ejpmr, 2016,3(4), 294-304

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

SJIF Impact Factor 3.628

Research Article

ISSN 3294-3211

EJPMR

FORMULATION DEVELOPMENT AND OPTIMIZATION OF EXTENDED RELEASE MATRIX TABLETS OF AZILSARTAN USING NATURAL AND SYNTHETIC POLYMERS

V.T. Iswariya*, G.L. Soujanya, Sai Santhoshi, Shobha Rani, Haseeba, Sabitha

Dept of Pharmaceutics, MRR College of Pharmacy, Hyderabad.

***Correspondence for Author: V.T. Iswariya**

Dept of Pharmaceutics, MRR College of Pharmacy, Hyderabad.

Article Received on 28/01/2016 **Article Revised on 19/02/2016** **Article Accepted on 10/03/2016**

ABSTARCT

The aim of the present study was to develop extended release formulation of azilsartan to maintain constant therapeutic levels of the drug for over 12 hrs. Azilsartan is an angiotensin II receptor antagonist used in the treatment of hypertension. Xanthan gum, Chitosan and HPMC K15M were employed as polymers. Preformulations studies were carried out for all the parameters such as angle of repose, bulk density, tapped density and Hausners ratio were found to be good. Drug and excipient compatability studies were carried out using FTIR and DSC, based on the results the it was found that there were no interactions. Various quality control evaluation parameters were carried out and the results were found to be good.Whereas from the dissolution studies it was evident that the formulation (F10) showed better and desired drug release pattern i.e., 99.75% in 12 hours. It contains the natural polymer HPMC K15M as extended release material. It followed peppas release kinetics mechanism.

KEYWORDS: Azilsartan, Xanthan gum, Chitosasn, HPMC, Extended release tablets.

INTRODUCTION[1]

The goal in designing extended or extended delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, extended release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or to a specified target organ.

Rationale for extended release dosage forms.[2,3]

Some drugs are inherently long lasting and require only once-a-day oral dosing to sustain adequate drug blood levels and the desired therapeutic effect. These drugs are formulated in the conventional manner in immediate release dosage forms. However, many other drugs are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic results. Multiple daily dosing is inconvenient for the patient and can result in missed doses, made up doses, and noncompliance with the regimen. When conventional immediate-release dosage forms are taken on schedule and more than once daily, they cause sequential therapeutic blood level peaks and valleys (troughs) associated with the taking of each dose . However, when doses are not administered on schedule, the resulting peaks and valleys reflect less than optimum drug therapy. For example, if doses are administered too frequently, minimum toxic concentrations of drug may be reached, with toxic side effects resulting. If doses are missed, periods of sub therapeutic drug blood levels or those below the minimum effective concentration may result, with no benefit to the patient. Extended-release tablets and capsules are commonly taken only 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 drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period (Fig.1).

The extended plasma drug levels provided by extended-release products oftentimes eliminate the need for night dosing, which benefits not only the patient but the caregiver as well.

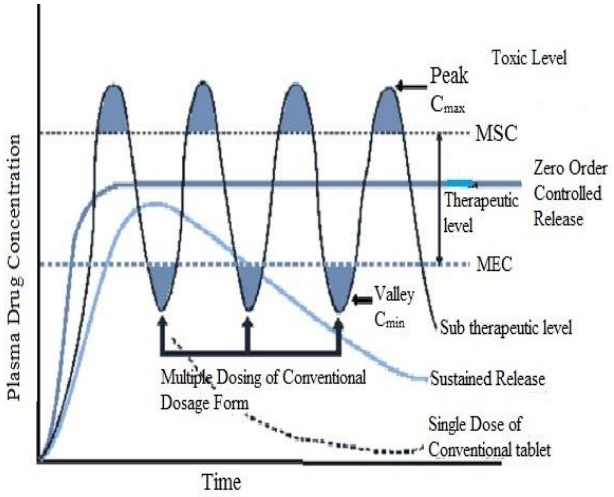

Figure 1 Hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of extended and controlled delivery formulations.

Terminology[4,5]

Modified release delivery systems may be divided conveniently in to four categories.

A) Delayed release
B) Extended release
- ✓ Controlled release
- ✓ Extended release

C) Site specific targeting
D) Receptor targeting

A) Delayed Release

These systems are those that use repetitive, intermittent dosing of a drug from one or more immediate release units incorporated into a single dosage form. Examples of delayed release systems include repeat action tablets and capsules and enteric-coated tablets where timed release is achieved by a barrier coating.

B) Extended release

During the last two decades there has been remarkable increase in interest in extended release drug delivery system. This has been due to various factor viz. the prohibitive cost of developing new drug entities, expiration of existing international patents, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems.

1. Controlled Release

These systems include any drug delivery system that achieves slow release of drug over an extended period of time.

2. Extended Release

Pharmaceutical dosage forms that release the drug slower than normal manner at predetermined rate & necessarily reduce the dosage frequency by two folds.

C) Site specific targeting

These systems refer to targeting of a drug directly to a certain biological location. In this case the target is adjacent to or in the diseased organ or tissue.

D) Receptor targeting

These systems refer to targeting of a drug directly to a certain biological location. In this case the target is the particular receptor for a drug within an organ or tissue. Site specific targeting and receptor targeting systems satisfy the spatial aspect of drug delivery and are also considered to be extended drug delivery systems.

Design and formulation of oral suatained release drug delivery system[6-10]

The oral route of administration is the most preferred route due to flexibility in dosage form, design and patient compliance. But here one has to take into consideration, the various pH that the dosage form would encounter during its transit, the gastrointestinal motility, the enzyme system and its influence on the drug and the dosage form. The majority of oral extended release systems rely on dissolution, diffusion or a combination of both mechanisms, to generate slow release of drug to the gastrointestinal milieu. Theoretically and desirably a extended release delivery device, should release the drug by a zero-order process which would result in a blood level time profile similar to that after intravenous constant rate infusion.

Extended (zero-order) drug release has been attempted to be achieved with various classes of extended drug delivery system:

A) Diffusion extended system.
i) Reservoir type.
ii) Matrix type

B) Dissolution extended system.
i) Reservoir type.
ii) Matrix type

C) Methods using Ion-exchange.

D) Methods using osmotic pressure.
E) pH independent formulations.

F) Altered density formulations.

Diffusion extended system:

Basically diffusion process shows the movement of drug molecules from a region of a higher concentration to one of lower concentration. The flux of the drug J (in amount / area -time), across a membrane in the direction of decreasing concentration is given by Fick's law.

$$J = - D \, dc/dx.$$

D = diffusion coefficient in area/ time
dc/dx = change of concentration 'c' with distance 'x'

In common form, when a water insoluble membrane encloses a core of drug, it must diffuse through the membrane.
The drug release rate dm/ dt is given by

$$dm/dt = ADK\Delta C/L$$

Where; A = Area.
K = Partition coefficient of drug between the membrane and drug core.
L= Diffusion path length (i.e. thickness of coat).
Δc= Concentration difference across the membrane.

i) Reservoir Type
In the system, a water insoluble polymeric material encases a core of drug (Figure 2). Drug will partition into the membrane and exchange with the fluid surrounding the particle or tablet. Additional drug will enter the polymer, diffuse to the periphery and exchange with the surrounding media.

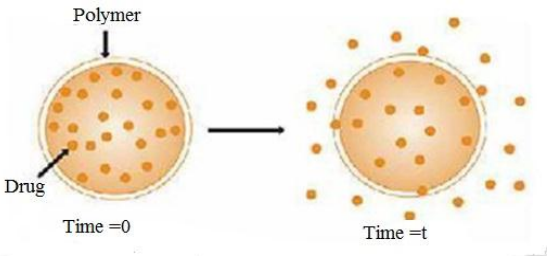

Figure 2: Schematic representation of diffusion extended drug release: reservoir system

ii) Matrix Type
A solid drug is dispersed in an insoluble matrix (Figure 3) and the rate of release of drug is dependent on the rate of drug diffusion and not on the rate of solid dissolution. Higuchi has derived the appropriate equation for drug release for this system:

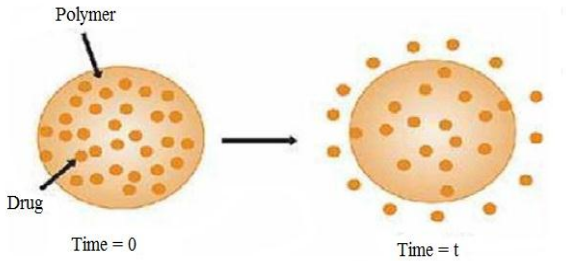

Figure 3: Schematic representation of diffusion extended drug release: matrix system.

DISSOLUTION EXTENDED SYSTEMS
In most cases, enteric coated dosage forms are not truly sustaining in nature, but serve as a useful function in directing release of the drug to a special site. The same approach can be employed for compounds that are degraded by the harsh conditions found in the gastric region.

i) Reservoir Type
Drug is coated with a given thickness coating, which is slowly dissolved in the contents of gastrointestinal tract. By alternating layers of drug with the rate controlling coats as shown in figure, a pulsed delivery can be achieved. If the outer layer is quickly releasing bolus dose of the drug, initial levels of the drug in the body can be quickly established with pulsed intervals.

ii) Matrix Type
The more common type of dissolution extended dosage form. It can be either a drug impregnated sphere or a drug impregnated tablet, which will be subjected to slow erosion

MATRIX TABLETS
One of the least complicated approaches to the manufacture of controlled release dosage forms involves the direct compression of blend of drug, retardant material and additives to formulate a tablet in which the drug is embedded in a matrix of the retardant. Alternatively drug and retardant blend may be granulated prior to compression. Examples of Retardant.

Table 1: Materials used to formulate matrix tablet

S. No	Matrix Characteristics	Material
1	Insoluble, Inert	Polyethylene, Polyvinyl chloride, Ethyl Cellulose
2	Insoluble, Erodible	Carnauba wax, Stearic acid, Polyethylene glycol

Polymers Used In The Matrix.[11]
The polymers most widely used in preparing matrix system include both hydrophilic and hydrophobic polymers.

A) Hydrophilic Polymers
Hydroxyl propyl methyl cellulose (HPMC), hydroxyl propyl cellulose(HPC), hydroxyl ethyl cellulose (HEC), Xanthan gum, Sodium alginate, poly(ethylene oxide), and cross linked homo polymers and co-polymers of acrylic acid.

B) Hydrophobic Polymers

This usually includes waxes and water insoluble polymers in their formulation Waxes: carnauba wax, bees wax, candelilla wax, micro crystalline wax, ozokerite wax, paraffin waxes and low molecular weight polyethylene. Insoluble polymers: Ammoniomethacrylate co-polymers (Eudragit RL100, PO, RS100, PO), ethyl cellulose, cellulose acetate butyrate, cellulose acetate propionate and latex dispersion of meth acrylic ester copolymers.

Drug Release From Matrix[12,13]

Drug in the outside layer exposed to the bathing solution is dissolved first and then diffuses out of the matrix. This process continues with the interface between the bathing solution and the solid drug moving toward the interior. It follows that for this system to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be much faster than the diffusion rate of dissolved drug leaving the matrix. Derivation of the mathematical model to describe this system involves the following assumptions.

- A pseudo-steady state is maintained during drug release;
- The diameter of the drug particles is less than the average distance of drug diffusion through the matrix;
- The bathing solution provides sink conditions at all times.

MATERIALS AND METHODS

Materials

azilsartan, xanthan gum, talc ,magnesium stearate, microcrystalline cellulose,povidone k-30, hydroxy propyl methyl cellulose ,chitosan

Methods

METHODOLOGY

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 2.The tablets were prepared as per the procedure given below and aim is to prolong the release of Azilsartan Total weight of the tablet was considered as 400mg.

Procedure

1) Azilsartan 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 2: Formulation composition for tablets

Formulation No.	Azilsartan	Xanthan gum	Chitosan	HPMC k15M	Mag. Stearate	Talc	PVP K30	MCC pH 102
F1	120	40	5	-	2	2	35	QS
F2	120	80	10	-	2	2	35	QS
F3	120	120	15	-	2	2	35	QS
F4	120	160	-	-	2	2	35	QS
F5	120	-	40	-	2	2	35	QS
F6	120	-	80	-	2	2	35	QS
F7	120	-	120	-	2	2	35	QS
F8	120	-	160	-	2	2	35	QS
F9	120	-	-	40	2	2	35	QS
F10	120	-	-	80	2	2	35	QS
F11	120	-	-	120	2	2	35	QS
F12	120	-	-	160	2	2	35	QS

All the quantities were in mg

Characterisation Of Azilsartan Matrix Tablets

Drug – Excipient compatibility studies by Fourier Transform Infrared (FTIR) spectroscopy

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in aligent spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

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.

Evaluation Parameters For Matrix Tablets Of Azalsartan

Preformulation parameters

The various characteristics of powder blends of azalsartan was tested as per Pharmacopoeia.

i) Flow properties by Angle of Repose :
ii) Bulk Density :
iii) Tapped density :
iv) Carr's index

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.

% Deviation = (Individual weight – Average weight / Average weight) × 100

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. Preweighed 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

% Friability = [(W1-W2) / W] × 100

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

In vitro drug release studies

Dissolution parameters

Apparatus Paddle Method	--	USP-II,
Dissolution Medium p H 6.8 Phophate buffer	--	0.1 N HCl,
RPM	--	50
Sampling intervals (hrs)	--	0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature	--	37°c ± 0.5°c

Procedure

900ml 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 was removed and pH 6.8 phosphate buffer was added process was continued from upto 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 249 and 243nm using UV-spectrophotometer.

RESULTS AND DISCUSSION

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

Standard graph of Azilsartan in 0.1N HCl

The scanning of the volumetric solution of Azilsartan in the ultraviolet range (200-400nm) against 0.1 N HCl blank gave the λ_{max} as 249 nm. The standard concentrations of Azilsartan(5-25 µg/ml) prepared in 0.1N HCl showed good linearity with R^2 value of 0.999, which suggests that it obeys the Beer-Lamberts law.

Table 3: Observations for graph of Azilsartan in 0.1N HCl (249nm)

Conc [µg/l]	Abs
0	0
5	0.202
10	0.386
15	0.578
20	0.786
25	0.997

It was found that the estimation of Azilsartan by UV spectrophotometric method at λ_{max} 249.0 nm in 0.1N Hydrochloric acid had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 5-25µg/ml. The regression equation generated was y = 0.039x-0.003.

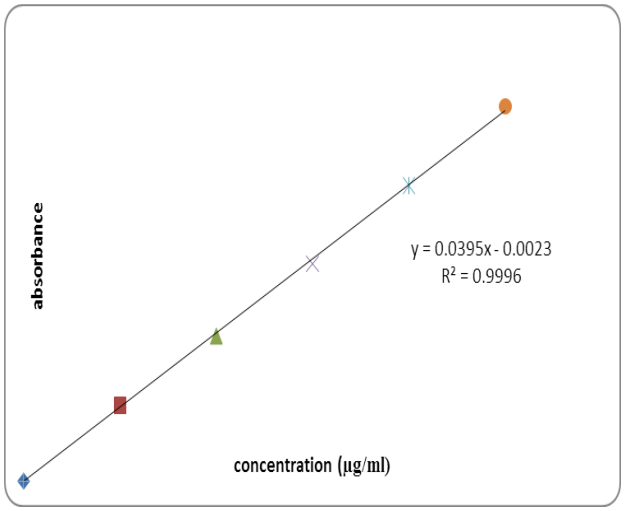

Figure 4: Standard graph of Azilsartan in 0.1N HCl

Table 4: Observations for graph of Azilsartan in p H 6.8 phosphate buffer (247nm)

Conc [µg/l]	Abs
5	0.107
10	0.215
15	0.337
20	0.447
25	0.559

It was found that the estimation of Azilsartan by UV spectrophotometric method at λ_{max} 247 nm in pH 6.8 Phosphate buffer. had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 5-25µg/ml. The regression equation generated was y = 0.022x - 0.003.

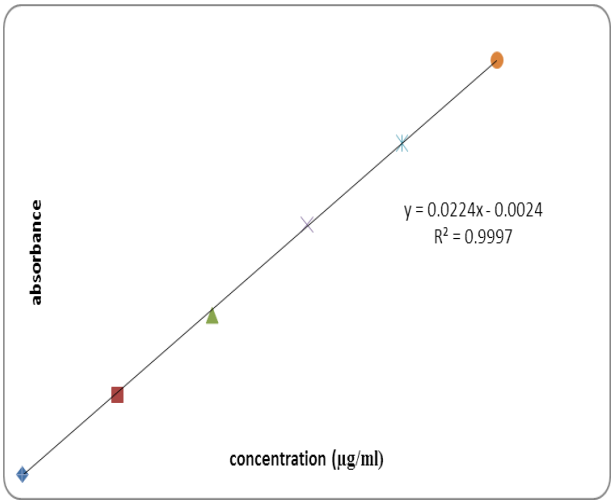

Figure 5: Standard graph of Azilsartan pH 6.8 phosphate buffer (247nm)

Drug – Excipient compatability studies

Fourier Transform-Infrared Spectroscopy

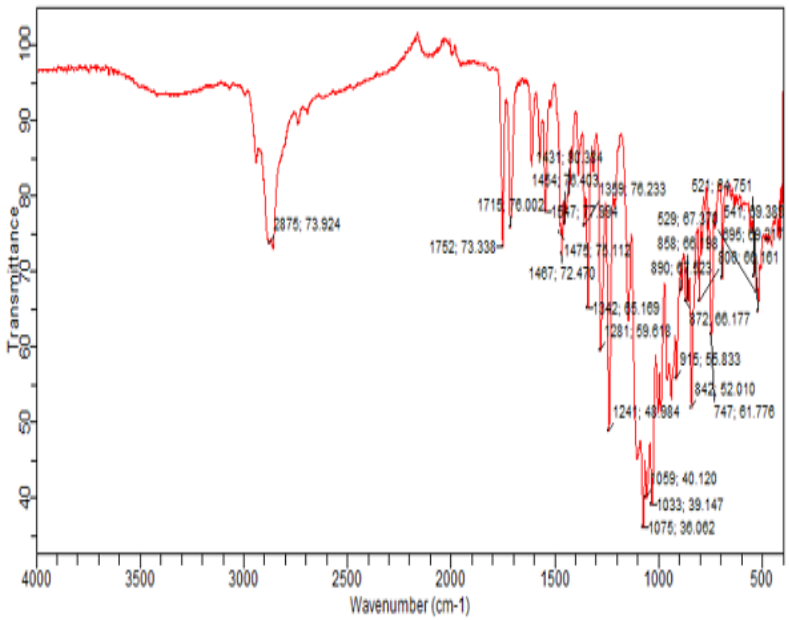

Figure 6: FT-IR Spectrum of Azilsartan pure drug

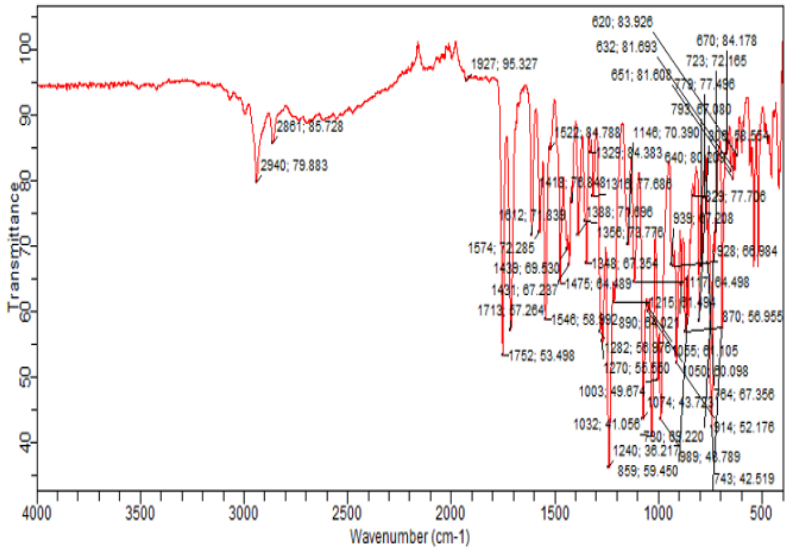

Figure 7: FT-IR Spectrum of Optimised Formulation

From the FTIR data it was evident that the drug and super disintegrates, other excipients doses not have any interactions**.** Hence they were compatible.

Preformulation parameters of powder blend

Table 5: Pre-formulation parameters of Core blend

Formulationcode	Angle of repose (Ɵ)	Bulk density(gm/cm3) gm/cm3) (gm/cm3)	Tapped density(gm/cm3)	Carr's index (%)	Hausner ratio (HR)
F1	28.16	0.566	0.654	13.45	1.16
F2	26.98	0.548	0.632	13.29	1.20
F3	23.98	0.58	0.689	14.71	1.17
F4	27.62	0.540	0.640	15.625	1.11
F5	27.68	0.53	0.631	15.87	1.13
F6	26.32	0.568	0.568	11.39	1.12
F7	24.29	0.537	0.582	14.38	1.16
F8	27.68	0.520	0.591	12.01	1.13
F9	26.98	0.512	0.611	16.2	1.19
F10	28.31	0.541	0.64	15.46	1.18
F11	27.15	0.55	0.632	12.97	1.14
F12	25.54	0.524	0.613	14.51	1.17

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 0.512 to 0.566 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.58 to 0.689 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 16 to 18 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friabili4ty, thickness, and drug release studies in different media were performed on the compression coated tablet.

Table 6: *In vitro* quality control parameters for tablets

Formulation codes	Average Weight (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	399.5	4.5	0.50	4.8	99.35
F2	403	4.5	0.51	5.5	99.53
F3	398	4.4	0.51	5.8	98.65
F4	402	4.5	0.55	5.6	98.74

F5	399	4.4	0.56	5.8	99.81
F6	398	4.5	0.48	5.6	100.9
F7	404	4.4	0.51	5.4	99.44
F8	399	4.3	0.62	5.9	98.82
F9	400	4.5	0.55	5.8	101.3
F10	398	4.4	0.58	6.2	99.45
F11	402	4.5	0.64	5.2	97.51
F12	399	4.5	0.58	5.8	99.56

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

***In-Vitro* Drug Release Studies**

Table 7: Dissolution Data of Azilsartan Tablets Prepared With xanthan gum In Different Concentrations

TIME **(hr)**	**CUMULATIVE PERCENT DRUG DISSOLVED**			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
0.5	23.15	16.41	12.21	8.65
1	30.35	23.72	17.65	11.26
2	38.46	31.66	22.43	18.24
3	45.61	40.48	25.58	24.38
4	60.13	53.46	32.87	28.53
5	75.46	59.45	40.35	34.88
6	87.46	65.46	48.22	40.45
7	99.45	71.58	56.49	49.27
8		87.32	65.37	56.65
9		97.45	74.35	64.26
10			85.39	72.65
11			90.85	80.32
12			99.27	88.27

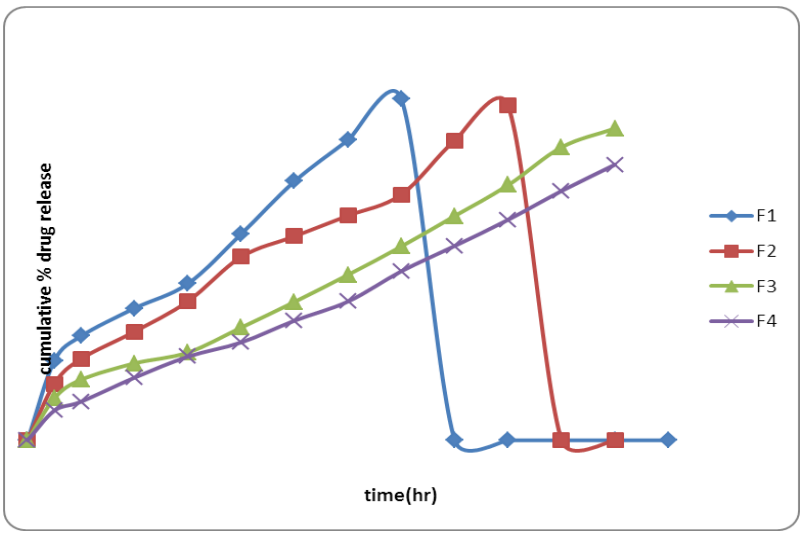

Fig 8: Dissolution profile of Azilsartan (F1, F2, F3, F4 formulations).

Table 8: Dissolution Data of Azilsartan Tablets Prepared With chitosan In Different Concentrations

TIME **(hr)**	**CUMULATIVE PERCENT DRUG DISSOLVED**			
	F5	**F6**	**F7**	**F8**
0	0	0	0	0
0.5	38.26	25.73	22.3	18.45
1	54.16	36.63	31.45	24.15
	72.01	45.04	39.80	30.56
3	88.26	58.25	45.25	39.74
4	97.10	65.33	58.24	45.62
5		76.41	66.73	51.33

6		84.84	71.34	60.15
7		97.2	75.52	67.48
8			87.10	76.45
9			98.2	83.64
10				99.41
11				
12				

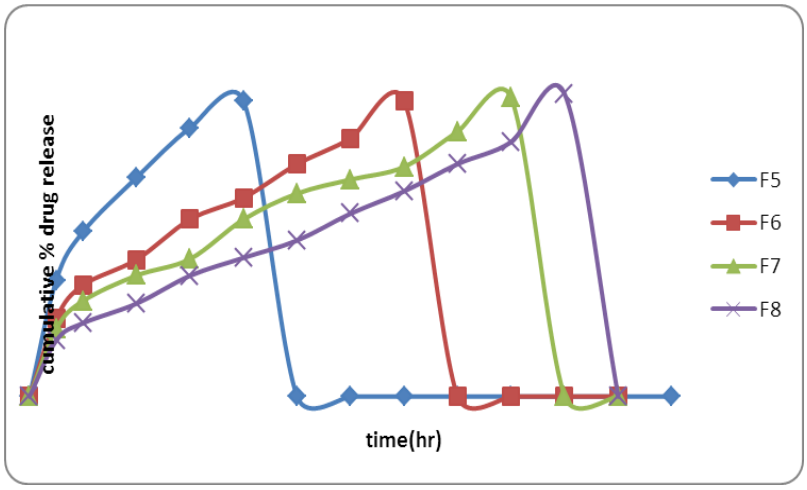

Fig 9: Dissolution profile of Azilsartan (F5, F6, F7, F8 formulations)

Table 9: Dissolution Data of Azilsartan Tablets Prepared With HPMC K15M In Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED			
	F9	F10	F11	F12
0.5	19.52	13.74	9.25	6.41
1	28.55	20.65	13.14	10.26
2	49.44	29.87	19.02	15.41
3	69.26	35.34	25.16	20.14
4	74.57	42.45	30.14	24.51
5	82.36	50.61	36.74	30.65
6	98.78	58.65	43.01	35.85
7		62.37	49.87	42.61
8		71.95	55.15	50.15
9		79.84	60.09	56.46
10		85.52	67.41	61.02
11		90.65	75.06	68.15
12		99.75	82.15	75.15

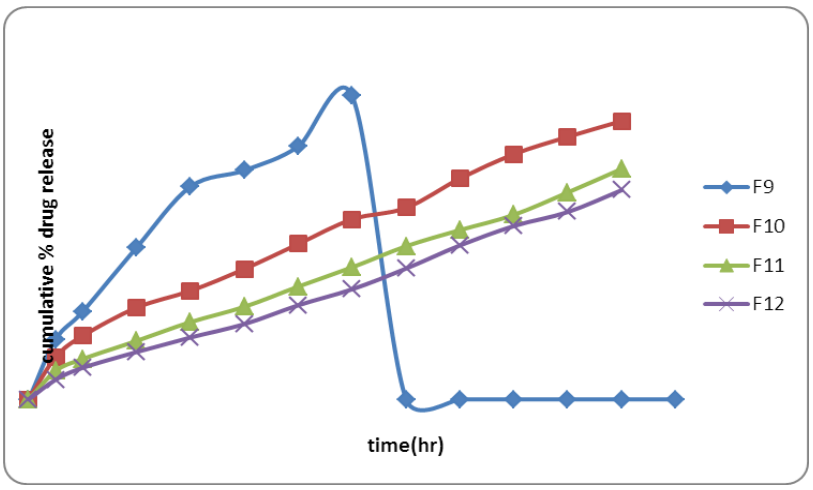

Fig 10: Dissolution profile of Azilsartan (F9, F10, F11, F12 formulations)

From the dissolution data it was evident that the formulations prepared with xanthan gum as polymer were retard the drug release up to desired time period i.e., 12 hours in the concentration of 120 mg. At low concentration it was unable to retard the drug release whenever increase the concentration of polymer it was more retardation of drug release after 12 hours also.

Whereas the formulations prepared with HPMC K15M retarded the drug release in the concentration of 80 mg (F10 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.75% in 12 hours with good retardation. Whenever increase the concentration of polymer it was release model more retardation of the drug release after 12 hours

The formulations prepared with Chitosan showed unable to retard the drug release up to 12 hours. Hence they were not considered.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze 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

Table 10: Release kinetics data for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining
0	0	0			2.000				100
13.74	0.5	0.707	1.138	-0.301	1.936	27.480	0.0728	-0.862	86.26
20.65	1	1.000	1.315	0.000	1.900	20.650	0.0484	-0.685	79.35
29.87	2	1.414	1.475	0.301	1.846	14.935	0.0335	-0.525	70.13
35.34	3	1.732	1.548	0.477	1.811	11.780	0.0283	-0.452	64.66
42.45	4	2.000	1.628	0.602	1.760	10.613	0.0236	-0.372	57.55
50.61	5	2.249	1.704	0.699	1.694	10.122	0.0198	-0.296	49.39
58.65	6	2.449	1.768	0.778	1.616	9.775	0.0171	-0.232	41.35
62.37	7	2.646	1.795	0.845	1.576	8.910	0.0160	-0.205	37.63
71.95	8	2.828	1.857	0.903	1.448	8.994	0.0139	-0.143	28.05
79.84	9	3.000	1.902	0.954	1.304	8.871	0.0125	-0.098	20.16
85.52	10	3.162	1.932	1.000	1.161	8.552	0.0117	-0.068	14.48
90.65	11	3.317	1.957	1.041	0.971	8.241	0.0110	-0.043	9.35
99.75	12	3.464	1.999	1.079	-0.602	8.313	0.0100	-0.001	0.25

CONCLUSION

The aim of the present study was to develop sustained release formulation of Azilsartan to maintain constant therapeutic levels of the drug for over 12 hrs. Xanthan gum, Chitosan and HPMC K15M were employed as polymers. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F10) showed better and desired drug release pattern i.e., 99.75 % in 12 hours. It contains the natural polymer HPMC K15M as sustained release material. It followed peppas release kinetics mechanism.

ACKNOWLEDGEMENT

We the authors take this opportunity to thank medilux laboratory pvt ltd for giving the gift sample of drug on request and also sura labs in Hyderabad for their suggestions in fulfilling our work.we also show our gratitude towards staff of M.R.R college of pharmacy who helped us in completion of the project

REFERENCE

1. Bogner RH. Bioavailability and bioequivalence of extended-release oral dosage forms. US Pharmacist, 1997; 22: 3–12.
2. Rogers JD, Kwan KC. Pharmacokinetic requirements for controlled-release dosage forms. In: John Urquhart, ed. Controlled-release Pharmaceuticals. Academy of Pharmaceutical Sciences. American Pharmaceutical Association, 1979: 95–119.
3. Madan PL. Sustained-release drug delivery systems, part II: Preformulation considerations. Pharm Manu fact, 1985; 2: 41–45.
4. Wani MS, Controlled Release System-A Review, 2008; 6 1: 56-62.
5. Banker GS, Anderson NR. The Theory and Practice of Industrial Pharmacy: Tablet,Lachman, (3rded) Varghese Publishing House, Bombay, 1990; 3: 293-303.
6. Lee VHL, Controlled Drug Delivery Fundamentals and Applications: Influence of drug properties on

design, Marcel Dekker, INC, and New York., 1987; 2: 16-29.
7. Manish R, Jayesh P, Siahboomi AR. Hydrophilic Matrices for Oral Extended Release: Influence of Fillers on Drug Release from HPMC Matrices. Pharma Times., 2010; 42(04): 67-73.
8. Kumar KP et al. Innovations in Sustained Release Drug Delivery System and Its Market Opportunities. J Chem Pharm Res., 2010; 2 1: 349-360.
9. Brahmankar DM, Sunil B. Jaishwal. "Controlled release medication" chapter 15th in "Bio pharmaceutics and Pharmacokinetics – A Treatise, 1st ed,, 2010; 1: 347- 353.
10. Stanley S. Davis, Formulation strategies for abs windows. Drug Discovery Today, 2005; 10: 249-257.
11. Aulton ME. Pharmaceutics: The Science of Dosage Form Design, 2005; 2: 296-298.
12. Wise DL. Handbook of Pharmaceutical Controlled Release Technology Inc., 2005; 2: 5-24.
13. Jantzen GM, Robinson JR. Sustained and Controlled- Release Drug Delivery systems Modern Pharmaceutics, 4thed, 2011; 121: 501-502.