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FORMULATION AND EVALUATION OF LOSARTAN POTASSIUM IMMEDIATE RELEASE CAPSULES

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ABSTRACT Hard gelatin capsule contains Losartan potassium granules. Losartan is an angiotensin-receptor blocker it is an antihypertensive drug which is used to treat hypertension.it was designed to achieve immediate release of drug from the dosage form,this was mainly designed to increase therapeutic efficacy and to improve patient compliance. Advantages of hard gelatin capsule are rapid drug release, flexibility of formulation and better bioavailability than tablets. The main aim of this present work is to release the drug immediately from the hard gelatin capsule containing losartan potassium. Losartan potassium granules were prepared by using wet granulation method by different concentrations of sodium starch glycolate and then the air dried granules are filled into empty hard gelatin capsules for the dissolution studies. The prepared granules were evaluated pre compressional and post comprssional properties. Stability study shows that there was no significant change in disintegration time, drug content and in-vitro drug release of the formulation. The, formulation F5 was considered as best formulation for immediate release of Losartan potassium.

KEYWORDS : Losartan potassium, sodium starch glycolate, in-vitro drug release

INTRODUCTION:

A hard gelatin capsule is a type of capsule that is usually used to contain medicine in the form of dry powder or very small pellets. The term capsule is derived from the latin word capsula, meaning a small container. Gelatin has the property of disintegrating when comes in contact with the water thereby releasing the medicament completely. The main advantage of hard gelatin capsules rapid drug release is possible, flexibility of the formulation which cant be obtained by tables and selead HGCs are good barriers to atmospheric oxygen. Main disadvantages of hard gelatin capsules are filling the bulky materials is a problem,equipment filling is slower than tableting and more costly than tablets.the process may be very simple or complex depending on the characteristics of powders.

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.

MATERIALS AND METHODS:

Losartan potassium, active pharmaceutical ingredient was procured from Research lab fine chem. Industries. Sodium starch glycolate (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.the entire chemicals of analytical grade and double distilled water used throughout the experiment[6-9].

Formulation and development of emulgel:

Granules were prepared by wet granulation method. losartan potassium, sodium starch glycolate 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 are filled to the Size #3 empty hard gelatin capsule. The composition of formulations has been examined in **Table 1.**

Table 1:composition of formulation

Ingredients (in gms)	F1	F2	F3	F4	F5	F6
Losartan potassium	50	50	50	50	50	50
Sodium starch gylcolate	20	25	29	30	35	38
lactose	16	19	15	14	9	6
Magnesium stearate	4	4	4	4	4	2
talc	2	2	2	2	2	2

Evaluation Parameters

Pre formulation tests

Percentage Yield losartan potassium granules were prepared by using wet granulation method.50mg of granules were weighed and percentage yield was calculated by using the following equation.

Yield=M/MoX100

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

2. Angle of Repose [6] 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. Bulk Density [7] 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)

$\rho b = M/Vb$

4. Tapped Density [8] 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:

$\rho t = M/Vt$

5. Hausner's Ratio [9] 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).

Hausner's ratio = ρt\ρb

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

6. Carr's Index [9] 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

Evaluation of losartan potassium capsules:.

1. Disintegration Time [10] Disintegration test on capsules were carried out using a disintegrating apparatus (Type: ZT3/1, Erweka® GmbH, Heusenstamn, Germany) at 37 ± 2 °C. The disintegration medium used was distilled water. A disk was placed on each capsule to prevent it from floating. The time taken for all six capsules to disintegrate leaving only remnants of gelatin shell on the mesh was recorded.

2. Drug Content [11] An accurately weighed amount of the granules equivalent to 50 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 50ml.the volume was filtered through what mann filter paper 41.the solution was diluted suitably and analyzed for the drug content at 246 nm using UV-visible spectrophotometer.

3. In-vitro Drug Release Study [11] This study was carried out using USP Dissolution Apparatus 2 (Veego, India) in 900 mL of phosphate buffer of pH 7.2 at a speed of 100 rpm and temperature of 37 ± 0.5 °C. Granules were first incorporated in empty hard gelatin capsule of size #3 and then placed in a dry basket at the beginning of each test. At 5, 10, 15,20,25,30,35,40,45,50,55 and 60 min, 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 Spectro photometer (Shimadzu UV – 1700 PharmaSpec, Japan) at wavelengths of 246 nm Cumulative percentage drug release was calculated using an equation obtained from a standard curve and plotted against time (Figure 1).

4. Stability Study As Per ICH Guideline Stablity study as per ICH guidelines were performed for one month under the conditions of 40°C±2°C 75 % RH ±5%. The formulation was evaluated for disintegration time, drug content and in-vitro drug release.

RESULTS AND DISCUSSION:

In the present study, hard gelatin capsules containing granules 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 97.21 to 99.0. Angle of repose was found to be in the range of 27.4 and 30.7. Bulk density was found to be between 0.3and 0.50 gm/cm3 and tapped density between 0.47and 0.6 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 1.26 to 1.37. All the batches show the good micromeritic properties for wet granulation and hence granules were prepared by using wet granulation method

Disintegration Time The disintegration time for hard gelatin capsule was found to be in the range of 2.0 to 2.6 min.

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.

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

Stability Study as per ICH Guideline Stability study of hard gelatin capsule containing granules of Losartan potassium was done to see the effect of temperature and humidity on capsules during the storage time. Capsules were evaluated periodically (0 and 1 months) for disintegration time, drug content and in-vitro drug release. Stability study results show that there was no significant change in disintegration time, drug content and in-vitro drug release of the formulation shown in Table 4.

Table 2:Evaluation of pre formulation properties of granules

Formulation Code	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Angle of Repose (θ)	Carr's Compressibility Index	Hausner's Ratio
F1	0.3525	0.4840	30.763	27.16	1.3731
F2	0.3279	0.4709	30.631	20.80	1.2628
F3	0.4355	0.5782	27.413	24.67	1.3277
F4	0.3661	0.4805	27.748	23.81	1.3126
F5	0.3852	0.4991	29.654	22.82	1.2956
F6	0.5039	0.6380	28.763	21.01	1.2660

Table 3: Evaluation of Losartan Potassium capsules

Formulation Code	Disintegration time (min)	Drug content (%)	Weight variation mg
F1	2.58	98.06	101.12
F2	2.10	97.21	102.23
F3	2.08	98.23	101.56
F4	2.23	98.41	100.02
F5	2.00	99.03	99.98
F6	2.61	98.67	103.56

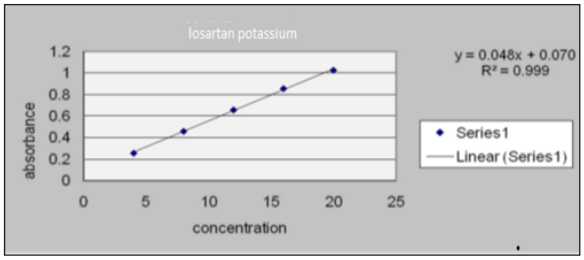

Figure 1:calibration curve of losartan potassium in phosphate buffer pH 6.8

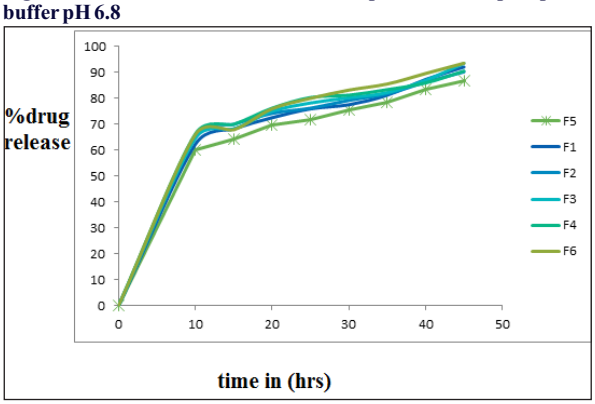

Figure 2: *In-vitro* drug release of losartan potassium immediate release capsules

CONCLUSION:

The aim of the present study was to develop an optimized formula for hard gelatin capsule containing granules of Losartan potassium. Losartan potassium was planned to formulate as an immediate 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 hard gelatin capsule containing granules of losartan potassium were also evaluated for disintegration time, drug content and in-vitro drug release. Stability study shows that there was no significant change in disintegration time, drug content and in-vitro drug release of the formulation. Thus, formulation was considered optimized formulation for immediate release of Losartan potassium.

Conflict Of Interest:

All the authors Rohini Reddy, Shanthi Priya, No conflicts of interest.

REFERENCES:

1. Augsburger L L. Hard and Soft Gelatin Capsules, In Modern Pharmaceutics, 3nd Edn; G. Banker and C T. Rhodes (Editors), Marcel Dekker, Inc., New York, NY, 1995.
2. Hostetler V, Bellard J Q. Capsules I. Hard Capsules, In Lachman, L., Lieberman, H.A., and Kanig, J.L. The Theory and Practice of Industrial Pharmacy, 2nd Edn; Lea and Febiger, Philadelphia PA, 389-404, 1976.
3. Granulation Process [Online]. 1995 Sep 28 [cited 2012 Oct 27]; Available from: URL: http://en.wikipedia.org/ wiki/Granulation_(process)
4. S C Sweetman. Martindale. The complete Drug reference, 35th Edn; Pharmaceutical Press, London; 1191-1192, 2007.
5. Krishna M K and Arunkumar S. Formulation and Evaluation of Losartan Potassium Sustained Release Matrix Tablets." RJPBCS, 3(2):524-533, 2012.
6. Martin A. Diffusion and Dissolution, Physical pharmacy, 3rd Edn; Lea and Febiger, Philadelphia, 399 444, 1983.
7. Fiese E F, Hagen T A. Preformulation. Lachman L., Lieberman H A., Kanig J L., The theory and practice of industrial pharmacy, 3rd Edn; Varghese Publishing House, Mumbai, 182 184, 1987.
8. Ansel H C, Popovich N G, Allen L V. Pharmaceutical dosage forms and drug delivery system. 8th Edn; B.I. Waverly Pvt. Ltd., New Delhi, 189(94):235-236, 1995.
9. Staniforth J N, Aulton M E. Powder flow. Aulton's Pharmaceutics: the design and manufacturing of medicines, 3rd Edn; Harcourt publisher ltd., Hungary, 175 79, 2007.
10. United States Pharmacopoeia. 28th Asian Edn, Rockvilne. United States Pharmacopoeial Convention Inc., 2005.
11. Indian Pharmacopoeia: Controller of Publications, Govt. of India, Ministry of Health & Family Welfare, New Delhi, 1, 135, 1996.