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DEVELOPMENT AND CHARACTERIZATION OF MATRIX TABLETS OF LOSARTAN BY USING SYNTHETIC POLYMERS

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ABSTRACT

The main objective of the present study was development and characterization of Losartan matrix tablets. These solid unit dosage formulated by utilizing Direct compression technique and by using synthetic polymers such as HPMC and Eudragit. Losartan drug as short plasma half-life it is used to treatment of hypertension. These dosage form were optimized for hardness, thickness, breakdown of the particle time and release rate of the drug studies. Optimized formulation of drug release was 99.16% in 8 hours along with satisfactory results. It was concluded that F6 formulation as best formulation compared with the other formulations based on the Drug release studies and physical parameters.

KEY WORDS

Losartan, HPMC, Carbopol 934, Direct compression technique, In vitro drug release studies.

INTRODUCTION

Conventional oral drug formulations, such tablets and capsules. They are prepared and deliver the drug rapidly after the administration through the oral, to produce speed and total systemic drug absorption. After administration of drug it enter into the circulate that supply to the blood after that drug will be absorbed from the tablets or capsule dosage form is complete, concentrations of drug plasma reduced.

A Matrix device consists of drug dispersed homogeneously throughout a polymer matrix. Two major types of materials are used in the preparation of matrix devices, which include hydrophobic carriers like glyceryl tri-stearate, fatty alcohols, fatty acids, waxes, carnauba wax, methyl methacrylate, polyvinyl chloride, polyethylene, ethyl cellulose and hydrophilic polymers. Losartan potassium is an angiotensin II receptor antagonist. The drug is readily absorbed from the GI tract, following oral administration. The drug undergoes extensive first pass metabolism; hence its bioavailability is only 32%. The drug has a low elimination half-life (1.5 to 2.5 hrs) and hence it is suitable for oral controlled release. Administration of conventional tablets of losartan potassium may exhibit fluctuations in the plasma drug levels, resulting either in manifestation of side effects or reduction in drug concentration at the receptor site. Accordingly, studies on regulation of drug release by formulating its controlled release systems would be advantageous as it would decrease the side effects and improve the patient compliance.

MATERIALS AND METHOD

MATERIALS

Losartan were purchased from Alkem pvt Ltd, HPMC, Eudragit, MCC were purchased from S.D fine chem. Pvt Ltd, Mumbai. All other ingredients used throughout the study were of analytical grade and were used as received.

METHOD

Formulation development

Table 1: Composition of Losartan floating tablets

Ingredients	Formulations							
	F1	F2	F3	F4	F5	F6	F7	F8
Losartan	50	50	50	50	50	50	50	50
HPMC K15M (mg)	100	75	50	-	-	-	-	-
Eudragit	-	-	-	100	75	50	75	50
MCC	47	72	97	47	72	97	72	97
Magnesium stearate (mg)	2	2	2	2	2	2	2	2
Talc (mg)	1	1	1	1	1	1	1	1
Total wt (mg)	200	200	200	200	200	200	200	200

Preparation of Formulation:

1. Drug and polymers transfer through 40 # screen individually and mix it for 3 minutes.
2. Above the powder particles and add diluents and other ingredients to the above mixture. Lastly add the Magnesium Stearate as glidant and Lubricant as Talc to the above the powder mix it for 2min.
3. Punching the above facilitated mix by utilizing 10mm round punches.

Evaluation parameters

Post compression parameters

Weight variation

Take prepared 20 tablets were unsystematic selected form each batch and separately weighed. After that average weight of tablets was calculated.

Thickness

The prepared dosage forms were unsystematically selected form single batch and these 10 thicknesses of the tablets was calculated by utilizing vernier caliper.

Hardness

Hardness of the tablet were measured utilizing a Pfizer apparatus. It is indicating in kg/cm. Take 3 tablets were unsystematically choose and hardness of the tablets were determined.

Friability

It is the disposition for a solid unit dosage break following compression. This is generally restricted to uncoated tablets during transportation. Prepared dosage forms were weighed and transfer in the friability instrument, it is then run for 25 rotations for 4 min. After rotation of the dosage forms were calculated.

% F = {1-(Wo/W)} ×100

Where,

Wo = Primary quantity of solid dosage form

W = final quantity of the tablet

Content Uniformity

Required amount of tablet powder transferred into 100 ml of suitable buffer such as 6.8 phosphate buffer by stirring it for 15 min. 1 ml of solution was pipette out into 10 ml VF and fill the volume of the flask with water. After that sample solution analyze the drug by taking drug absorbance at 235 nm using reagent blank.

***In- Vitro* Release study**

Release rate of the drug studies were as a process utilizing tablet dissolution test apparatus USP II at 100 rpm. The dissolution bowls 900 ml of Standard buffer pH 1.2 l for 2 hr and followed by pH 6.8-time interval. And the Temperature maintained at 37±5. The aliquots were remove at particular time period and equal amount of dissolution medium. From that 1 ml sample, 1 ml aliquots were withdrawn and transfer in a 10 ml VF and make the volume with buffer. These aliquots were analysing by taking the absorbance at suitable wavelength (235 nm) against the standard.

Stability studies

Losartan tablets were placed on desiccant and stored at ambient conditions such as 37 °C and 40±2°c and refrigerator 2-8°C for a period of 3 months.

RESULTS

Precompression parameters

Table 2: List of Micromeritic properties of directly compressible powder

Parameter	F1	F2	F3	F4	F5	F6	F7	F8
Angle of repose	23.45±0.1	25.44±0.3	22.20±0.15	27.25±0.15	29.12±0.10	28.12±0.09	29.12±0.10	28.12±0.09
Bulk density	0.412±0.2	0.420±0.3	0.413±0.20	0.450±0.27	0.429±0.22	0.431±0.20	0.429±0.22	0.431±0.20
Tapped density	0.497±0.17	0.503±0.22	0.498±0.15	0.508±0.21	0.503±0.26	0.501±0.25	0.503±0.26	0.501±0.25
%Compressibility	12.53	14.04	13.81	13.65	12.28	12.39	12.28	12.39
Hausner's ratio	1.13	1.14	1.14	1.14	1.05	1.03	1.05	1.03

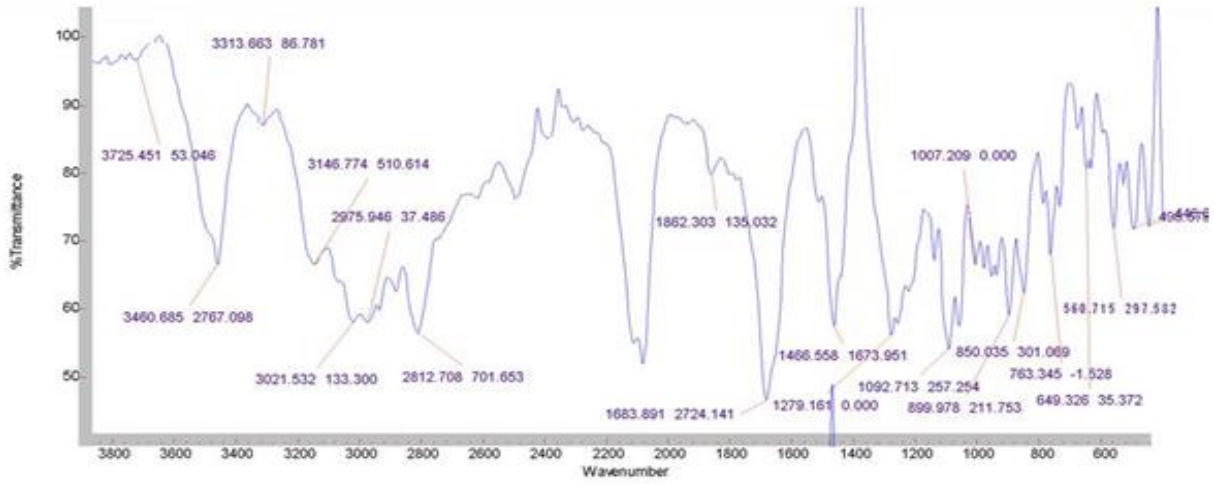

Figure 1: FTIR Studies for Pure drug

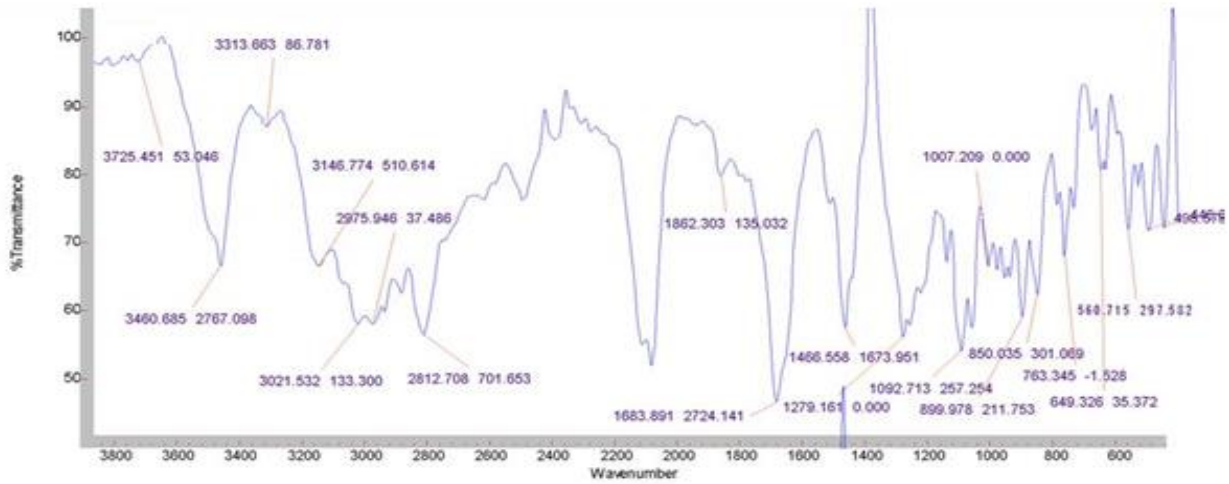

Figure 2: FTIR Studies for Optimized formulation

Post compression parameters

Table 3: List of Post compression parameter results

Parameter	F1	F2	F3	F4	F5	F6	F7	F8
Weight variation	199.9±2	298.1±2	193.8±2	197.7±2	194.1±2	200.8±2	199.7±2	`198.1±2
Thickness (mm)	5.4±0.2	5.5±0.2	5.2±0.2	5.3±0.2	5.4±0.2	5.8±0.2	5.3±0.2	5.4±0.2
Hardness kg/cm²)	8.7±1.3	7.2±1.2	8.1±1.3	6.7±0.9	8.1±1.7	8.8±1.3	6.1±0.9	7.3±1.5
Friability	0.13%±0.2	0.15%±0.2	0.14%±0.1	0.14%±0.2	0.15%±0.2	0.16%±0.1	0.15%±0.2	0.17%±0.2
Content uniformity	96.01%±0.	95.3%±0.4	95.5%±0.3	96.5%±0.2	97.7%±0.3	98.9%±0.3	94.2%±0.4	97.6%±0.3

Drug release studies

Table 4: Dissolution data for F1-F8

	%Drug Release							
Time	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
0	0	0	0	0	0	0	0	0
1	13.43	14.33	15.58	16.65	18.92	17.56	17.22	17.89
2	26.92	24.45	25.90	24.65	26.55	25.87	26.67	28.45
3	35.65	36.92	42.25	47.58	47.44	52.25	57.99	47.44
4	46.92	56.73	54.95	59.98	54.18	74.95	72.98	61.19
5	62.58	66.88	70.94	62.10	63.92	85.94	81.10	73.78
6	78.45	78.82	81.45	75.98	75.58	91.16	88.45	81.68
7	88.24	82.13	89.16	81.56	85.51	95.87	91.98	92.78
8	94.12	91.74	95.16	93.77	95.58	99.16	96.45	98.58

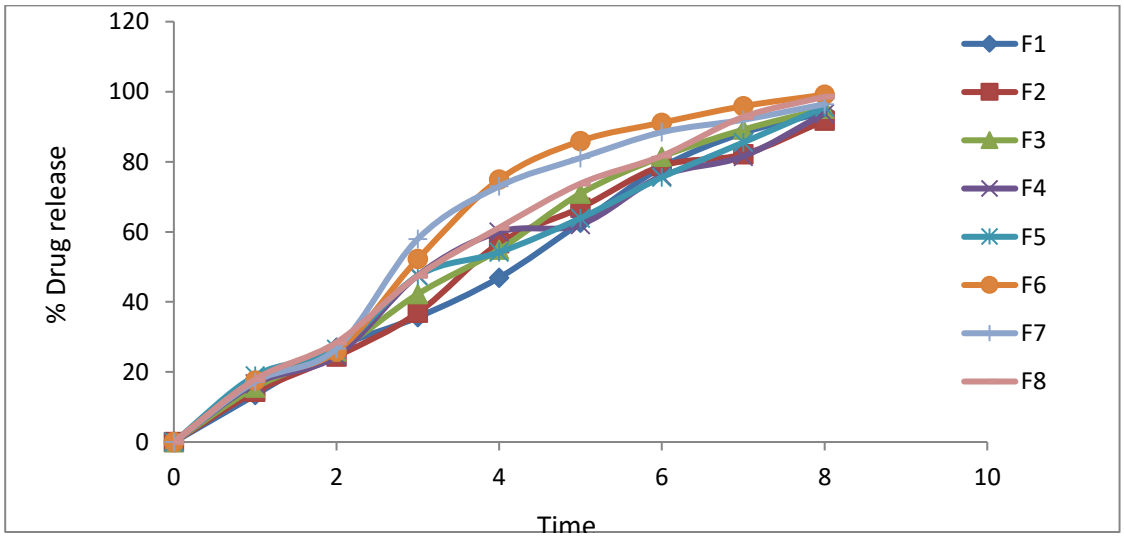

Figure-3: Drug release studies of all formulation

Drug release kinetics

Table 5: Kinetic studies of Losartan

Release kinetics	R^2	Intercept	slope
Zero order	0.934	10.49	3.29
First order	0.953	4.964	-0.14
Higuchi	0.934	11.0	25.61
Korsmeyer peppas	0.991	0.66	0.74

Dissolution- Zero Order kinetics

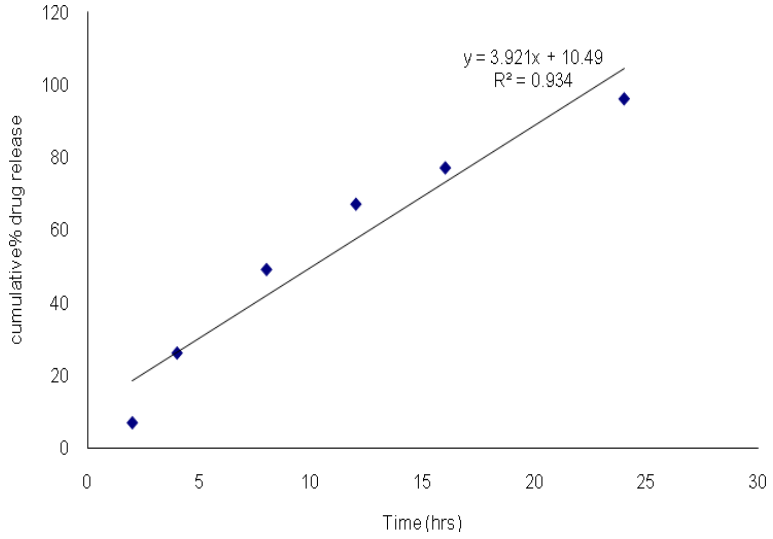

Figure 4: Graph for the formulation optimized -Zero Order Kinetics

Dissolution - First Order Kinetics

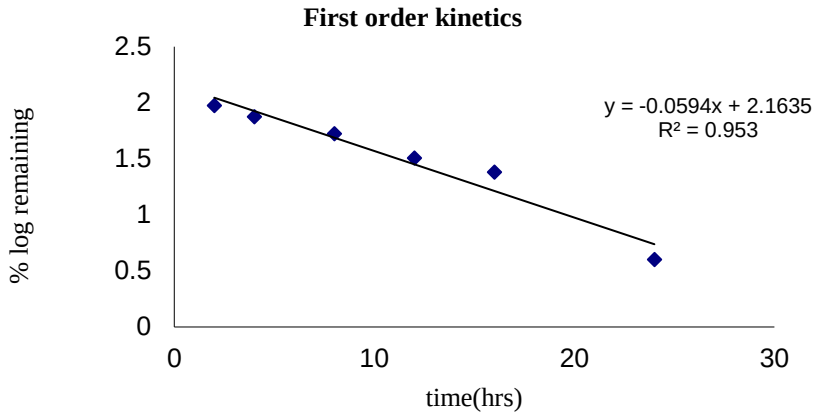

Figure 5: Graph for the formulation Optimised First Order Kinetics

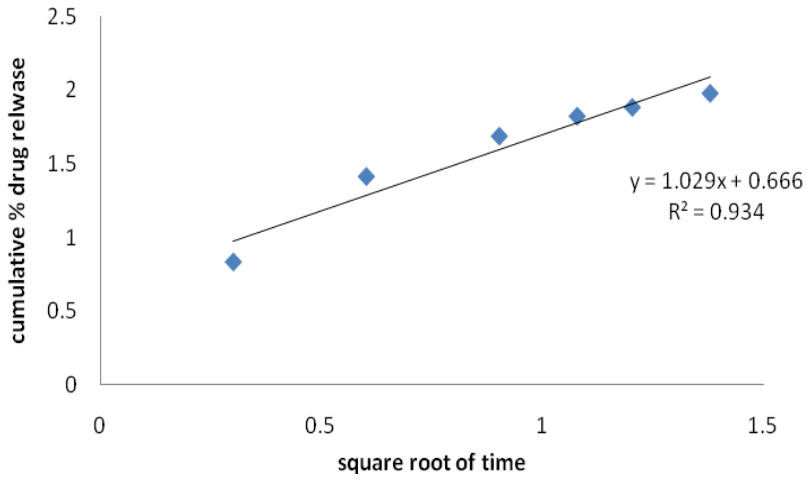

Figure 6: Graph for the formulation Optimised Higuchi model

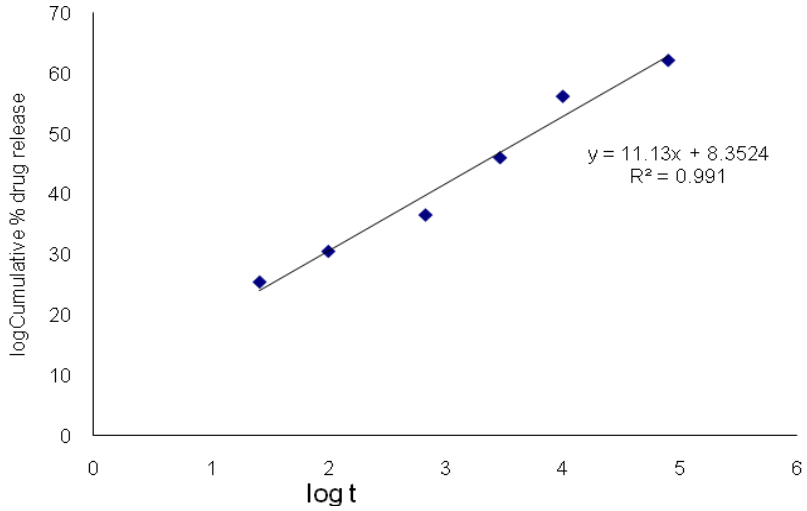

Figure 7: Drug Release Kinetic for Optimised Korsmeyer-Peppas

Stability studies

Table 6: Stability Studies of Optimized Formulation

S.NO	Time in days	Physical changes	Mean % drug content ± SD		
			Losartan		
			$25^0C/60\%$	$30^0C/75\%$	$40^0C/75\%$
1.	01	No Change	99.16	99.28	99.32
2.	30	No Change	99.16	99.31	99.42
3.	60	No Change	99.16	99.41	99.50

CONCLUSION

In the present work, attempts were made to development and characterization of Losartan matrix tablets. Losartan was subjected to preformulation studies; based on the results obtained Losartan sustained release tablets were successfully formulated. Formulations prepared by direct compression technique using HPMC, eudragit as polymers showed desired in vitro release. Set of trials were formulated for which physical parameters (B.D, T.D, compressibility index, hausner's ratio, weight, thickness, hardness) were found to lie within the specifications the %drug content(F6) values were found to be in the range of 98.9%. Dissolution study was performed in USP type II apparatus at 100 RPM in 0.1 HCL for 2 hours followed by pH 6.8 phosphate buffer. The eight formulations are done in this F6 formulation release the drug 99.16% up to the 8hrs. It is compared to innovator it releases the drug. *In-vitro* release showed that the formulation F6 had better dissolution profile along with sustained action as compare to other formulations. From the results of the *in vitro* study it appears that the release of the Losartan was significantly influenced by the characteristics of the polymer used.

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