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Research Article

Formulation and *In-Vitro* Evaluation of Losartan Potassium Sustained Release Matrix Tablets

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ABSTRACT

The objective of the present study was to develop a sustained release matrix tablets of Losartan potassium, an anti hypertensive drug. The sustained release tablets were prepared by wet granulation and formulated using different polymer such as Hydrophilic polymer HPMC and natural polymers like xanthan Gum and (XG), guar gum., in different ratios. All the formulations were analysed by measuring different parameters: hardness, consistent weight uniformity friability assay and in-vitro drug release and tested for the physiochemical equivalence of tablets through the evaluation of both official and non-official standers to check if they comply with specification of USP. The in-vitro drug release kinetics of drug was studied by using Zero order, First order, Higuchi, and Korsemeyer-peppas models based on the correlation coefficient (r^2) value. The formulations F2, F3, F4, F5 and F8 showed compliance with USP Requirement and FDA Guideline. This Formulation showed acceptable tablet properties and in vitro drug release. The resulting formulations produced matrix tablets with optimum hardness, consistent weight uniformity friability and assay. All tablets but five formulation exhibited gradual and near completion sustained release for losartan potassium and Not less than 70% released at the end of 10hrs. The results of dissolution studies indicated that five formulations (F2, F3, F4, F5 and F8) are the most successful of the study and exhibited drug release pattern very close to theoretical release profile. A decrease in release kinetics of the drug was observed on increasing polymer percentage.

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Introduction

Sustained release dosage form is new drug delivery system which release the active agent for longer period of time at expected rate after its single dose administration of drug delivery system is to provide a therapeutic amount of drug

to the specific site in the body to achieve promptly and then maintain the desired drug concentration(Viswanath et al., 2016).

Losartan potassium is a competitive antagonist, which is more selective for Angiotensin 1 (AT1) than for angiotensin 2(AT2) receptor. It is potent drug, its bioavailability is only 33% due to first pass metabolism and plasma half-life is ranging from 1.5-2.5 hr. To reduce the frequency of administration, side effect and to improve patient compliance, sustained-release formulation of Losartan potassium is desirable. Drug is freely soluble in water hence right selection of release-retarding excipients is necessary to achieve a constant in vivo input rate of the drug. The most of suitable method of preparation of this drug is to include in matrix system. Because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery to obtain a desirable drug release profile, cost-effectiveness, and broad regulatory acceptance (BG and Patel, 2010). Sustained release drug delivery gives the safe and easy method of drug utilization since medication is promptly terminated in case of toxicity Developing a sustained release matrix tablet of losartan potassium is desirable for effective treatment of hypertension (Shanmugam, 2011).Drug release for extended duration, particularly for highly water-soluble drugs, using a hydrophilic matrix system is restricted because of rapid diffusion of the dissolved drug through the hydrophilic gel network. For such drugs with high water solubility, hydrophobic polymers are suitable, along with a hydrophilic matrix for developing sustained-release dosage forms. Hydrophobic polymers provide several advantages, ranging from good stability at varying pH values and moisture levels to well-established safe applications(Prajapati, 2010).

Losartan potassium is water-soluble drug when this drug given via the oral route has very low gastric residence time due to the first pass effect and thus cannot ensure maximum bioavailability and better utilization of drug for the targeted site thus the need has emerged to formulate a sustained release matrix tablets(Prajapati, 2010)**.**The aim of this research study is preparation of sustained release matrix tablet with better patient compliance. This dosage form enables to maintain therapeutic blood or tissue levels of the drug for an extended period by reducing first pass metabolism and increase bioavailability. The lesser dose could provide desirable effect hence we will be able to minimize first pass metabolism and thus that help to reducing adverse drug reaction.

Material and Method

Method of Preparation of Mucoadhesive tablets

The wet granulation method was employed to prepare sustained tablets of LosartanPotassium using different polymers, such as HPMC k 100, Xanthan gum and Guar gum, in different ratios.

Preparation

Sustained matrix tablets containing 50 mg of furosemide were prepared by the wet granulation method (using isopropyl alcohol) and PVPK-30. All the ingredients except lubricants were mixed in the order of ascending weights and blended for 10 min in an inflated polyethylene pouch, and then Losartan Potassium was added to this mixture and mixed for 2 min for uniform mixing. Granulation was performed with a binder solution (Prajapati, 2010) of PVPK-30 that was previously dissolved in isopropyl alcohol, and this damp mass passed through a 10 no. Sieve. This was dried in a hot air oven at 60 °C for 1 hour and passed through 16 no. Sieve and lubricants, such as magnesium stearate and talc, were mixed and then compressed with a 10station rotary compression machine into a 450 mg tablet to a hardness of 6-10 kg/cm^{2}using a 6.5 mm punch.

Evaluation of granules of Losartan Potassium

All the prepared mucoadhesive tablets were evaluated for the following parameters.

Bulk density and Tap densities

Exactly 15 gm of polymer was weighed on a chemical balance and transferred into a 50 ml measuring cylinder. The cylinder was dropped on a wooden plat form a height of 2.5 cm three times at 2 second intervals. The volume occupied by the granules was recorded as the bulk volume. The cylinder wasthen tapped on the wooden platform until the volume occupied by the powder blend remains constant. This was

repeated three times for the blend. The data generated was used in calculating Carr's compressibility index (Prajapati, 2010).

$$\text{Bulk density} = \frac{\text{Mass}}{\text{Untapped volume}}$$

$$\text{Tapped density} = \frac{\text{Mass}}{\text{Tapped volume}}$$

Carr's Index

The compressibility index of the granules was determined by Carr's index. Carr's index can be calculated by using the following formula (Panda et al., 2018).

$$\textbf{Carr's Index} = \left(1 - \frac{\textbf{Tapped volume}}{\textbf{Fluppy/Bulk volume}}\right) * 100$$

Swelling Index

Selling index was determined by using following procedure

– Conical flask was taken and weighted.

– About 1 gm of polymer was added to it separately followed by addition of 10 ml of water.

– It was left for 24 hours.

– After 24 hours excess water was strained and the weight of conical flask was measured.

– Weight of swollen polymer was determined by subtracting it from weight of empty flask finally swelling index was calculated by using following formula (Prajapati, 2010).

$$\text{Swelling index} = \frac{\text{weight of swellen polymer}}{\text{weight of polymer}} \times 100$$

Loss on Drying

Determination of loss on drying of polymer is important drying time during granulation was optimized depending LOD value. LOD of each polymer were tested at 105°C for 1 hour by using Hot-air oven.LOD was determined by using following formula (Prajapati, 2010).

$$\text{Loss on dring \%} = \frac{W1 - W2}{W1} \times 100$$

Where,

W1= initial weight of sample

W2= weight of sample after drying.

Standard Calibration of Losartan Potassium in Phosphate Buffer of pH 6.8

100mg of Losartan potassium was accurately weighed and dissolved in100ml of pH 6.8 phosphate buffer to obtain a concentration of 1000µg/ml. From the above 10ml was withdrawn and diluted to 100ml to obtain a concentration of 100µg/ml. From this stock solution aliquots of 2.5ml, 5ml, 7.5ml, 10ml, 12.5 and 15ml were diluted in 100ml volumetric flask with phosphate buffer to give concentrations in range of 2.5µg/ml to 15µg/ml respectively, absorbance was measured at 234nm(El-Deen et al., 2017)

Pre-formulation evaluation

Solubility of Drug

Solubility of losartan potassium was determined by taking an approximate amount of drug in a test tube, in various medium.

Table 1: Relation between solubility and volume of solvent in ml per solute

Descriptive terms	Approximate volume of solvent in ml/gm of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble form	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10000
Practically insoluble	10000 and over

Bulk, Tapped density, Carr's Index, Angle of Repose and Hasuner Ratio of powder blend was analyzed by taking 15 g of powder

Evaluation of Furosemide Tablets

Friability

Friability is the measure of tablet strength. A Roche-type friabilator was used for testing the

friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed, and the percentage loss was determined (Ankit et al., 2013).

$$\% \text{ loss} = \frac{(\text{initial weight- final weight})}{\text{Initial weight}} * 100$$

***In-vitro* dissolution studies**

The release of the drug from the Furosemide tablet was determined using a USP dissolution apparatus type II, and 50 rpm speed in 900 ml of 0.1 N hydrochloric acid (gastric simulated fluid, pH 1.3) as a dissolution medium for first 2 hours and next 3 to 10 hours in intestinal simulated fluid (buffer solution, pH 6.8). The amount of drug dissolved after 1hr, 2hr, 4hr, 8hrand 10hr, in the surrounding dissolution medium were determined by UV visible spectrophotometer at 234 nm (Jayasree et al., 2014, Mohapatra et al., 2018).

Table 2: USP Requirement and FDA Guidance for Modified Release Dosage Form (Fuhrman, 2006)

Time (Hour)	Amount dissolved
1	15-40 %
2	25-60 %
3	35-75 %
4	Not less than 70 %

Hardness

Hardness was measured using a Monsanto hardness tester. For each batch, three tablets were tested.

Thickness

Three tablets were selected randomly from each batch, and thickness was measured by using a Vernier caliper.

Weight Variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets were calculated. The batch passed the test for the weight variation test if not more than two of the individual tablet weights deviated from the average weight by more than the percentage shown in Table No.3 and none deviated by more than twice the percentage shown.

Table 3: Percentage deviation allowed under the weight variation test

Average wt. of Tablets (mg)	Percentage
130 or less	10
130-324	7.5
More than 324	5

Assay

Assay was determined by accurately weighing 20 tablets and crushing them in mortar, an accurately weighed quantity of powder equivalent to 20 mg of drug was transferred to a 100 ml volumetric flask. Water was added and shaken for 15 min. Volume was made up to 100 ml with distilled water. The solution was filtered through Whatman's filter paper. 5 ml of the filtrate was diluted to 100 ml with 0.1N HCl. Then absorbance of the resulting 10 µg/ml solution was recorded at 234 nm. Assay was calculated using formula (Khan et al., 2014, Viswanath et al., 2016)

$$\% \text{ Assay} = \frac{spcl.abs}{std.abs} \times \frac{std.wt}{spl.wt} \times \frac{spcl.Dilution}{std.dilution} \times \frac{100 - LOD}{100} \times \text{purity } \%$$

Where, Spcl. abs = Absorbance of sample; Std. abs = Absorbance of standard; Std.wt = weight of standard Spcl. Wt = weight of sample; LOD = Loss on drying.

Release kinetics

For the release kinetic the various formulation were tested for Zero order, First Order, Higuchi model and Korsmeyer- Peppas Model (Fuhrman, 2006, Ramteke et al., 2014, Gouda et al., 2017)

Table 4: Composition of Different Formulations

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8
Losartan Potassium (mg)	50	50	50	50	50	50	50	50
HPMC (mg)	45	90	135	-	-	-	-	-
Xanthum gum (mg)	-	-	-	45	90	135	-	-
Gaur gum (mg)	-	-	-	-	-	-	45	90
Pvk 30 (mg)	22	22	22	22	22	22	22	22
Mccp 101	325.5	280.5	235.5	325.5	280.5	235.5	325.5	280.5
Talc (mg)	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Magnesium stearate (mg)	3	3	3	3	3	3	3	3
Isopropyl alcohol (mg)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total (mg)	450	450	450	450	450	450	450	450

Result and Discussion

Calibration Curve

Standard calibration curve was obtained by plotting the values of the concentration versus respective absorbance for each of concentration from 2.5 to 15µg/ml of reference losartan potassium. The analysis for linearity showed that the solvent used in the estimation of losartan potassium and in-vitro release are suitable and have no interference while taking absorbance in UV-Visible Spectrophotometer. From the calibration curve, the correlation coefficient (R^2) values and regression equation of losartan potassium standard in 0.1 N HCL and pH 6.8 phosphate buffer was found to be 0.990 and 0.997.

Polymer Characterization Bulk Density, Tapped density, Carr's Index, Swelling index and Loss on drying

Bulk density of different polymers was determined and it was found that the value was between 0.48 to 0.71. HPMC had minimum bulk density whereas xanthan gum had maximum value of bulk density. The value of bulk density,Tapped density between 0.62 to 0.0.88. The HPMC had minimum value of tapped density whereas xanthum gum had maximum value of tapped density, Carr's index of different polymers was found in the range of 19.61 to 22.54 percent, Swelling index was in range of 215 to 482, Loss on drying of different polymer was found in range of 2 to 4%. This was showed in table

Table 5: Absorbance of Losartan Potassium Standard at Various Concentrations in 0.1 N HCL

Concentration (µg/ml)	Absorbance
2.5	0.133
5	0.268
7.5	0.372
10	0.564
12.5	0.651
15	0.850

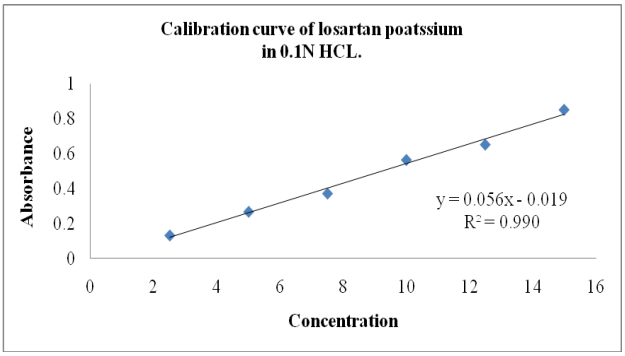

Fig.1: Calibration curve of losartan potassium standard in 0.1 N HCl.

Table 6: Absorbance of Losartan Potassium Standard at Various Concentrations in pH 6.8 Buffer.

Concentration (µg/ml)	Absorbance
2.5	0.122
5	0.247
7.5	0.358
10	0.512
12.5	0.641
15	0.742

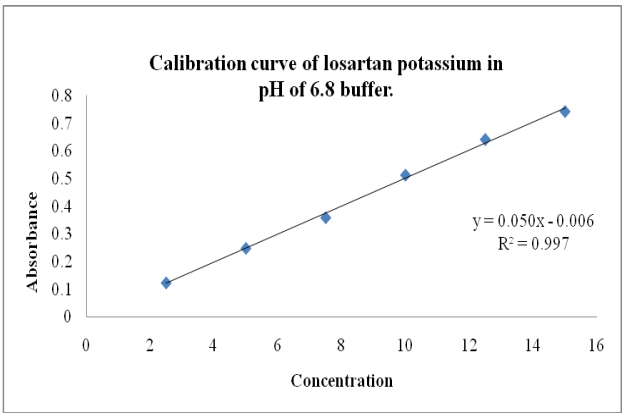

Fig.2: Calibration Curve of Losartan Potassium Standard in pH of 6.8 Buffer.

Polymer Characterization

Bulk Density,Tapped density, Carr's Index, Sweeling index and Loss on drying

Bulk density of different polymers was determined and it was found that the value was between 0.48 to 0.71. HPMC had minimum bulk density whereas xanthan gum had maximum value of bulk density. The value of bulk density,Tapped density between 0.62 to 0.0.88. The HPMC had minimum value of tapped density whereas xanthum gum had maximum value of tapped density, Carr's index of different polymers was found in the range of 19.61 to 22.54 percent, Swelling index was in range of 215 to 482, Loss on drying of different polymer was found in range of 2 to 4%. This was showed in table

Table 7: Characterization of Polymer

Polymer	Bulk Density	Tapped Density	Carr's index	Swelling index	LOD
HPMC 100000	0.48	0.62	22.54	444	2%
Xanthum gum	0.71	0.88	17.97	336	4%
Gaur gum	0.52	0.65	20.40	400.66	4%

Evaluation of Physical Properties of Losartan Potassium Powder Blends

Bulk Density, Tapped density, Carr's index, Angle of repose and Hausner ratio

Bulk density of different formulation was determined and it was found that the value was between 0.345 to 0.416. The formulation F1 and F2 had minimum value bulk density the formulation F3 had maximum value of bulk density, Tapped density of different formulation was determined and it was found that the value was between 0.430 to 0.520. The formulation F1 and F2 had minimum value of tapped density whereas the formulation F3 had maximum value of tapped density, Carr's index of different formulation was found to be in the range of 14.85 to 22.72 percent, The angle was found to be in the range of 23.21° to 34.29°,The hausner ratio of different formulation was found to be in range of 1.17 to 1.29.

Post Compression Evaluation of Losartan Potassium SR tablets

Physical Inspection

All examined formulated products were found to be pale white in color and round in shape without any defect.

Thickness and Hardness

The thickness of different formulation of Losartan potassium SR matrix tablets was found to be in ranging from 4.41mm to 4.74mm. The result of thickness is given in Fig.3. Among the eight formulations, it was found that the

formulation F3 had minimum thickness whereas the formulation F5 had maximum thickness. The minimum SD in average thickness was seen in formulation F5 (0.014) whereas the formulation F3 (0.096) had maximum SD value.The hardness of different formulation of losartan potassium SR matrix tablets was found to be in ranging from 5.2 kg/cm^2 to 9 kg/cm^2.Among the eight formulations, it was found that the formulation F1 had minimum hardness of 5.2 kg/cm^2 whereas the formulation F6 had maximum hardness of 9 kg/cm^2. The minimum SD in average hardness was seen in formulation f4, F7and F8 (0.84) whereas the formulation F3 (1.40) had maximum SD value.

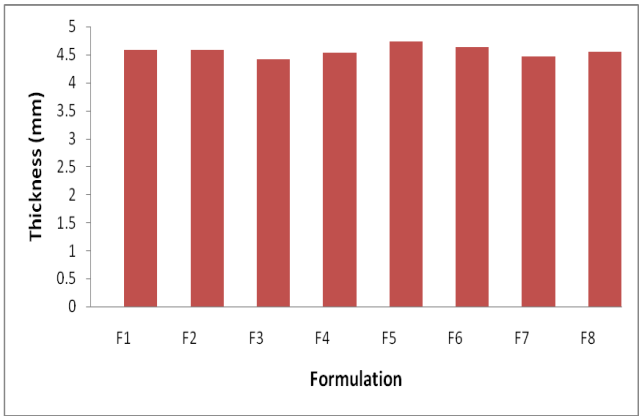

Fig. 3: Average Thickness of Different Formulation of Losartan Potassium SR Matrix Tablets.

Table 8: Thickness, Hardness and Friability Test of the all Formulation

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)
F1	4.59±0.01	5.2±1.31	0.67
F2	4.58±0.02	6.2±1.31	0.022
F3	4.41±0.09	5.4±1.40	0.033
F4	4.54±0.06	7.8±0.04	0.011
F5	4.74±0.04	6.4±1.15	0.022
F6	4.64±0.02	9±1	0.000
F7	4.47±0.03	5.8±0.84	0.033
F8	4.55±0.01	5.8±0.84	0.022

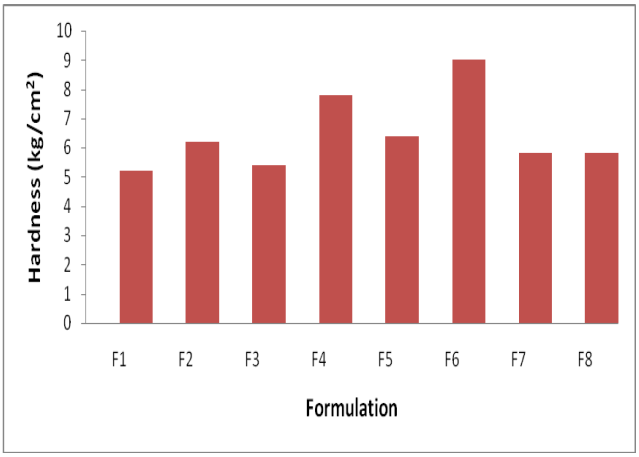

Fig. 4: Average Hardness of Different Formulation of Losartan Potassium SR Matrix Tablets.

Effect of Hardness on Dissolution

The relationship between hardness and dissolution was found to be inversely proportional. When hardness of tablets was increased, the dissolution was decreased. In formulation F6, hardness was found to be 9 kg/cm^2 it's dissolution was decreased with 9.45%. However, when hardness was decreased from 9kg/cm^2 to 5.2kg/cm^2 and 5.4kg/cm^2 in formulation F1 and F3 and value of their dissolution was increased with 36.91% and 21.31% respectively.

Weight Variation

The weight variation of eight formulations of losartan potassium SR matrix tablets was found in ranging from 447.3mg to 453.35. The result is shown in Fig. 5. Among the eight formulations, it was found that the formulation F2 (447.3) had minimum weight whereas formulation f7 (453.35) had maximum value of weight. The maximum SD in average weight was seen in formulation F4 (11.16) whereas F3 (6.047) had minimum SD value. It was observed that all the formulation was found within ranged of limit of ±7.5% of respective average weight.

Table 9: Weight Variation Test (mg) of the all Formulations

F1	F2	F3	F4	F5	F6	F7	F8
453	446	450	456	447	445	445	448
445	453	439	466	458	442	448	441
448	458	442	445	461	454	455	439
447	442	448	439	462	459	447	438
452	456	459	450	450	449	452	458
453	458	452	455	452	448	462	438
451	444	458	469	450	438	451	449
456	439	451	440	461	444	453	450
359	440	455	435	463	457	452	452
458	440	453	438	466	464	444	453
459	442	442	442	465	450	458	466
441	445	444	454	457	451	460	465
456	448	449	460	445	453	458	460
459	446	453	457	444	458	461	447
444	439	446	458	438	455	463	462
459	442	461	459	439	451	442	463
460	451	446	463	441	435	455	458
440	452	452	466	447	441	459	439
444	450	455	469	448	449	458	440
448	455	456	440	451	450	444	448
451.6	447.3	450.55	453.05	452.25	449.65	453.35	450.7
6.59	6.59	6.04	11.16	8.83	7.32	6.58	9.60

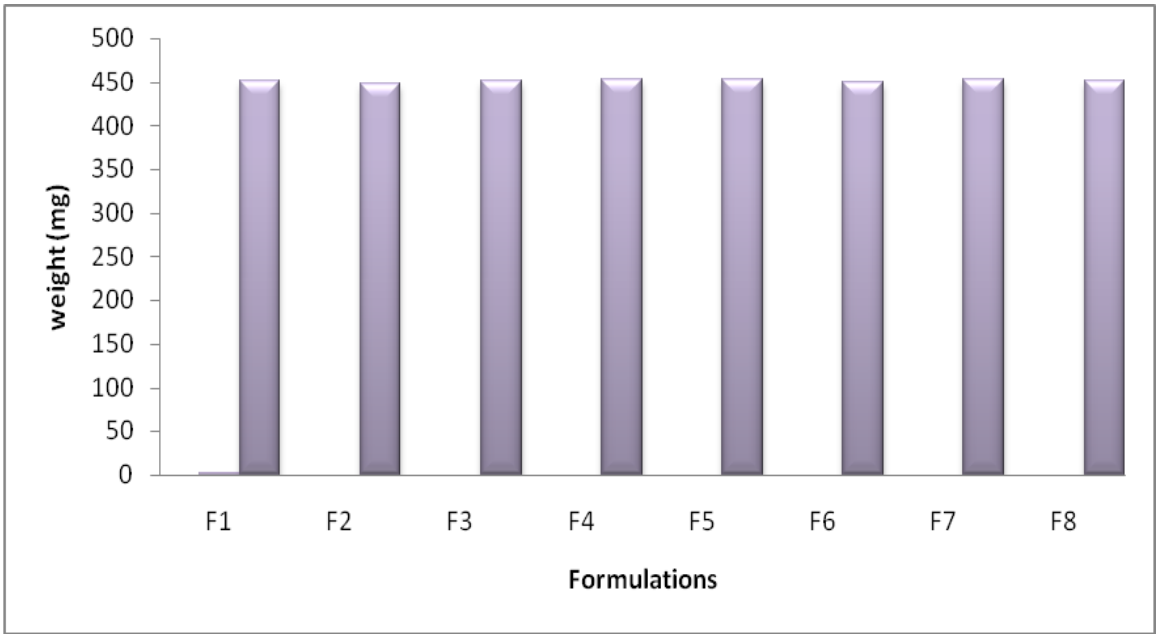

Fig. 5: Average Weight of Different Formulation of Losartan Potassium SR Matrix Tablets

Friability Test

The friability value of eight formulations of losartan potassium SR matrix tablets was found in ranging from 0.000% to 0.67% The result are shown in Fig. 6. Among the eight formulations, it was found that the formulation F1 (0.67%) had maximum value of friability whereas formulation F3 (0.000%) had minimum value of friability.

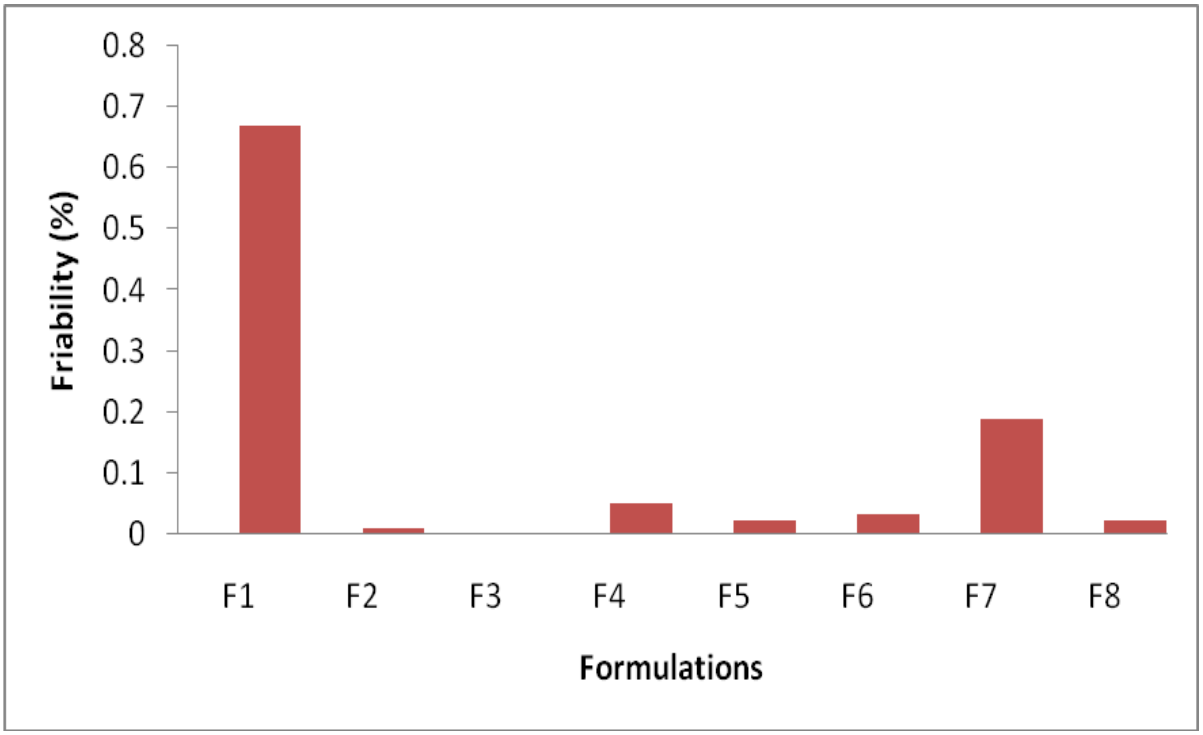

Fig.4: Average Friability (%) of Different Formulation of Losartan Potassium SR Matrix Tablets

Assay

% Assay of eight formulations was fond in ranging from 89.11% to 99.88%. The result of assay is showed in Fig.7 and Table 9. Among eight formulation the formulation F3 (89.11%) had minimum value of percentage assay whereas the formulation F5 (99.88) had maximum value of % assay. The result obtained from eight formulations of losartan potassium SR matrix tablets showed all formulation had the value within the USP specification limit of 90-110%.

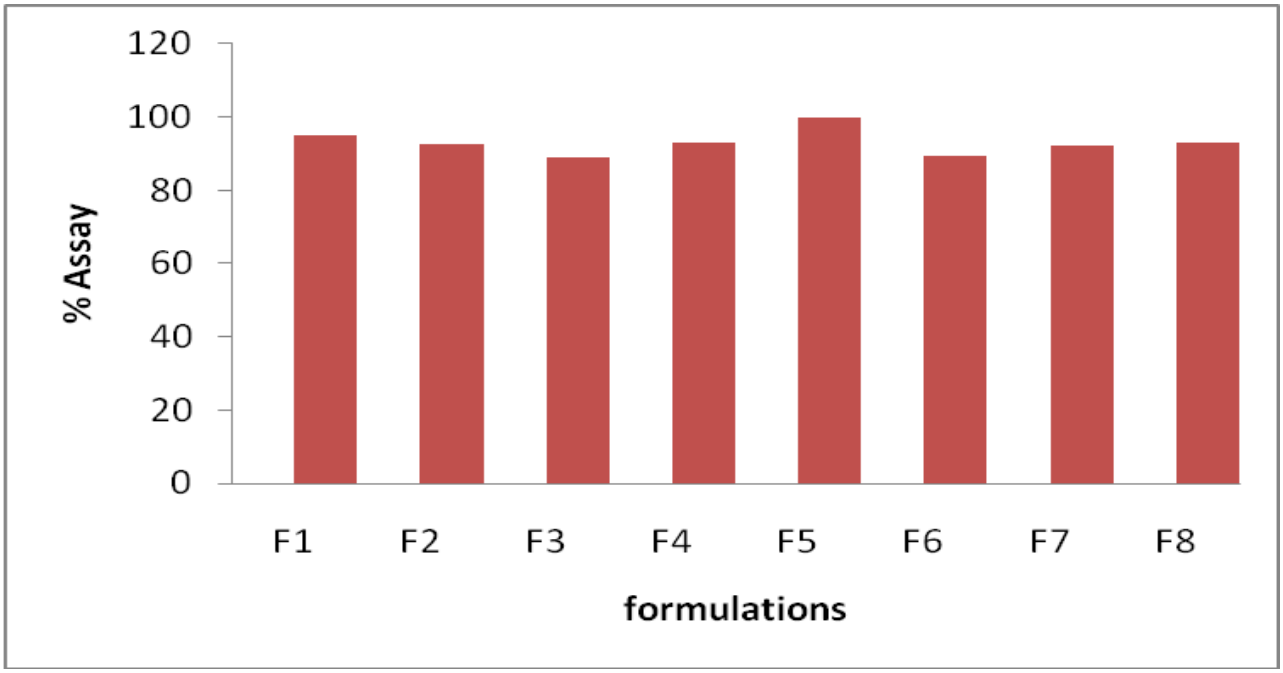

Fig.5: Average Friability (%) of Different Formulation of Losartan Potassium SR Matrix Tablets

Table 10: Assay (%) of the all Formulations

Formulation	Assay (%)
F1	95.01±1.30
F2	92.78±2.56
F3	89.11±1.66
F4	93.21±4.78
F5	99.88±3.45
F6	89.42±5.86
F7	92.22±3.78
F8	93.14±2.53

Dissolution Test

The dissolution profile of eight formulations of losartan potassium SR matrix tablets is given in Fig.8. The results of percentage of amount of losartan potassium dissolved after 1hrs,2hrs,4hrs, 6hrs, 8hrs and 10hrs.

According to result, the value of drug release percentage of the all formulation was found to be within range of 15-40% in 1st hour except F6 and F7 formulation. The formulation F6 (9.45%) showed the minimum value of drug release percentage whereas formulation F7 (56.18) showed maximum value of drug release percentage within 1 hour. All the formulations except F1, F2 and F6 were found to be value of drug release percentage within range of 25-60% in 2 hour. The formulation F6 showed minimum value of drug release percentage whereas the formulations F1 and F7 showed the maximum value of 72.35% and 66.59% respectively in 2 hour. All the formulations except F1 and F7 showed that value of drug release percentage within range of 35-75% after 4 hour. Both formulations of F1 (90.18) and F7 (91.24) showed the maximum value of drug release percentage within 4 hour. All the formulations except F6 showed that value of drug release percentage within not less than 70% in 8 hour. The formulation F6 (57.33%) showed minimum value of drug release percentage within 8 hour. (Average ± SD).

Effect of Polymer on Dissolution

The result of dissolution of different formulations of losartan potassium SR matrix tablet showed that the relationship between concentration of different polymer and dissolution was found to be inversely proportional. When low concentrations of polymer were used, the dissolution was increased. 10% of HPMC of total weight of tablets was used in the formulation F1 and 10% gaur gum of total weight of tablets was used in F7 formulation and their dissolution were increased of 36.91% and 56.18% within 1 hour respectively. However, when concentration of polymer increased from 10% to 30%, 30% of HPMC were used in formulation F3 and 30% 0f xanthum gum were used in formulation F6 and their dissolution value was decreased into 21.31% and 9.45% within 1 hour in formulations F3 and F6 respectively.

Different kinds of polymer showed different role in drug dissolution in same concentration. In formulation F2, the polymer (HPMC) concentration was 20% of total weight of tablets whose dissolution was 101.54% within 10 hour whereas formulations F5, the polymer (xanthum gum) and F8, the polymer (gaur gum) their concentration was 20% of total weight of formulations and their dissolution was found to be 83.49% and 96.69% within 10 hour. Hence dissolution rate depend on the types of formulation.

Table 11: Average % Drug Release Profile of the all Formulations

	% DR					
Formulation	1 hour	2 hour	4 hour	6 hour	8 hour	10 hour
F1	36.91±1.93	72.55±2.61	90.18±2.15	-	-	-
F2	28.20±3.16	38.48±6.91	61.28±4.34	81.28±1.58	92.49±2.34	101.54±5.25
F3	21.31±4.35	26.27±3.53	63.88±6.45	73.64±2.67	87.79±1.20	96.99±2.86
F4	18.55±2.26	32.05±3.54	58.77±6.11	68.50±8.46	77.09±10.03	87.55±10.22
F5	17.01±1.06	27.29±3.65	40.66±2.30	62.52±2.44	73.82±3.50	83.41±3.12
F6	9.45±0.83	12.43±1.56	37.75±3.60	49±2.08	57.33±2.23	65.71±2.09
F7	56.18±1,81	66.59±2.69	91.25±3.45	-	-	-
F8	32.65±5.73	41.48±4.75	66.18±4.41	77.28±3.35	86.40±2.29	96.69±2.81

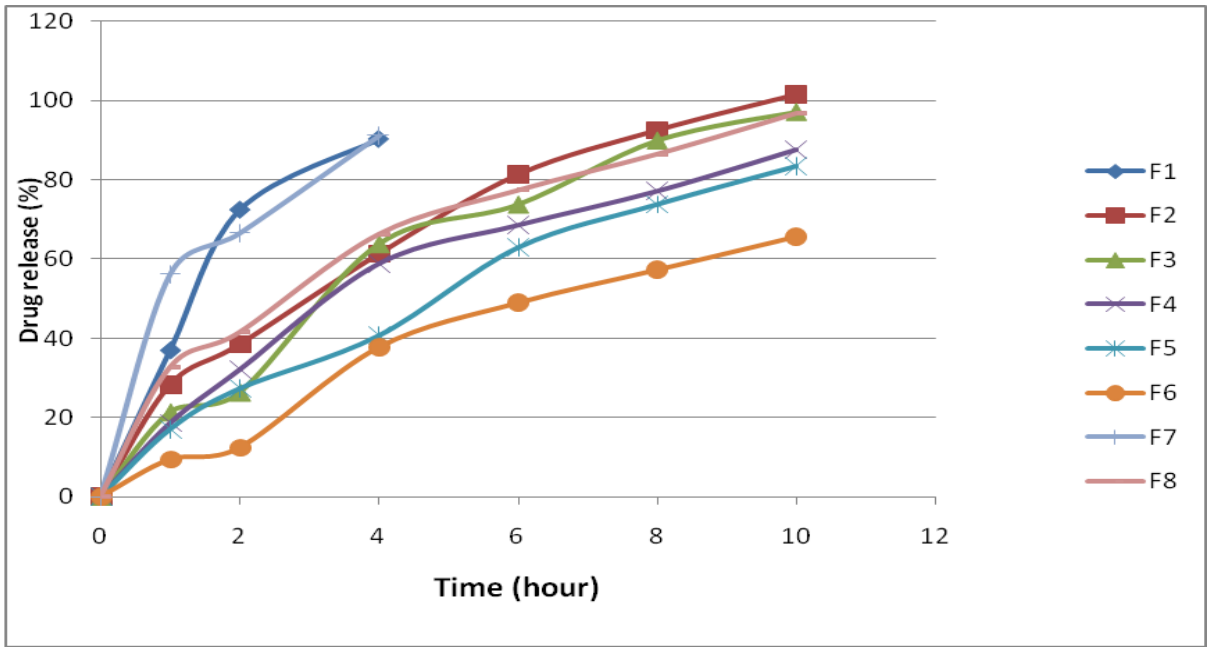

Fig.8: Drug Release Percentage of Different Formulation of Losartan potassium SR Matrix Tablets

Drug Release Kinetic Study

The release data analysis was carried out using the different kinetic model. The Regression coefficient (R^2) value of different kinetic model was tabulated below**.** This indicated that the in-vitro drug release of losartan potassium SR matrix tablet was best explained by korsemeyerpeppas model as plot showed that highest linearity (R^2 = 0.911), (R^2 = 0.991), (R^2 = 0.962), (R^2 = 0.980), (R^2 = 0.980), (R2 = 0.959), (R^2 = 0.964) and (R^2 = 0.990) respectively.

Table 12: Release Kinetics of the all Formulations

Formulation	Zer0 0rder R^2 value	First order R^2 value	Higuchi R^2 value	Korsmeyer peppas R value
F1	0.863	0.986	0.923	0.911
F2	0.971	0.911	0.993	0.991
F3	0.939	0.976	0.971	0.962
F4	0.937	0.987	0.983	0.980
F5	0.983	0.984	0.987	0.980
F6	0.954	0.987	0.978	0.959
F7	0.998	0.970	0.981	0.964
F8	0.959	0.926	0.990	0.990

Conclusion

Losartan potassium is a competitive antagonist, which is more selective for Angiotensin 1 (AT1) than for angiotensin 2(AT2) receptor. It is potent drug, its bioavailability is only 33% due to first pass metabolism, and plasma half-life is ranging from 1.5-2.5 hr. To reduce the side effect and to improve patient compliance, sustained-release formulation of Losartan potassium is suitable. Drug is freely soluble in water hence right selection of release-retarding excipients is necessary to achieve a constant in vivo input rate of the drug. The most of suitable method of preparation of this drug is to include in matrix system. Because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery to obtain a desirable drug release profile, cost-effectiveness, and broad regulatory acceptance.

Sustained release drug delivery gives safe and easy method of drug utilization since medication is promptly terminated in case of toxicity. When given in adequate doses losartan potassium matrix tablet appeared to be as ACE inhibitors in the treatment of hypertension. Hence developing a sustained release matrix tablet of losartan potassium is desirable for effective treatment of hypertension.

The eight formulations of losartan potassium SR matrix tablets were formulated by varying percentage of polymer like HPMC, xanthum gum and gaur gum by wet granulation. The pre-evaluation of granulation was carried out and all

the granulation of formulation showed satisfactory flow ability and compressibility. All the formulation passed the limit of weight variation, friability test and percentage of assay. The formulations F2, F3, F4, F5 and F8 passed limit of dissolution, which is given in USP Requirement and FDA Guidance for Modified Release Dosage. Formulation F2, F3, F5 and F8 passed the limit of dissolution because they had high amount of polymer and formulation F4 passed limit of dissolution even it contain lower amount of polymer but it was higher hardness. The formulations F1, F6 and F7 did not pass the limit of dissolution, which is given in USP Requirement and FDA Guidance for Modified Release Dosage. Because F1 and F7 had lower amount of polymer. Similarly, formulation F6 was found to be lower dissolution rate because it had higher amount of polymer also it was higher hardness. According to above result it showed that the decrease in release kinetic of drug on increasing amount of polymer and hardness. Therefore, it can be concluded that HPMC and natural polymer is potential candidates for the development of sustained release losartan potassium matrix tablets. The best-proposed formulation F2, F3, F4, F5 and F8 may be used for the development of sustained release losartan potassium matrix tablet to meet the patient's demand for the management of hypertension.

Conflict of Interest

The authors declare no conflict of interest

Disclosure Statement

There are no conflicts of interest.

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