Formulation and Evaluation of Sustained Release Tablets of Losartan Potassium

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ABSTRACT:

The present study was undertaken to develop sustained release (SR) tablets of Losartan potassium, an angiotensin-II antagonist for the treatment of hypertension. The tablets were prepared by wet granulation method, with ethyl cellulose. The amount of Losartan potassium remains fixed (100 mg) for all the six formulations whereas the amounts of ethyl cellulose were 50mg,60mg,70mg,80mg,90mg and 100mg for F-1, F-2, F-3, F-4, F-5 F-6 & F7 formulations respectively. The evaluation involves three stages: the micromeritic properties evaluation of granules, physical property studies of tablets, and in-vitro release kinetics studies. The USP apparatus type II was selected to perform the dissolution test, and the dissolution medium was 900 mL phosphate buffer pH 6.8. The test was carried out at 75 rpm, and the temperature was maintained at $37^oC \pm 0.5^oC$.

KEYWORDS:- *Losartan potassium, Sustained release, ethyl cellulose, in-vitro drug release and anti-hypertensive drug*

1. INTRODUCTION:

The objective of an ideal drug delivery system is to deliver adequate amount of drug for an extended period for its optimum therapeutic activity. Most drugs are inherently not long-lasting in the body, and require multiple daily dosing to achieve the desired blood concentration to produce therapeutic activity. To overcome such problems greater attention has been focused on sustained release drug delivery system[1].

Losartan is an angiotensin-receptor blocker (ARB) that may be used alone or with other agents to treat hypertension.It is well absorbed Losartan may be used to treat hypertension, left ventricular hypertrophy and diabetic nephropathy. It may also be used as an alternative agent for the treatment of systolic dysfunction, myocardial infarction, coronary artery disease, and heart failure. The objective of the present investigation were to prepare sustained release tablets of Losartan Potassium by using ethyl cellulose at six different concentrations, and to compare the in-vitro characteristics (weight variation, thickness and diameter, hardness, friability, drug content,) of the developed tablets[2].

2. MATERIALS AND METHODS:

Losartan potassium, active pharmaceutical ingredient was procured from Research lab fine chem. Industries. Ethyl cellulose (Loba Chemie Pvt. Ltd., Mumbai, India), starch (Qualigens Fine Chemicals, Mumbai, India), Magnesium sterate (Prime laboratories, Hyderabad), talc(S.D Fine chemicals, Hyderabad, India were procured and used in this investigation [3].

2.1 Formulation and Development of Sustained Release Tablets:
Granules were prepared by wet granulation method[4]. Losartan potassium, ethyl cellulose and lactose are weighed and mixed uniformly. Required quantity of starch paste was prepared and added drop wise to the blend. The wet granules prepared were passed through sieve #10 & dried for 15 minutes. The air dried granules are again passed through sieve #22, magnesium stearate & talc were accurately weighed added to the granules. The prepared granules compressed into tablets by using tablet compression machine. The composition of formulations has been examined in **Table 1.**

Table 1: Composition of formulation

Ingredients (in gms)	F1	F2	F3	F4	F5	F6	F7
Losartan potassium	100	100	100	100	100	100	100
Ethyl cellulose	50	60	70	80	90	100	110
lactose	130	120	110	100	90	80	70
Magnesium stearate	10	10	10	10	10	10	10
talc	10	10	10	10	10	10	10

3. EVALUATION PARAMETERS [4-9]

Pre formulation tests

3.1 Percentage Yield: losartan potassium granules were prepared by using wet granulation method. 100mg of granules were weighed and percentage yield was calculated by using the following equation.

$$\textbf{Yield=M/MoX100}$$

Where, M = weight of granules and Mo = total expected volume

3.2 Angle of Repose : This was determined by using the funnel method. Granules was allowed to flow freely from the funnel at a distance of 2 cm from the tip of the funnel to the horizontal surface to form a heap. The heap of the cone was marked and the pile of granules was also poured off. The average of the two diameters were also determined. The angle of repose was then calculated from the height of the heap (h) and the radius (r) from the relation:

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

3.3 Bulk Density: Apparent bulk density (ρb) was calculated by placing presieved drug excipients blend into a graduated measuring cylinder and measuring the volume (Vb) and weight (M)

$$\rho b = M/Vb$$

3.4 Tapped Density: The measuring cylinder containing a known mass of powder blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using following formula:

$$\rho t = M/Vt$$

3.5 Hausner's Ratio: It indicates the flow properties of the powder. It is usually determined from the ratio between the tapped density (TD) and the bulk density (BD).

$$\text{Hausner's ratio} = \rho t \backslash \rho b$$

Where, ρt = Tapped density and ρb = Untapped bulk density

3.6 Carr's Index The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated as follows:

$$C = (\rho t - \rho b) / \rho t * 100$$

Where, ρt = Tapped density and ρb = Untapped bulk

4. Evaluation of losartan potassium Sustained Release Tablets[10-11]:

Post formulation studies like weight variation, thickness, friability and hardness were performed according to the standard procedures

4.1 Drug Content: An accurately weighed amount of the granules equivalent to 100 mg of Losartan potassium was taken in stoppered volumetric flask. The content was dissolved in phosphate buffer pH 6.8 and the volume made upto 100ml.the volume was filtered through whatmann filter paper 41.the solution was diluted suitably and analyzed for the drug content at 205 nm using UV-visible spectrophotometer.

4.2 In-vitro Drug Release Study: This study was carried out using USP Dissolution Apparatus 2 (Veego, India) in 900 mL of phosphate buffer of pH 6.8 at a speed of 72 rpm and temperature of 37 ± 0.5 °C. Granules were first compressed into tablets using tablet compression machine. At1,4,8,12,16,20,24 hours, 5 mL of each sample were withdrawn and replaced with fresh dissolution medium maintained at 37 ± 0.5 °C. The samples withdrawn were then filtered through whatman filter paper (No. 5) and assayed using the UV Spectrophotometer (Shimadzu UV – 1700 PharmaSpec, Japan) at wavelengths of 205 nm Cumulative percentage drug release was calculated using an equation obtained from a standard curve and plotted against time (Figure 1).

5. RESULTS AND DISCUSSION:

In the present study, sustained release tablets of Losartan potassium were prepared by wet granulation method. For each batch, blend of drug and excipients were prepared and evaluated for micromeritic properties shown in Table 2. The percentage yield was found to be in the range of 97.05 to 99.05. Angle of repose was found to be in the range of 26.1 and 29. Bulk density was found to be between 0.47and 0.55 gm/cm3 and tapped density between 0.56and 0.63 gm/cm3 for all formulations. From density data % compressibility was calculated and was found to be between 20.80% and 27.16%. Hausner's ratio was found to be between and 1.13 to 1.23. All the batches show the good micromeritic properties for wet granulation and hence granules were prepared by using wet granulation method

5.1 Drug Content: The percentage drug content of all the six formulation's were found to be between 97.21% to 99.03 %, which was within the acceptable limits as per IP.

5.2 In- vitro Drug Release: The % cumulative drug release of all the six formulations were shown in Figure 2. The results of all the six formulations for disintegration time, drug content and in-vitro drug release were shown in Table 3

Table 2: Evaluation of pre formulation properties of granules

Formulation Code	Angle Of Repose (θ)	Bulk Density g/ml	Tapped Density g/ml	Carr' S Index	Hausner's Ratio
F1	26.1	0.55	0.63	13.1	1.15
F2	26.8	0.51	0.60	14.63	1.17
F3	25.0	0.51	0.60	14.6	1.17
F4	27.4	0.50	0.56	11.12	1.13
F5	29.0	0.47	0.58	14.96	1.17
F6	27.4	0.52	0.61	15.44	1.23
F7	27.9	0.51	0.63	13.47	1.15

Table 3: Evaluation of Losartan Potassium sustained release tablet

Formulation Code	Weight Variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Drug Content (%)
F1	303	2.72	14	0.1	97.5
F2	304	2.73	15	0.09	99.5
F3	303	2.72	13	0.06	95.2
F4	302	2.73	16	0.05	99.6
F5	301	2.72	12	0.03	89.3
F6	302	2.74	15	0.13	98.2
F7	301	2.75	14	0.06	97.5

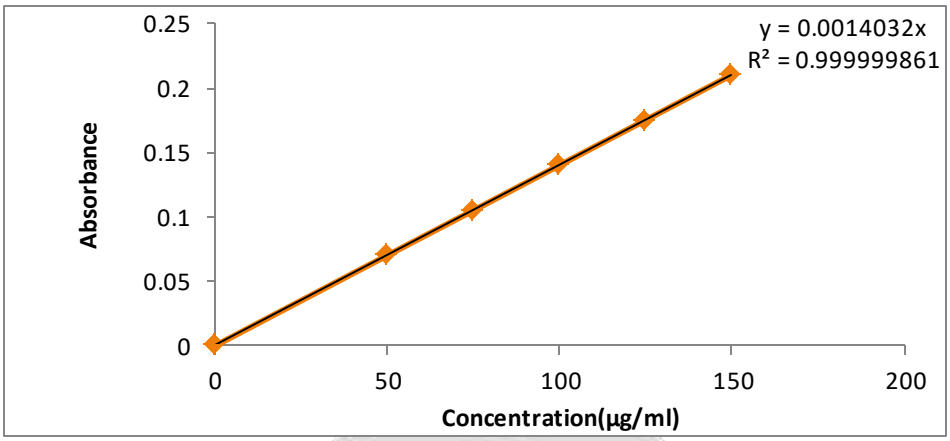

Figure 1: calibration curve of losartan potassium in phosphate buffer pH 6.8

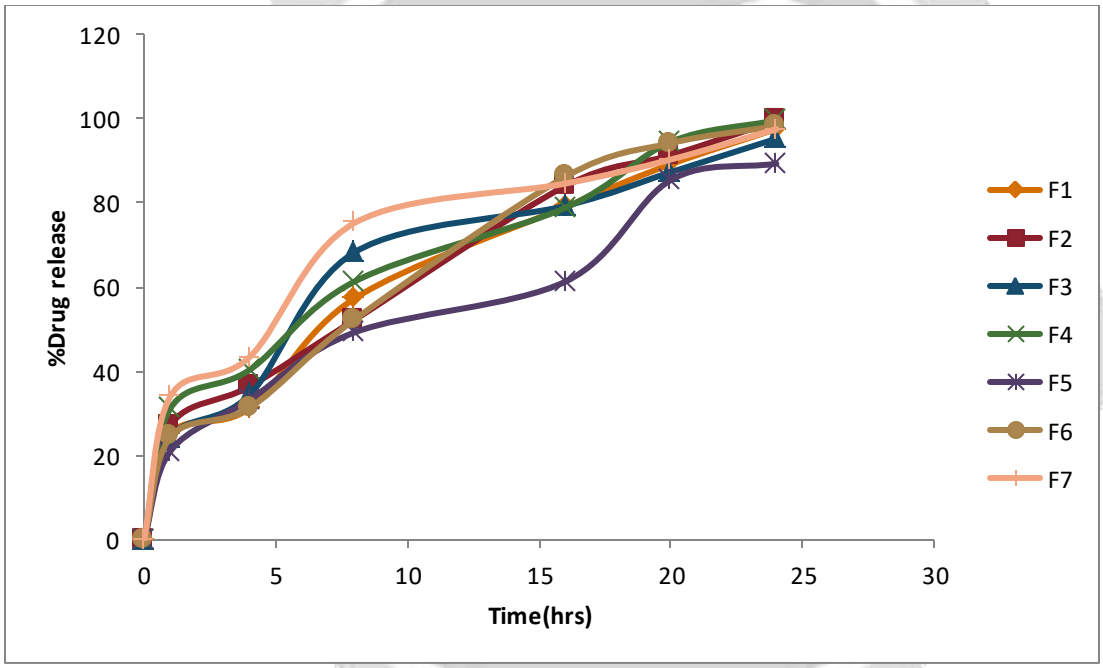

Figure 2: *In-vitro* drug release of losartan potassium sustained release tablets

6. CONCLUSION:

The aim of the present study was to develop an optimized formula for sustained release tablets containing Losartan potassium. Losartan potassium was planned to formulate as an sustained release system. The prepared granules were evaluated for percentage yield, angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index. The sustained release tablets of losartan potassium were also evaluated for, drug content and in-vitro drug release. F-7 formulation was considered optimized formulation for sustained release tablets of Losartan potassium as the drug release was 97.56 at 24 hours.

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