INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

FORMULATION AND INVITRO EVALUATION OF GASTRO RETENTIVE FLOATING TABLETS OF LOSARTAN POTASSIUM

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ABSTRACT

In the present study, Gastro Retentive Floating Drug Delivery systems (GRDDS) of Losartan potassium, an antihypertensive drug, with an oral bioavailability of only 33% (because of its poor absorption from lower gastrointestinal tract) have been designed to increase the therapeutic efficacy & gastric residence time and to reduce frequency of administration. Losartan potassium having a short biological half-life of 1.5 -2 h is eliminated quickly from the body leading to low therapeutic efficacy. Therefore a sustained release medication was advantageous so as to achieve the prolonged therapeutic effect and to reduce peak and valley effect in plasma concentration. This can be achieved by formulating modified gastro retentive sustained release dosage forms which resides in the stomach for sufficient time to release the drug in vicinity of the absorption zone. The tablets were prepared by hot melt extrusion method, by employing semi-synthetic and natural polymers like HPMCK15M, Guar gum and Xanthan gum respectively in various concentrations. Bees wax was used as a melting aid and sodium bicarbonate as gas generating agent to reduce floating lag time. The prepared granules were evaluated for angle of repose, bulk density; tapped density, compressibility index and Hausner's ratio and results obtained were in compliance with the pharmacopoeial standards. Compressed formulations were further evaluated for thickness, friability, hardness, floating lag time swelling index and in-vitro dissolution studies. All the formulations showed good results which were in compliance with pharmacopoeial standards. *In vitro* dissolution study was carried out in 0.1 N Hcl pH 1.2 buffer. From *in vitro* dissolution studies, it has been found that increase in polymer concentration diminishes drug release profile. The *in vitro* cumulative % drug release of all formulations ranged from 79.92% – 95.89% at the end of 10 hrs with more than 12h buoyancy. The release kinetics was analyzed by using zero-order, first-order Higuchi's and korsmeyer-peppas model equations. The in vitro drug release followed first order kinetics and the drug release mechanism was found to be non- fickian type.

Keywords: Losartan potassium, Hot melt extrusion.

INTRODUCTION

The oral route is considered as the most promising route of drug delivery among all the routes that have been explored for the systemic delivery of drugs .Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics helps to achieve stable therapeutic plasma drug concentrations in contrary to the conventional formulations. These dosage forms show better patient compliance and predictable drug release profiles. However these were not designed to counter the

problems associated with physiological conditions of the body such as gastric emptying, which significantly affects the bioavailability and in turn the therapeutic efficacy of the dosage form. Thus gastro retentive dosage forms such as hydro dynamically balanced systems, altered density systems, muco adhesives were formulated which have aimed at the prolongation of gastric emptying time (GET) and concentrates the dosage form in GIT. (The GET has been reported to be from 2-6 hrs in humans in the fed state). These systems will remain in the stomach for several hours and significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high p^H environment and release the drug in absorption zone and prolong the gastric residence time by counteracting gastric emptying process. This channels the complete controlled release of the drug in absorption zone before elimination of the dosage form from the body thus improving the bioavailability of the drug.

Losartan potassium is an orally active class-II anti-hypertensive agent called as angiotensin-II receptor antagonists used in the treatment of hypertension .It has an oral bioavailability of only 33%, while the remaining is excreted unchanged in faeces. This is because of its poor absorption in lower G.I tract and its elimination half life is 1.5-2 hrs. Therefore, it is selected as a suitable drug for the design of a gastro retentive floating drug delivery system (GRDDS) with a view to improve its oral bioavailability. In the present work, an attempt has been made to formulate GRDDS of Losartan potassium using polymers such as HPMC K15M, guar gum, xanthan in order to prolong the drug release and impart floating properties to the matrix tablet formulations.

MATERIALS AND METHODS

Losartan potassium was obtained from Lupin pharmaceuticals, Xanthan and guar gum were obtained from Himedia laboratories; HPMC K15M was obtained from spectrum pharma; beeswax was obtained from ambrosia natural products; Lactose, Magnesium stearate and Talc were obtained from S.D. Fine chemicals; sodium bicarbonate was obtained from Nice laboratories. All chemicals and reagents used were of analytical grade.

PREPARATION OF LOSARTAN POTASSIUM FLOATING TABLETS

Tablets were prepared by Hot Melt Extrusion (HME) method. It is the process of embedding drug in a polymeric carrier. Specifically, HME dosage forms are complex mixtures of API, functional excipients, and processing aids, which are blended uniformly. The calculated amount of bees wax was melted in a china dish. To this, geometrical mixture blend of polymers, diluents was added followed by the active pharmaceutical ingredient. Mix it well before solidification and later the mass was removed from hot plate by scrapping until it attains room temperature and the coherent mass passed through sieve no 36 to form granules. The formed granules were then made to pass through sieve no 100 to remove any fines. The formed granules are then mixed with calculated amount of glidant and lubricant for the processing operations and the granules are then compressed using rotary tablet punching machine (cad mach) to obtain 200 mg tablets. Composition of all formulations was given in (Table 1).

EVALUATION PARAMETERS

PRE COMPRESSION PARAMETERS

Angle of repose (θ)

It is 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,

$$\theta = \tan^{-1}(h/r)$$

Where, θ = angle of repose
h = height of pile,
r = radius of the base of the pile.

Bulk density (D_b)

It is the ratio of mass of the powder taken to its 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,

$$D_b = M / V_o$$

Where, D_b = Bulk density (gm/cc)
M =Mass of powder (g)
V_o = Bulk volume of powder (cc)

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,

$$D_t = M / V_t$$

Where, D_t = Tapped density (gm/cc)
M = Mass of powder (g)
V_t = Tapped volume of powder (cc)

Compressibility Index
An indirect method of measuring powder flow from bulk densities was developed by carr. The percentage compressibility of powder was a direct measurement of the potential powder arch or the bridge strength and stability. Carr's index of each formulation was calculated according to equation given below:

$$\% \textbf{ compressibility} = \frac{Dt - Do}{Dt} \mathbf{x\ 100}$$

Where,
D_t = Tapped density, D_o = Bulk density

Hauser's ratio
Hausner's ratio is an index of ease of powder flow; it is calculated by the following formula.

$$\textbf{Haussler's ratio} = D_t / Do$$

Where, D_t = Tapped density,
D_o = Bulk density

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

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/cm^2.Three tablets were randomly picked and hardness of the tablets was determined.

Friability
Tablet strength was tested by using Roche Friabilator. 20 tablets were weighed and placed in the friabilator and operated for 100 revolutions (25 rpm for 4min), taken out and were dedusted. The percentage weight loss was calculated by reweighing the tablets. The % friability was then calculated by,

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

Weight variation
Ten tablets were selected randomly from each batch were weighed individually and together in a single pan balance. The average weight was noted. The tablet passes the test if not more than two tablets fall outside the percentage limit and none of the tablet differs by more than double the percentage limit.

$$PD = \frac{(W_{avg}) - (W_{initial})}{(W_{avg})} \times 100$$

Where, PD = Percentage deviation,
W_{avg} = Average weight of tablet,
$W_{initial}$ = individual weight of tablet

Uniformity of drug content
The drug content was performed to check the dose uniformity in the formulation. Randomly ten tablets were weighed and powered. A quantity equivalent to 100mg of Losartan potassium was added in to a 100ml volumetric flask and dissolved in 0.1N HCl, shaken for 10 minutes and made up to the volume with 0.1N HCl. After suitable dilutions the drug content was determined by UV spectrophotometer (Elico Ltd. SL 159) at 234nm against blank.

Swelling Index
Measurement of swelling rate of the floating matrix tablet was carried to gain insight the observed phenomenon of drug release with the rates of polymer hydration. Swelling index of the dosage form is conducted by using USP dissolution apparatus-II(LABINDIA DS 8000) in 900 ml of 0.1N HCl which is maintained at 37±0.5°C, rotated at 50 rpm. At selected regular intervals, the tablet was withdrawn and the excess water was blotted with tissue paper and the swelling index was calculated using following formula.

$$\textbf{\% Swelling Index} = \{(W_t) - (Wo)/ (Wo)\} \times 100$$

Where, Wt = weight of the swollen tablet
Wo = initial weight of the tablet.

Buoyancy studies
The *in-vitro* floating behavior (buoyancy) of the tablets was determined by floating lag time. The tablets were placed in 100 ml beaker containing 0.1 N HCl (pH 1.2). The floating lag time (time taken by the tablet to reach the surface) and total floating time (floating duration of the tablet) were determined.

In vitro Drug Release Study

The release rate of Losartan potassium floating tablets was determined using USP Type II Apparatus (paddle type). The dissolution test was performed using 900ml of 0.1N HCl, at 37± 0.5˚C at 50 rpm for 12 hrs. A 5ml sample was withdrawn from the dissolution apparatus at specified time points and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µm membrane filter and diluted if necessary. Absorbance of these solutions were measured at 234 nm using U.V-Visible Spectrophotometer.

Drug release kinetics

To study the drug release kinetics, the data obtained from in vitro drug release studies were plotted in various kinetic models: zero order (Equation 1) as cumulative amount of drug release v_s time, first order (Equation 2) as log % drug remaining v_s time, and Higuchi's model (Equation 3) as cumulative % of drug released v_s square root of time.

$$C=K_0t \quad \text{..... (1)}$$

Where K_0 is the zero order constant expressed in units of concentration/time and t is the time in hours. A graph of concentration v_s time would yield a straight line with a slope equal to k_o and the intercept origin of the axes [15].

$$\text{Log } C = \text{Log } C_O - Kt/2.3 \quad \text{..... (2)}$$

Where Co is the initial concentration of drug is the first order constant, and t is the time[16].

$$Q=kt^{1/2} \quad \text{..... (3)}$$

Where K is the constant reflecting the design variables of the system and t is the time in hours. Hence, drug release rate is proportional to the reciprocal of the square root of time.

Mechanism of drug release

To evaluate the mechanism of drug release from Losartan potassium floating tablets, data of drug release were plotted in korsmeyer et al's equation (Equation 4) as log cumulative percentage of drug release v_s log time and the exponent n was calculated through the slope of the straight line.

$$M_t/M\infty = Kt^n \quad \text{..... (4)}$$

Where $M_t/M\infty$ is the fractional solute release, t is the release time, K is a kinetic constant characteristics of the drug/polymer system, and n is exponent that characterizes the mechanism of release of tracers [(18)] .For cylindrical tablets, if the exponent n=0.45,then the drug release mechanism is Fickian diffusion and if 0.45<n<0.89, then it is non-fickian or anomalous diffusion. An exponent's value is 0.89 it is indicative of case-II transport or typical zero-order release.

Stability studies of the optimized formulation

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies are adopted. The International Conference on Harmonization (ICH) Guidelines titled "Stability testing of New Drug Substances and Products" describes the stability test requirements for drug registration application in the European Union, Japan and the States of America.

ICH specifies the length of study and storage conditions.

Long-Term Testing: 25°C ± 2°C / 60% RH ± 5% for 12 Months .

Accelerated Testing: 40°C ± 2°C / 75% RH ± 5% for 6 Months.

Stability studies were carried out at 40°C / 75% RH for the optimized formulation for 3 months. The floating tablets were stored at 40°C / 75% RH in closed high density polyethylene bottles for 3 months. The samples were withdrawn after periods of 1 month, 2 month and 3 month. The samples were analyzed for its hardness, floating characteristics, drug content and In vitro drug release.

RESULTS AND DISCUSSION

For each designed formulation, blend of drug and excipients was prepared and evaluated for micromeritic properties and were tabulated in table-2. Bulk density was found to be between 0.245 to 0.409gm/ml and tapped density between 0.269 to 0.455gm/ml for all formulations. Hausner's ratio was found below 1.19 and Carr's compressibility index between 8.80 to 14.99% for all formulations, which indicates that the prepared granules of all the formulations have good flow property .The angle of repose is known to be a measure of flow ability and the angle of repose of all formulations was found between 20.14 to 29.2, it indicates good flow properties of granules.

All batches of tablets were evaluated for various physical parameters and were tabulated in table-3.The weight variation of all formulations was within the ranges of 197.4 to 203.6 mg. The hardness of the tablets was within the range of 5.06 to 6.82 kg/cm^2.The friability of all tablets was below 1%(0.58%-0.81%).The thickness and drug content of all tables was within the range of 2.98 to 3.20mm and 97.93 to 99.95 respectively. Thus all the physical properties of these tablets were satisfactory as specified in the pharmacopoeia (IP, 1996).

In vitro buoyancy studies were performed in 1.2 pH 0.1N HCl and all formulations exhibited floating time more than 12 hours in dissolution medium subjected to rotation and floating lag time ranging from 63-98secs and are tabulated in (Table4) .The buoyancy lag-time of tablets depends on the amount of sodium bicarbonate involved in CO_2 formation. For a floating system, the ideal matrix material should be highly permeable to dissolution media in order to initiate rapid generation of CO_2 and allow release of CO_2 to promote floating. The floating time of all formulations was found to be increasing with the increasing amount of polymer concentration and as the concentration of gas generating agent ($NAHCO_3$) increases the floating lag time decreases. The bees wax incorporated in the formulation also aid as floating enhancer giving the required buoyancy to the system. The formulations were evaluated for degree of swelling and results were tabulated in (Table 4) and it was found that natural polymers exhibited greater degree of swelling compared to semi synthetic polymers.

In vitro dissolution studies were performed in 0.1N HCL (1.2 pH) and results are tabulated in (Table 5-7) and graphs were depicted in (Figure 3-5). Formulations F1,F2,F3 F4,F5,F6,F7,F8 and F9 showed drug release of 97.45,93.95,88.44,93.05,88.58,81.69,98.89,85.36 and 79.92% respectively at the end of 10 hours.

Among all the formulations, formulation F7 was found to be most promising formulation as it has shown most consistent drug release (98.89%) up to 10 hrs as compared to other formulations. From the above data, it is evident that the proportion of polymer in the formulation increases, cumulative percentage drug release in 10hrs decreases. An increase in polymer concentration causes increase in viscosity of the gel as well as the gel layer with longer diffusion path. This could cause a decrease in effective diffusion coefficient of the drug and a reduction in drug release rate.

The *in-vitro* drug release data of the floating tablets were evaluated kinetically by zero order kinetics, first order kinetics, Higuchi model, and Korsemeyer Peppa's models. The regression co-efficient obtained for first order kinetics were found to be higher (R^2:0.9989 to 0.9662), when compared with those of zero order kinetics (R^2:0.8535 to 0.9468), indicating that the drug release follows first order kinetics (Table 8).To evaluate drug release mechanism from the floating tablets, plots of cumulative percentage release $v_{s.}$ square root of time as per Higuchi's equation were constructed. These plots were found to be linear in all formulations (R^2:0.9862 to 0.9917), indicating that the drug release from the floating tablets was diffusion mechanism the data were fit into Korsemeyer equation. All the formulations show good linearity (R^2:0.9831 to 0.9981), with slope (n) values 0.57 to 0.69 and is between "0.45 to 0.85". This indicates that the drug release depends on swelling, diffusion, and erosion. All formulations follow the non-Fickian/anomalous type of diffusion.

Stability studies

The stability studies were carried out on the optimised formulation F7. The formulation was stored at 40±2^{0}C/75±5% for three months to assess their stability studies. Samples were analyzed for Hardness, *In-vitro* buoyancy studies, Drug content and *In-vitro* drug release at the end of each month for three months. And values obtained are tabulated in table-8. No statistically significant differences were observed in the percentage drug released; Hardness, % drug content and Floating lag time in optimized formulation at the end of three months of stability studies. So it can be concluded that the formulation is stable for short term storage conditions.

CONCLUSION

This study discusses the formulation and evaluation of gastro retentive tablets of Losartan potassium. The effervescent-based floating drug delivery was a promising approach to achieve in vitro buoyancy. The addition of gel-forming polymer HPMC K15M, natural polymers and gas-generating agent sodium bicarbonate was essential to achieve in vitro buoyancy. Formulation F7 showed desired drug release profile over 10 hrs following Higuchi release kinetics and all formulations followed non-fickian diffusion. Optimised GRDDS of Losartan potassium was found to be stable at 40^{o}c/75% following a three months of stability study. Finally, it is concluded that the rate of drug release from the formulation depends upon polymer

concentration in the formulation and delivers the drug at a controlled rate at a specific site and GRDDS of Losartan potassium provides a better strategy for increasing the bioavailability and treating hypertension by allowing a better control of fluctuations observed in contrary to conventional dosage forms.

ACKNOWLEDGEMENTS

The authors wish to thank: Lupin Pharmaceuticals, Aurangabad, India for providing Losartan Potassium as gift sample and also to the Management of MLR Institute of Pharmacy, Hyderabad for providing the all facilities required for carrying out this research work.

Table 1: Formulae of Losartan potassium GRDDS

Ingredients(mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Losartan potassium	50	50	50	50	50	50	50	50	50
Guar gum	30	45	60	_	_	_	_	_	_
Xanthan gum	_	_	_	30	45	60	_	_	_
HPMC K15M	_	_	_	_	_	_	30	45	60
Bees wax	30	30	30	30	30	30	30	30	30
Sodium bicarbonate	53	38	23	53	38	23	53	38	23
Mg stearate	16	16	16	16	16	16	16	16	16
Talc	6	6	6	6	6	6	6	6	6
Lactose	15	15	15	15	15	15	15	15	15

Total weight: 200mg

Table: 2 Pre compression flow properties of powder blends

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Average weight variation(mg)	Drug content
F1	2.98	5.82	0.81	202.3	98.88
F2	3.05	5.14	0.69	203.6	98.56
F3	3.00	5.06	0.75	198.9	99.95
F4	3.01	6.02	0.59	204.2	99.33
F5	3.20	5.94	0.58	201.6	97.95
F6	3.17	5.30	0.73	200.2	97.93
F7	3.11	6.82	0.77	197.4	98.35
F8	3.03	5.24	0.60	199.79	99.58
F9	3.16	6.06	0.78	202.4	99.95

Table: 3 Physical evaluation parameters and drug content

Formulation code	Floating lag time (sec)	Floating duration (hrs)	Swelling Index (%)
F1	63	>12	82.47±0.05
F2	75	>12	76.92±0.04
F3	95	>12	71.68±0.04
F4	70	>12	64.11±0.03
F5	85	>12	67.45±0.06
F6	97	>12	61.48±0.06
F7	74	>12	54.91±0.07
F8	91	>12	58.44±0.06
F9	98	>12	67.59±0.05

Table 4: In vitro buoyancy and swelling properties of Losartan potassium GRDDS

Formulation	Angle of repose	Bulk Density (gm/cc)	Tapped density (gm/cc)	Hausner's Index (%)	Compressibility Index (%)
F1	22.47	0.404	0.455	1.12	11.10
F2	25.11	0.375	0.441	1.17	14.63
F3	28.5	0.361	0.423	1.16	14.82
F4	24.19	0.245	0.269	1.09	8.80
F5	23.17	0.365	0.429	1.19	14.99
F6	24.10	0.409	0.425	1.04	10.07
F7	28 .1	0.391	0.451	1.15	13.33
F8	20.14	0.355	0.394	1.11	10.12
F9	29. 2	0.326	0.377	1.15	13.63

I) Initial stage at 30 seconds. II) Middle stage at 65 seconds III) Final stage at 74 seconds.

Fig. 1: In-vitro buoyancy studies of tablets of formulation F7

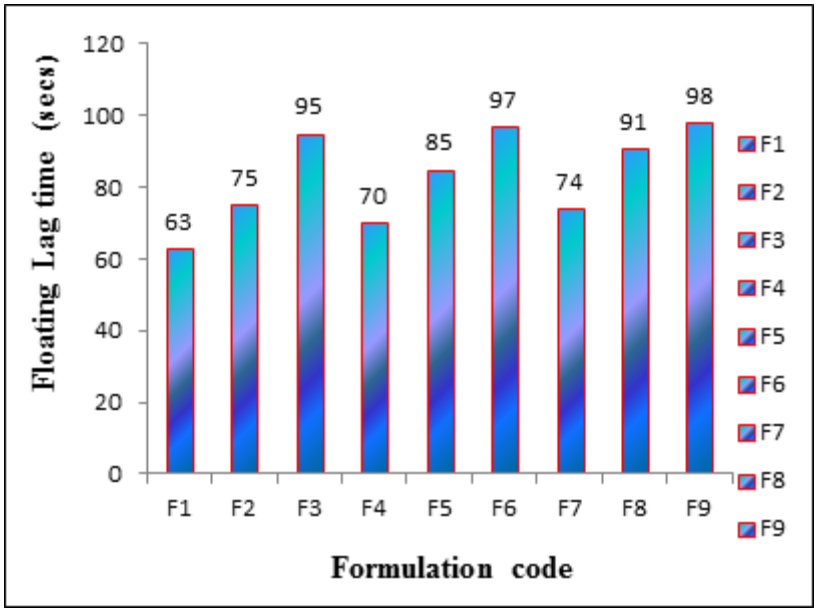

Fig. 2: Floating lag time observed for formulations F1 toF9

In vitro dissolution studies

Table: 5 Cumulative percent drug release of formulations (F1-F3)

Time (hrs)	Percentage drug release of Formulations		
	F1	F2	F3
1	25.391±0.91	25.047±0.93	21.989±0.42
2	41.255±0.16	40.450±0.70	35.353±0.60
3	55.203±0.15	53.700±0.46	47.59 ± 0.69
4	68.730±0.73	66.423±1.40	55.92 ± 1.49
5	80.050±1.15	77.733±0.84	65.49 ± 0.88
6	88.894±0.26	86.883±0.23	73.51 ± 0.14
7	89.846±0.17	89.639±0.31	82.57 ± 0.43
8	92.557±0.30	91.368±1.30	86.27 ± 0.27
9	95.220±0.17	93.452±0.18	87.50 ± 0.47
10	97.452±0.21	93.955±0.22	88.44 ± 0.73

All the values are expressed as a mean ± SD., n=3

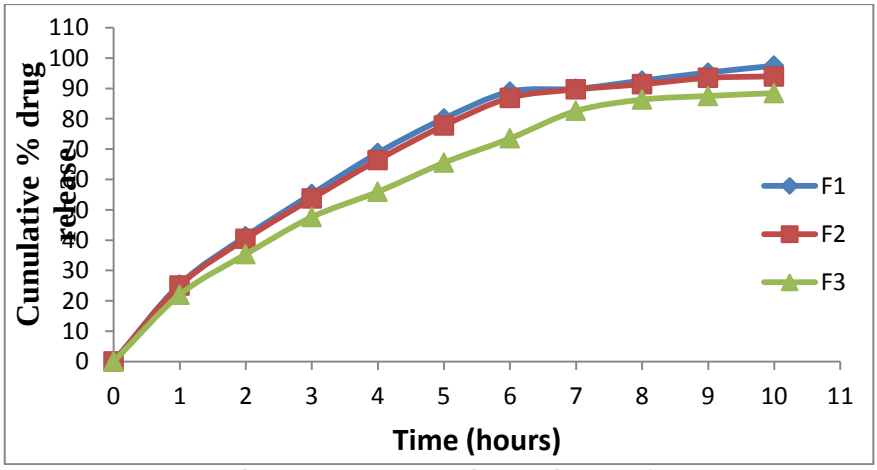

Fig. 3: Percentage drug release of Losartan potassium from Formulation F1 toF3

Table 6: Cumulative percent drug release of formulations (F4-F6)

Time (hrs)	Percentage drug release of Formulations		
	F4	F5	F6
1	26.24 ± 0.27	23.073±0.23	20.302±1.09
2	39.159±0.06	34.24 ± 0.18	29.206±0.38
3	53.70 ± 0.47	45.43 ± 0.27	38.871±0.61
4	67.70 ± 0.47	56.665±0.19	47.398±1.28
5	77.36 ± 0.53	66.658±0.10	55.829±0.36
6	85.91 ± 0.30	73.831±0.46	62.656±0.72
7	88.93 ± 0.38	80.495±0.68	69.001±0.71
8	90.331±0.26	84.972±0.82	76.676±0.60
9	91.51 ± 0.98	87.488±0.45	80.023±0.82
10	93.05 ± 0.60	88.585±0.27	81.691±0.18

All the values are expressed as a mean ± SD., n=3

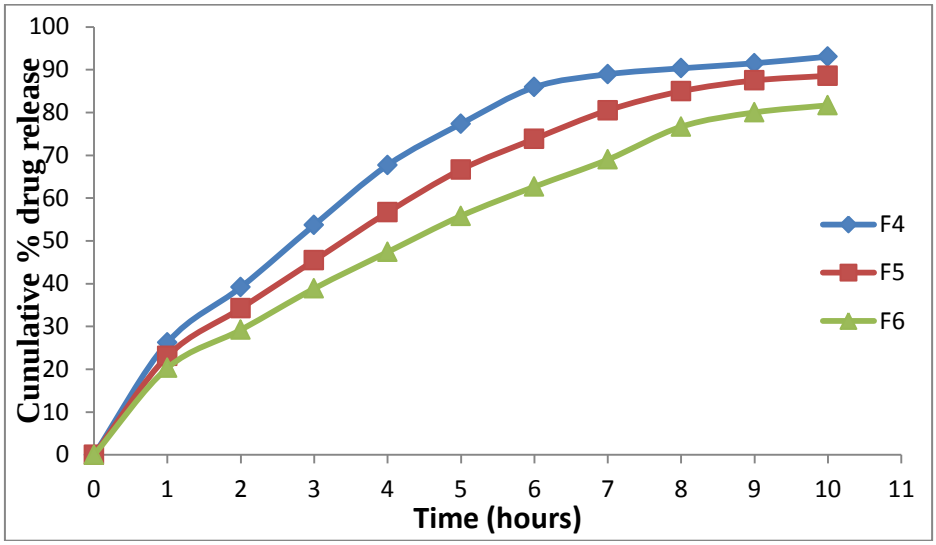

Fig. 4: Percentage drug release of Losartan potassium from Formulation F4 to F6

Table 7: Cumulative percent drug release of formulations (F7-F9)

Time (hrs)	Percentage drug release of Formulations		
	F7	F8	F9
1	22.109 0.47	19.763±0.86	15.958±0.05
2	35.456±0.94	32.571±0.73	28.291±0.07
3	46.395±1.59	41.707±0.56	38.865±0.31
4	57.393±0.62	52.524±1.48	46.405±0.40
5	66.179±1.27	59.635±0.27	55.717±0.60
6	72.879±1.31	67.666±0.83	61.617±1.29
7	80.003±1.08	73.489±1.27	66.839±1.37
8	86.223±0.17	78.859±1.88	71.509±1.26
9	91.929±1.69	83.329±0.72	75.986±0.68
10	98.892±0.51	85.366±0.59	79.926±0.70

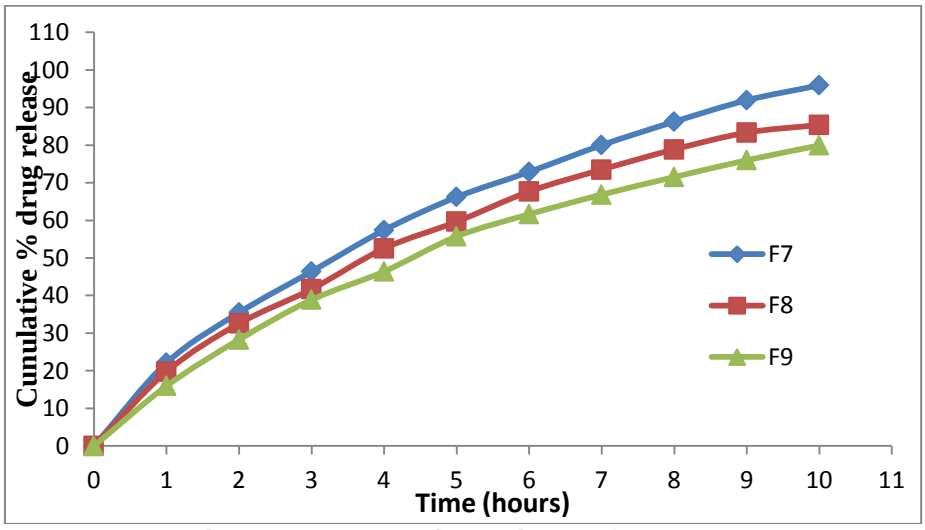

Fig. 5: Percentage drug release of Losartan potassium from Formulation F7 to F9

Table 8: Release kinetics of optimized formulation

S.No	Formulation	Zero order	First order	Higuchi	Korsemeyer-peppa's	
					R^2	*n* value
1	F1	0.8645	0.9914	0.9870	0.9840	0.5968
2	F2	0.8640	0.9917	0.9862	0.9842	0.5953
3	F3	0.9141	0.9927	0.9906	0.9942	0.6268
4	F4	0.8535	0.9900	0.9855	0.9831	0.5782
5	F5	0.9156	0.9967	0.9913	0.9949	0.6174
6	F6	0.9469	0.9964	0.9890	0.9977	0.6374
7	F7	0.9398	0.9662	0.9917	0.9981	0.6431
8	F8	0.9349	0.9968	0.9911	0.9969	0.6464
9	F9	0.9468	0.9989	0.9880	0.9957	0.6950

Table 9: Stability study data of various parameters of formulation F7 at initial and different stability periods

Stability period	Parameters			
	Hardness (kg/cm^2)	Floating lag time(seconds)	% drug content	% Drug release
Initial	5.24	91	99.58	99.19
First month	5.16	93	99.47	99.09
Second month	5.08	97	99.32	98.87
Third month	5.08	103	99.21	98.74

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