	800	800	800	800	800	800	800

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Evaluation Parameters**Pre Compression Parameters****A. Bulk density (D_b)**

It is the ratio of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured into graduated measuring cylinder through large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in gm/cc and is given by,

$$D_b = M / V_o$$

B. Tapped density (D_t)

Ten grams of powder was introduced into a clean, dry 100ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and tapped volume was read. It is expressed in gm/cc and is given by,

$$D_t = M / V_t$$

C. Compressibility index: The compressibility of the powder was determined by the Carr's compressibility index.

$$CI = \frac{\rho_{tap} - \rho_{bulk}}{\rho_{tap}} \times 100$$

D. Hausner ratio:

$$\text{Hausner ratio} = \text{tapped density} / \text{bulk density}$$

E. Angle of repose (θ)

It is defined as the maximum angle possible between the surface of pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height (h), above a flat horizontal surface on which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of funnel. The angle of repose was then calculated using the formula,

$$\theta = \tan^{-1} \left(\frac{h}{r} \right)$$

Post Compression Parameters**A. Thickness and diameter**

Control of physical dimension of the tablet such as thickness and diameter is essential for consumer acceptance and tablet uniformity. The thickness and diameter of the tablet was measured using Vernier calipers. It is measured in mm.

B. Hardness

The Monsanto hardness tester was used to determine the tablet hardness. The tablet was held between a fixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of hardness of the tablet. Hardness was expressed in Kg/cm².

C. Friability (F)

Tablet strength was tested by Friabilator USP EF-2. Pre weighed tablets were allowed for 100 revolutions (4min), taken out and were dedusted. The percentage weight loss was calculated by rewriting the tablets. The % friability was then calculated by,

$$F = \frac{(W_{\text{initial}}) - (W_{\text{final}})}{W_{\text{(initial)}}} \times 100$$

D. Weight variation test

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. First the total weight of 20 tablets from each formulation is determined and the average is calculated. The individual weight of the each tablet is also determined to find out the weight variation.

E. Uniformity of drug content.

Five tablets of various formulations were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in different buffers, the drug content was determined using a UV/Visible Spectrophotometer (Single beam spectrophotometer).

In-vitro release study:**Table.2 In vitro Studies**

Apparatus	USP XXIV dissolution testing apparatus II (Paddle method)
Dissolution medium	0.1N HCl, 6.8 pH phosphate buffer,
Temperature	37± 0.5° C
RPM	50
Vol. withdrawn and replaced	5ml every 1 hour
λ max	233 nm in pH 1.2 buffer and 233 nm in pH 6.8
Blank solution	Buffers used
Duration of study	12 hours
Volume of dissolution media	900ml

Procedure:

The release rate of Eprosartan from tablets was determined using The United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle type). The dissolution test was performed using 900 ml of pH 1.2, for first 2 hours and followed by phosphate buffer (pH 6.8; 900 mL) for remaining hours at 37.5±0.5°C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 12 hours, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with respected dissolution medium. Absorbance of these solutions was measured using a UV-Visible Spectrophotometer (Single beam spectrophotometer). Cumulative percentage of drug release was calculated.

Kinetic Analysis of In-Vitro Release Rates of Controlled Release Tablets:

The results of in vitro release profile obtained for all the formulations were plotted in modes of data treatment as follows:-

1. Zero – order kinetic model – Cumulative % drug released versus time.
2. First – order kinetic model – Log cumulative percent drug remaining versus time.
3. Higuchi's model – Cumulative percent drug released versus square root of time.
4. Korsmeyer equation / Peppas's model – Log cumulative percent drug released versus log time.

1. Zero Order Kinetic

It describes the system in which the drug release rate is independent of its concentration.

$$Q_t = Q_0 + K_0 t$$

2. First Order Kinetic

It describes the drug release from the systems in which the release rate is concentration dependent.

$$\log Q_t = \log Q_0 + kt / 2.303$$

3. Higuchi Model

It describes the fraction of drug release from a matrix is proportional to square root of time.

$$M_t / M_\infty = kHt^{1/2}$$

4. Korsmeyer-Peppas model (Power Law)

The power law describes the drug release from the polymeric system in which release deviates from Fickian diffusion, as expressed in following equation.

$$M_t / M_\infty = ktn$$

$$\log [M_t / M_\infty] = \log k + n \log t$$

RESULTS AND DISCUSSION**PREFORMULATION STUDIES****Determination of melting point**

The melting point of Eprosartan was found to be 249°C which compiled with BP standards, indicating purity of the drug sample. which was determined by capillary method.

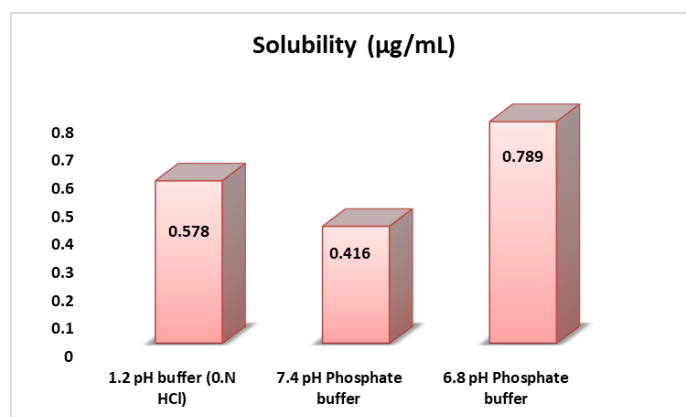
Solubility studies:

Figure.1 Solubility studies of Eprosartan

Discussion: From the above solubility studies, it was observed that among that 3 buffer solutions (0.1N HCl i.e pH 1.2, 7.4 pH Phosphate buffer and 6.8 pH phosphate buffer) the drug was soluble freely in 6.8 pH buffer.

FTIR studies:**Drug-Excipient compatibility studies:**

The IR spectrum of pure drug was found to be similar to the standard spectrum of Eprosartan. From the spectra of Eprosartan, combination of Eprosartan with polymers, it was observed that all characteristic peaks of Eprosartan were not altered and present without alteration in the combination spectrum, thus indicating compatibility of the drug and polymers. FTIR spectra of Eprosartan, and Optimized formulation are shown in Figure respectively.

FTIR Spectra of Pure drug:

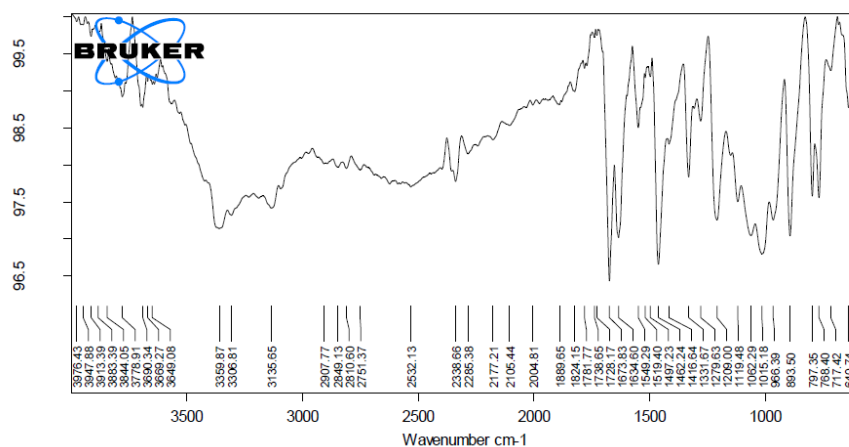


Figure.2 FTIR Spectra of Pure drug

FTIR Spectra of Drug and Excipients:

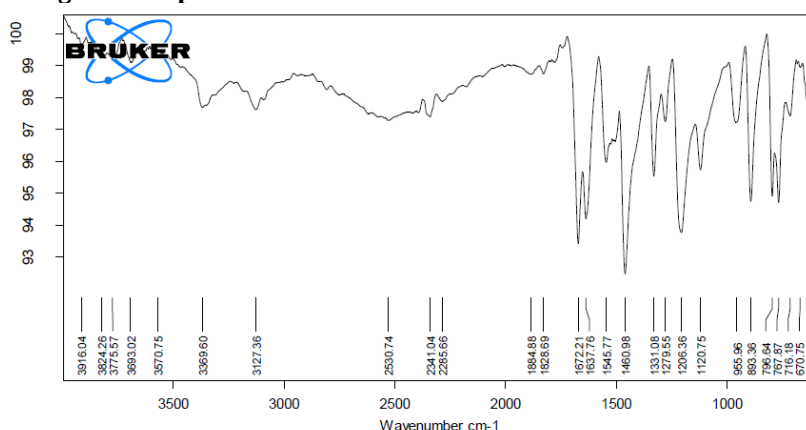


Figure.3 FTIR Spectra of Drug and Excipients

Discussion: From the drug excipients compatibility studies we observe that there are no interactions between the pure drug and (drug+ excipients) which indicates there are no physical changes.

UV Determination:

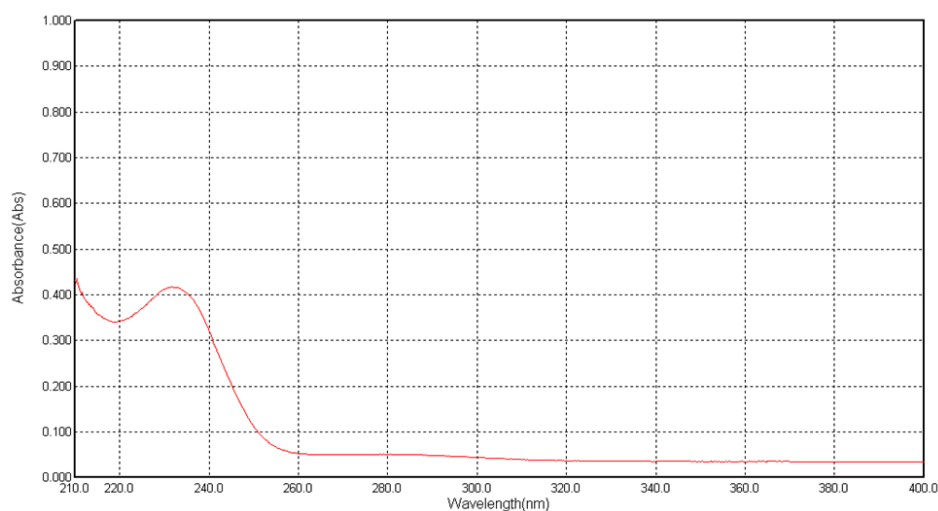
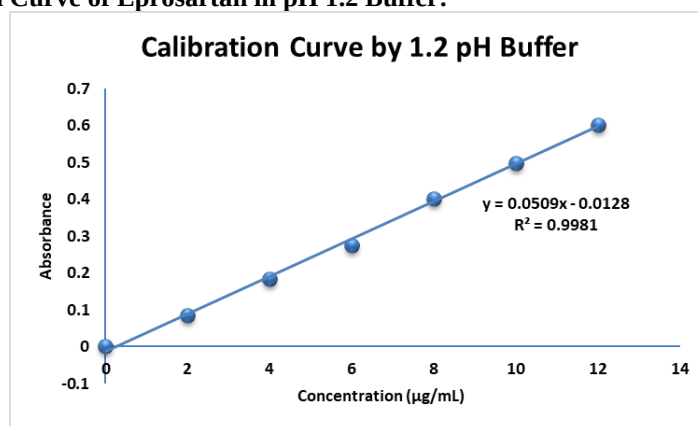
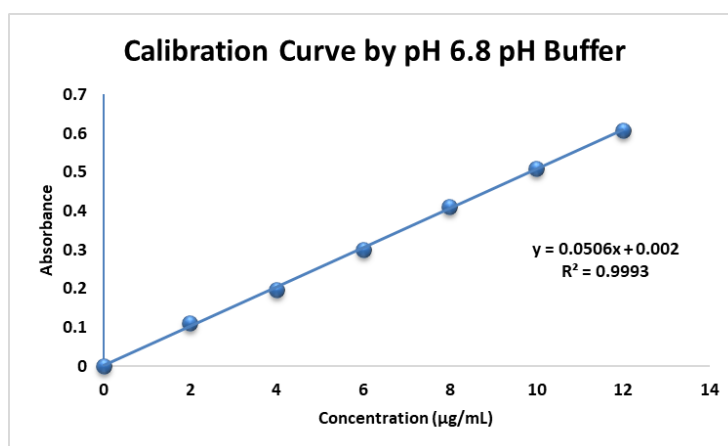


Figure.4 Uv spectrum of Eprosartan

Discussion: A solution of Eprosartan containing the conc. 8µg/ ml was prepared in 6.8pH buffer and UV spectrum was taken using Single Beam Spectrophotometer (YIS-294). The solution was scanned in the range of 200 – 400 nm. The maximum absorbance was found to be at 233 nm.

Standard Calibration Curve of Eprosartan in pH 1.2 Buffer:**Figure.5 Standard calibration curve of Eprosartan in pH 1.2****Discussion:**

The standard calibration curve shown 0.998, through that the drug obeys Beers and Lamberts law in the concentration range of 0 to 12 µg/mL. A standard graph was plotted by keeping the known concentration on X – axis and obtained absorbance on Y – axis.

Standard Calibration Curve of Eprosartan in pH 6.8:**Figure.6 standard calibration curve Eprosartan in pH 6.8 Phosphate Buffer****Discussion:**

The standard calibration curve shown R^2 value 0.999 which is near to 1 shows the linearity, through that the drug obeys Beers and Lamberts law in the concentration range of 0 to 12 µg/mL. A standard graph was plotted by keeping the known concentration on X – axis and obtained absorbance on Y – axis.

Evaluation of Eprosartan controlled release matrix Tablets**Table.3 Pre Compression Parameters of Eprosartan controlled release Tablets**

FC	Bulk density	Tapped density	Carr's index	Hausner's ratio	Angle of Repose
F1	0.345±0.002	0.427±0.002	20.24±1.14	1.19±0.01	28.12±1.14
F2	0.339±0.001	0.430±0.001	19.49±1.27	1.18±0.02	29.24±1.29
F3	0.356±0.003	0.441±0.002	18.67±1.14	1.17±0.01	27.51±1.43
F4	0.340±0.002	0.436±0.003	19.45±1.20	1.18±0.02	27.76±1.51
F5	0.359±0.001	0.448±0.002	18.10±1.37	1.17±0.01	28.35±1.24
F6	0.363±0.002	0.452±0.004	17.35±1.45	1.15±0.02	27.42±1.37
F7	0.342±0.002	0.435±0.002	16.24±1.05	1.15±0.01	26.12±1.15
F8	0.356±0.003	0.446±0.003	14.45±1.34	1.13±0.01	25.45±1.14
F9	0.371±0.002	0.465±0.001	12.69±1.14	1.11±0.02	24.37±1.26
F10	0.342±0.001	0.431±0.002	17.12±1.24	1.17±0.01	28.12±1.45
F11	0.356±0.002	0.445±0.003	16.45±1.43	1.15±0.01	27.45±1.57
F12	0.365±0.003	0.452±0.002	15.37±1.20	1.14±0.01	25.19±1.24

Discussions:

The angle of repose of different formulations (F1-F12) was found to be in the range of 29.24 ± 1.29 to 24.37 ± 1.26 . But the formulation F9 having the excellent flow property with 23.48 ± 0.20 . So, it was confirmed that the flow property of blends was free flowing.

The bulk density of blend was found between 0.339 ± 0.001 to 0.365 ± 0.003 . The Tapped density was found between 0.427 ± 0.002 to 0.465 ± 0.001 . These values indicate that the blends had good flow property.

Carr's index for all the formulations was found to be between 20.24 ± 1.14 to 12.69 ± 1.14 and Hausner's ratio from 1.19 ± 0.01 to 1.11 ± 0.02 , which reveals that the blends have good flow character.

Post Compression Parameters of Eprosartan controlled release tablets:**Table.4 Physical properties of tablet formulation (F1 to F12)**

FC	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Weight Variation (mg)	Drug Content (%)
F1	2.89 ± 0.04	7.12 ± 0.04	0.80 ± 0.03	802.15 ± 1.42	$94.43 \pm 1.42\%$
F2	2.85 ± 0.02	7.27 ± 0.02	0.72 ± 0.02	801.34 ± 1.16	$95.25 \pm 1.26\%$
F3	2.90 ± 0.03	7.35 ± 0.05	0.67 ± 0.02	801.12 ± 1.37	$96.63 \pm 1.39\%$
F4	2.85 ± 0.01	7.24 ± 0.06	0.76 ± 0.01	799.24 ± 1.58	$93.18 \pm 1.25\%$
F5	2.83 ± 0.02	7.51 ± 0.08	0.65 ± 0.02	798.48 ± 1.75	$95.25 \pm 1.26\%$
F6	2.86 ± 0.03	7.76 ± 0.04	0.51 ± 0.03	801.19 ± 1.34	$95.43 \pm 1.38\%$
F7	2.85 ± 0.04	7.34 ± 0.07	0.69 ± 0.02	802.37 ± 1.49	$97.67 \pm 1.45\%$
F8	2.87 ± 0.02	7.51 ± 0.02	0.46 ± 0.02	798.45 ± 1.92	$98.35 \pm 1.26\%$
F9	2.95 ± 0.03	7.75 ± 0.09	0.33 ± 0.01	800.12 ± 1.35	$99.74 \pm 1.38\%$
F10	2.82 ± 0.02	7.37 ± 0.04	0.67 ± 0.02	801.08 ± 1.47	$96.47 \pm 1.51\%$
F11	2.84 ± 0.01	7.46 ± 0.09	0.59 ± 0.03	802.45 ± 1.88	$97.47 \pm 1.17\%$
F12	2.86 ± 0.02	7.59 ± 0.07	0.45 ± 0.04	799.95 ± 1.62	$98.68 \pm 1.84\%$

Discussion:

Thickness of the Eprosartan tablets were found to be in the range of 2.82 ± 0.02 mm to 2.95 ± 0.03 mm. Hardness of the Eprosartan tablets were found to be in the range of 7.12 ± 0.04 to 7.76 ± 0.04 kg/cm². Friability of the Eprosartan tablets were found to be in the range of 0.45 ± 0.04 to $0.80 \pm 0.03\%$. The Weight Variation of the Eprosartan tablets were found to be in the range of 798.48 ± 1.75 mg to 802.37 ± 1.49 mg. Drug content of the Eprosartan tablets were found to be in the range of $94.43 \pm 1.42\%$ to $98.68 \pm 1.84\%$.

In-vitro drug release studies:

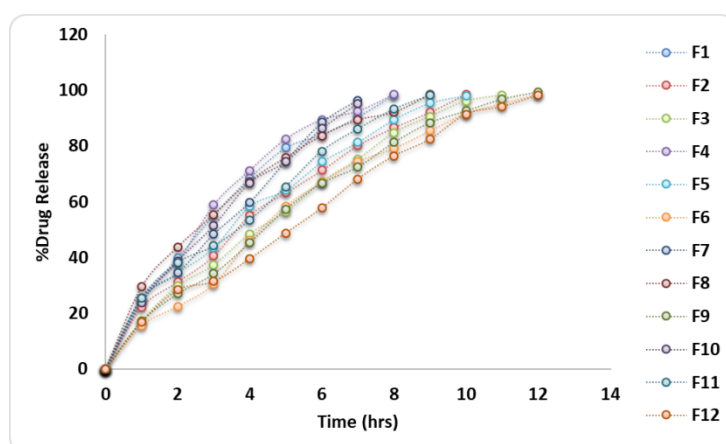
In-vitro drug release studies were carried out using USP XXII dissolution apparatus type II (Lab India DS 8000) at 50 rpm. The dissolution medium consisted of 900 ml of buffer, maintained at $37 \pm 0.50^\circ\text{C}$. The drug release at different time intervals was measured using an ultraviolet visible spectrophotometer (PG Instruments). The study was performed in triplicate

Table.5 In vitro dissolution studies with formulation F1 to F6

Time (hrs)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	24.58 ± 1.35	22.12 ± 1.46	17.39 ± 1.15	25.52 ± 1.18	25.19 ± 1.24	15.58 ± 0.14
2	39.74 ± 1.42	31.24 ± 1.86	29.87 ± 1.24	38.37 ± 1.24	34.52 ± 1.42	22.47 ± 1.24
3	55.12 ± 1.96	40.57 ± 1.24	37.37 ± 1.48	58.85 ± 1.45	43.51 ± 1.26	30.45 ± 1.21
4	68.51 ± 1.65	55.20 ± 1.36	48.54 ± 1.12	71.27 ± 1.46	58.46 ± 1.24	46.19 ± 1.25
5	79.42 ± 1.35	63.27 ± 1.45	56.37 ± 1.45	82.51 ± 1.27	64.15 ± 1.42	58.48 ± 1.17
6	84.14 ± 1.27	71.32 ± 1.15	67.25 ± 1.42	89.42 ± 1.34	74.36 ± 1.20	67.15 ± 1.28
7	90.45 ± 1.25	80.24 ± 1.75	75.34 ± 1.21	92.51 ± 1.69	81.42 ± 1.84	74.41 ± 1.15
8	98.36 ± 1.45	86.69 ± 1.63	84.85 ± 1.45	98.54 ± 1.24	89.57 ± 1.12	79.16 ± 1.42
9		92.24 ± 1.15	90.68 ± 1.42		95.54 ± 1.20	85.45 ± 1.21
10		98.67 ± 1.28	96.21 ± 1.45		98.12 ± 1.75	91.68 ± 1.10
11			98.28 ± 1.34			95.14 ± 1.48
12						98.58 ± 1.44

Table.6 In vitro dissolution studies with formulation F7 to F12

Time (hrs)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
1	25.47±1.48	29.47±1.45	17.14±1.22	23.87±1.46	25.47±1.24	16.72±1.21
2	34.47±1.19	43.77±1.22	26.98±1.45	38.82±1.22	38.18±1.54	28.42±1.67
3	48.47±1.45	55.42±1.16	34.20±1.45	51.46±1.14	44.14±0.25	31.46±1.22
4	59.87±1.47	67.41±1.01	45.35±1.19	66.84±1.22	53.48±0.15	39.58±1.44
5	74.58±1.65	75.92±1.24	57.41±1.20	74.48±1.54	65.47±0.15	48.82±1.51
6	88.47±1.25	83.72±1.36	66.75±1.64	86.25±1.28	78.21±0.19	57.77±1.13
7	96.48±1.62	89.35±1.87	72.54±1.48	95.36±1.26	86.15±0.18	68.21±1.27
8		92.08±1.11	81.38±1.20		93.24±0.11	76.48±1.25
9		98.47±1.24	88.45±1.14		98.18±1.06	82.46±1.57
10			92.68±1.42			91.49±1.64
11			96.87±1.15			94.16±1.95
12			99.45±1.38			98.24±1.47

In Vitro Drug Release Studies:**Figure.7 In Vitro Drug Release Studies of F1-F12 Formulations****Discussion:**

From the in vitro drug release studies of Eprosartan controlled release tablets using HPMC K15 M, Carbopol 940, Pectin and Gellan Gum in three different polymer ratios using lactose as a diluent, MCC as a binder and PVP K30 as filler.

From Formulations, the F1-F3 were formulated using HPMC K15 M in three different ratios like 150mg, 200mg, and 250mg, the drug release of F1 was 98.36±1.45% at the end of 8th hour, F2 was 98.67±1.28% at the end of 10th hour and F3 was 98.28±1.34% at the end of 11th hour.

So, when the polymer concentration increases the drug release time was increased but F3 showing the highest release at the end of 11th hour only. So further dissolution was takes on the polymer Carbopol 940.

The formulation F4-F6 were formulated by using Carbopol 940 in three different ratios like 150mg, 200mg, and 250mg, the drug release of F4 was 98.54±1.24% at the end of 8th hour, F5 was 98.12±1.75% at the end of 10th hour and F6 was 98.58±1.44% at the end of 12th hour.

So, further studies were done with Pectin. The formulations from F7-F9 were formulated by using Pectin in three different ratios like 150mg, 200mg, and 250mg. So, the drug release of F7 was 96.48±1.62% at the end of 7th hour, F8 was 98.47±1.24% at the end of 9th hour and F9 was 99.45±1.38% at the end of 12th hour.

In this turn, with the polymer Pectin the formulation F9 shows the better results up to 12th hour.

Next the formulations from F10 to F12 with Gellan Gum shows the release of F10 was 95.36±1.26% at the end of 7th hour, F11 was 98.18±1.06% at the end of 9th hour and F12 was 98.24±1.47% at the end of 12th hour. So in this dissolution studies with Gellan Gum also shows good results at the end of 12th hour.

But when comparted to all the formulations the Formulation of drug with the polymer Pectin in the concentration of 250mg shows the highest drug release at the end of 12th with 99.45±1.38% which results in the drug was released in controlled manner up to 12 hour. Hence, the formulation F9 was identified as the Optimized formulation. So further Release kinetics was done to this formulation.

Drug Release Kinetics:

Zero Order:

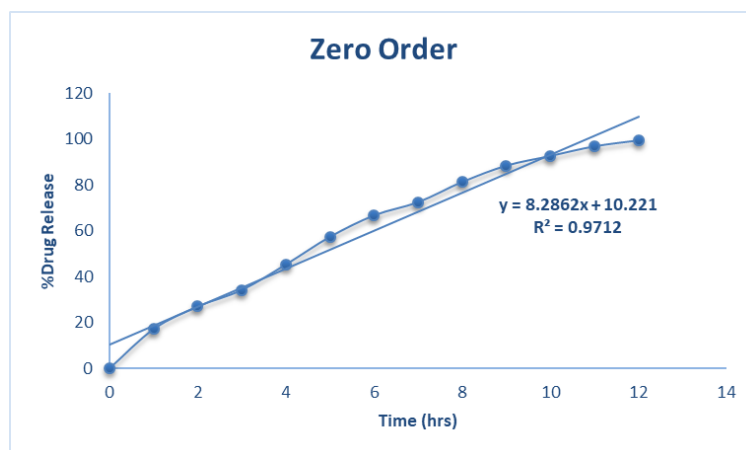


Figure.8 Zero order graph of optimized formulation(F9)

First Order:

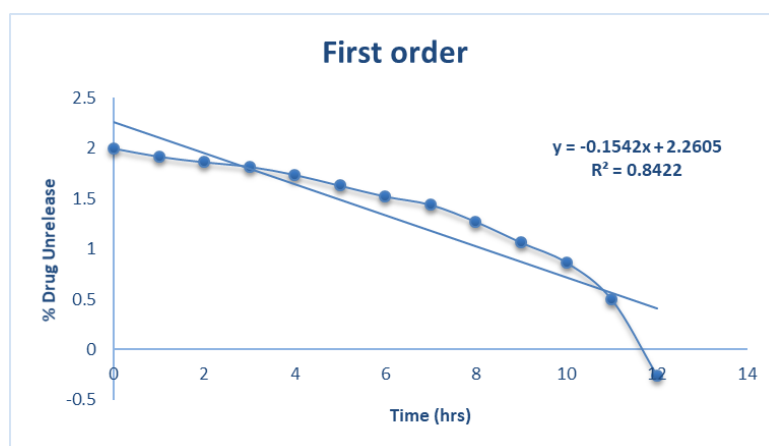


Figure.9 First order graph of optimized formulation(F9)

Higuchi Plot:

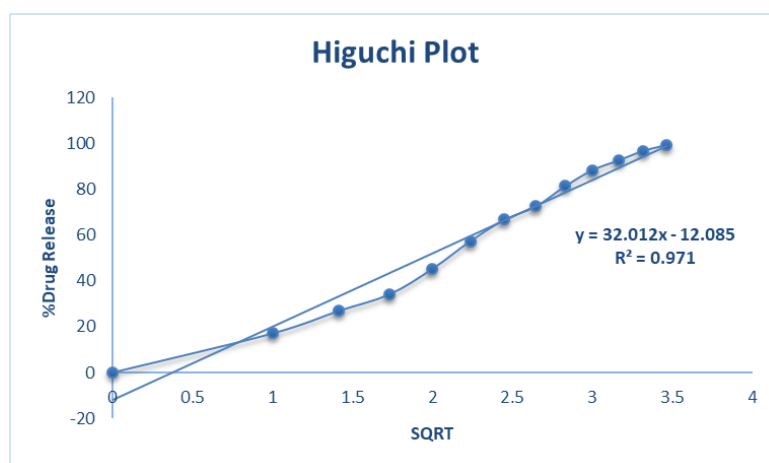
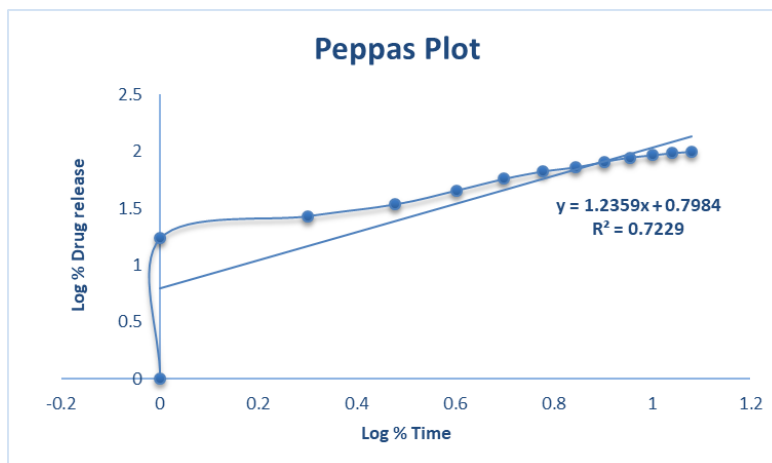


Figure.10 Higuchi graph of optimized formulation(F9)

Peppas Plot:**Figure.11 Peppas graph of optimized formulation(F9)****Discussions:**

The *in vitro* dissolution data for the optimized formulation F9 were fitted in different kinetic models i.e., zero order, first order, Higuchi and korsmeyer-peppas equation. Optimized formulation F9 shows R^2 value 0.971. As its value nearer to the '1' it is conformed as it follows the Zero order release. The mechanism of drug release is further confirmed by the korsmeyer and peppas plot, if $n = 0.45$ it is called Case I or Fickian diffusion, $0.45 < n < 0.89$ is for anomalous behavior or non-Fickian transport, $n = 0.89$ for case II transport and $n > 0.89$ for Super case II transport. The 'n' value is 1.235 for the optimized formulation (F9) i.e., n value was > 0.89 this indicates super case transport. The release kinetics for the optimized formula are shown in table.

SUMMARY & CONCLUSION

In this study, controlled release tablets of Selexipag were prepared by Direct compression method, using HPMC K15 M, Carbopol 940, Pectin and Gellan Gum polymers. The pre compression and post compression parameters show that the values were found to be acceptable within the range. FTIR studies revealed that the drug and excipients used weren't have any interactions. The drug-polymer ratio was found to influence the release of drug from the formulations.

Different parameters like hardness, friability, weight variation, drug content uniformity, *in-vitro* drug release were evaluated in all the parameters the optimized formulation F9 yields best results and among in all 12 formulations F9 formulation containing 250mg of Pectin controls the drug release up to 12 hours. So Pectin was considered to be suitable for the formulation of Selexipag controlled release tablets. Based on these results formulation F9 was found to be the most promising formulations. The regression coefficient (R^2) of Zero order of Optimized formulation F9 shows R^2 value 0.971. The 'n' value is 1.235 for the optimized formulation (F9) i.e., n value was > 0.89 this indicates super case transport

REFERENCES

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. Gayle W. Robins & Lesley J. Scott, Eprosartan A Review of its Use in the Management of Hypertension, Volume 65, pages 2355–2377, (2005)
5. Indian pharamacopeia. Government of India Ministry Health and FamilyWelfare. Delhi: Controler of publication;1996: 750,151.
6. Dollery C. Therapeutic drugs. London: Churchill Livingstone: 1991; 2: p 7-25.
7. G. Hardman, Lee E. Limbird. Goodman and Gilman's. The pharmacological basis of therapeutics. Mc Graw-Hill Publihing house. 10th ed. p 991-992, 1758-1760.
8. Ainle Y, Paul JW. Handbook of pharmaceutical excipients. Mongraph 2nd edition. Lodon:Pharmaceutical Press; 2000:51.52, 128, 138-139, 257.113,19.
9. Lachman Leon, Lieberman Herbert A. Pharmaceutical Dosage Forms: Tablets. In: The Theory and Practice of Industrial Pharmacy. Lea and Febiger, U.S.A,1991; 3rd edition: 293-345.
10. Subrahmanyam CVS. Textbook of physical pharmaceutics. 2nd ed. Delhi:Vallaba prakashan;2003.p.180-234.

11. Korsemeier RW, PeppasNA. Macromolecular and modeling aspects of swelling – controlled Systems. In: Mansdrofsz, Roseman TJ, ad, Controlled Release Delivery systems. New – York, NY: Marcel Dekker; 1983:77.
12. ICH Q1A (R2) stability testing guidelines: stability testing of new drug substances and products. [Online]. 2003 [cited 2008 Nov10].
13. Subrahmanyam CVS. Textbook of physical pharmaceutics. 2nded. Delhi: Vallaba prakashan;2003.p.180-234.
14. Reddy KR, Mutalik S, Reddy S. Once-Daily Sustained-Release Matrix Tablets of Nicorandil: Formulation and In Vitro Evaluation. AAPS PharmSciTech2003; 4(4): article 61.
15. Murali Mohan Babu GV. et. al., Development of new controlled released formulation of flurbiprofen, in-vitro in-vivo correlation”. Ind J of Pharm Sci.2002 ;64(1):37-43.
16. NerkurJ,JunHW,ParkJC,ParkMO.Controlled-release matrix tablets of ibuprofen using cellulose ethers and carrageenans: effect of formulation factors on dissolution rates.Eur J Pharm Biopharm 2005 61(1-2) 56-68.