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FORMULATION AND EVALUATION OF MATRIX TABLETS OF LOSARTAN POTASSIUM

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ABSTRACT

The current study was designed to develop sustained release matrix tablets of losartan potassium used to treat hypertension. The sustained release matrix tablets were prepared by direct compression method using different polymer ratio with the drug, nine such formulations were prepared (F1 to F9). The polymers with hydrophilic (HPMC) and hydrophobic (Ethyl cellulose) nature as well as one natural polymer (Gaur Gum) were used. The drug compatibility with the excipients was evaluated. The compatibility showed by formulations was in compliance with the limits prescribed in pharmacopoeia. The formulation F7 showed remarkable pre-compression and post compression parameters when compared with other formulations as it had robust nature with optimum hardness, uniformity weight and friability. In-vitro dissolution study of F7 showed the sustained release of drug losartan potassium (96.26%) release at the end of 12th hrs. Increased polymer ratio showed decrease in release kinetics of drugs.

KEYWORDS: Losartan potassium, Gaur Gum, Hydroxypropyl methylcellulose K4M, Ethyl cellulose, Direct Compression Method.

INTRODUCTION

Oral delivery of the drug is the most common method of delivery of the drug because of its flexibility and ease of administration in the design of the drug form. It is known as the same dose of modified medicine dose may provide many advantages in the formulation of immediate release. Oral administration has different ways of designing modified dosage forms. It is usually expected that the design of the modified drug product will improve the release of the therapeutic treatment by providing a continuous and slow connection to the drug during the entire dose period and also providing greater comfort and compliance to the patient.[1]

Matrix tablet as a sustained release gave a new revolution to the new drug delivery system in pharmaceutical technology. Matrix is the release system that controls the prolongation and prolongation of drugs. The matrix is defined as a well-mixed combination of one or more drugs with a sweating agent, i.e. water-soluble polymers. The matrix tablets use traditional facilities, rental treatment variables and a larger dose of drugs. There is still interest in the development of new preparations that allow for the sustained release of drugs using inexpensive, easily available formulas by drafting the matrix rules to the desired location. It excludes complex production procedures such as polarization and coating during manufacturing. The rate of release of the drug is controlled from the dosage form by the type and proportion of polymer used in the preparation.

Matrix system is preferred because of its simplicity and patient compliance etc., then delivery of traditional drugs that have many defects such as repeated administration, fluctuation in blood concentration level and so on. The development of matrix tablets for continuous oral release of water-soluble drugs with a constant release rate has always been a challenge for the pharmaceutical technologist.[2]

Matrix delivery systems are an interesting and promising option when developing an oral release regimen. This review focuses on the progress made in the design of release dosage forms that are controlled using different types of matrices as a vector of active components. Sustained drug release system changed into designed to keep plasma drug degrees to release the medicine in a prolonged rate. The half-life of medicine having shorter and these are suitable for the sustained drug transport system. The principle goal in designing sustained transport machine is to increasing the movement and decreasing dosing frequency. Inside the matrix systems drug molecules are indicates higher sustained drug release profile in by means of specific mechanisms.[3]

Sustained release Matrix tablet has given a brand -new revolution for novel drug delivery machine inside the Pharmaceutical era. Matrix device is the discharge device which controls and prolongs the release for the drug, that's dispersed or dissolved. A matrix is defined as a properly-combined composition of the one or more than one drugs with gelling agent i.e. hydrophilic

polymers. Matrix tablets are the utilize the conventional centres, rent processing variables and accommodate large drug dose. There final interest in increase the unconventional formulations that allow for the sustained drug release using without difficulty to be had less expensive excipients via formula of matrix bases to favoured web page. Its regulations out procedures of complicated production including polarization and coating for the duration of Manufacturing and rate of drug release from the dosage shape is managed by the type Especially and percentage of polymer used inside the arrangements.

Hydrophilic matrix systems are the most typically used for oral managed drug shipping due to the fact they could reproduce a appropriate drug profile and their powerful cost. The drug release mechanism of leading from hydrophilic matrices occurs whilst the polymer swells inside the contact with the aqueous medium to shape a gel layer on the surface of the system. The drug then releases utilized by diffusion, dissolution.[4]

MATERIALS AND METHODS

Materials

Losartan potassium was gift sample by Micro Lab.Ltd., Bangalore. Gaur Gum, HPMC K4M was produced by Molychem Pvt. Ltd. Mumbai. Ethyl Cellulose, Polyvinyl pyrrolidine was purchased from Central Drug House Ltd. New Delhi. Micro crystalline cellulose produced by Ozone international, Mumbai. Magnesium stearate, Talk was purchased from Loba Chemical Pvt. Ltd. Mumbai.

Methods

Estimation of losartan potasium

Spectrophotometric method depends on the measurement of absorbance at 250 nm of U.V region in Distilled water, pH 1.2, and pH 6.8 was used for the estimation of losartan potassium.

Standard curve of losartan potassium in pH 1.2 (0.1 N HCL):

100 mg of Losartan Potassium was weighed and dissolved in 10 ml distilled water and volume was made up to 100 ml with 0.1N HCl. This was primary stock solution containing 1000µm/ml. From this stock solution,1ml was pipette out and transferred in to a 100 ml volumetric flask and volume was made up to100 ml with 0.1 N HCl which contained the concentration of 1µg/ml (second stock solution).from this second stock solution aliquots equivalent to 2-10 µg(2,4,6,8,and 10ml were pipette out in series of 100 ml volumetric flask and volume was made up to 10 ml with 0.1 N HCl .the absorbance of these solution was measured against the 0.1 N HCl as blank at 250 nm using UV –visible double beam spectrophotometer. then calibration curve was plotted taking concentration in µg/ml on X-axis and absorbance on Y-axis.

Standard curve of losartan potassium in pH 6.8 (phosphate buffer)

100 mg of Losartan Potassium was weighed and dissolved in 10 ml distilled water and volume was made up to 100 ml with phosphate buffer this was primary stock solution containing 1000µm/ml. From this stock solution,1ml was pipette out and transferred in to a 100 ml volumetric flask and volume was made up to100 ml with phosphate buffer which contained the concentration of 1µg/ml (second stock solution). from this second stock solution aliquots equivalent to 2-10 µg(2,4,6,8,and 10ml were pipette out in series of 100 ml volumetric flask and volume was made up to 10 ml with phosphate buffer. the absorbance of these solution was measured against the phosphate buffer as blank at 250 nm using UV –visible double beam spectrophotometer. then calibration curve was plotted taking concentration in µg/ml on X-axis and absorbance on Y-axis.

Method for preparation matrix tablet of losartan potassium

The sustained matrix tablets of losartan potassium were prepared by the direct compression method. The drug, polymers and other excipients were passed through sieve # 80. The total weight of tablet was 400mg and each tablet contains 80 mg of Losartan Potassium and the sustained release tablets containing drug, matrix materials, diluents, binder and lubricants were mixed uniformly and compressed on 10 station tablet machine using 8 mm round and flat punches with hardness between 5-7 kg/cm^{-2}.

Characterization Methods

1. **Fourier transform infrared spectroscopy (FTIR)**
   Interaction between drug–polymer was studied by infrared spectroscopy using FTIR spectrometer with diffuse reflectance principle. Sample preparation involved mixing the sample with potassium bromide, triturating in glass mortar and finally placing in the sample holder. And the FTIR spectra were recorded between 4000-400cm^{-1} ranges.[5]
2. **Differential scanning calorimetric analysis(DSC)**
   DSC of losartan potassium, Mβ-CD, physical mixtures and inclusion complexes were carried out the use of DSC Q2000 V24.2 build 107 devices. The mass of empty pan and reference pan has been taken under consideration for calculation of warmth float. The pattern mass varied from 3-10 + 0.5 mg and it became placed in sealed aluminium pans. The coolant used becomes liquid nitrogen. The samples have been scanned at 10°C/min from 20°C to 30°C.[6]

Evaluation Parameters

1. **Hardness**
   Hardness of the tablets was determined by using a hardness testing apparatus (Pfizer tester). A tablet hardness of 5-7 kg/cm^{-2} is considered adequate for mechanical stability.[7]

2. Friability

Roche friability test apparatus changed into used to determine the friability of the tablets. 20 pre weighed drugs had been positioned within the equipment, it become worked at 25 rpm for 4mins also tablets have been determined even as rotating. The drugs were then taken after 100 rotations, retested and reweighed. The percentage friability turned into calculated the use of the components.[8]

$$\% \text{ Friability} = \frac{\text{Initial weight- Final weight} \times 100}{\text{Initial weight}}$$

3. Weight variation

To study weight version character weights (WI) of 20 tablets from every component have been stated the usage of digital stability. Their average weight of (WA) turn into calculated. Common weight of the tablets changed into calculated.[9]

$$\% \text{ weight variation} = \frac{(WA–WI)}{WA} \times 100$$

4. Drug content

Ten tablets were randomly selected & allowed to equilibrate with 6.8 pH phosphate buffer solution overnight and the solution were filtered (0.45µ,milipore). After 12 hours, suitable dilutions were made with 6.8 pH buffer solution to get the concentration in Beer's Range. Absorbance of the solution was noted at 250 nm using 6.8 buffer solutions as blank and drug content per tablet was calculated.[10]

5. In-vitro drug release study

In-vitro drug release study was carried out using a USP-II rotating dissolution tester. The dissolution was carried out at 37±0.5°C and 100rpm speed. Release of drug from the tablets was premeditated in 900ml acidic medium of pH 1.2 for 2 hours, in alkaline medium of pH 6.8 phosphate buffer for remaining hours till end of the study. At predetermined time intervals 5ml aliquots were withdrawn and same volume of fresh solution were replaced. The amount of drug released was analysed using UV spectrophotometer at 250nm. The drug release data were fitted to various mathematical models as under to know which model is best fitting the obtained release profiles.[11]

6. Stability Studies

The accelerated stability of losartan potassium sample was evaluated according to ICH guidelines for 3 months at 40°C/75% RH. Samples were removed periodically (1, 2 and 3 months) and examined for drug content and particle size.[12]

RESULT

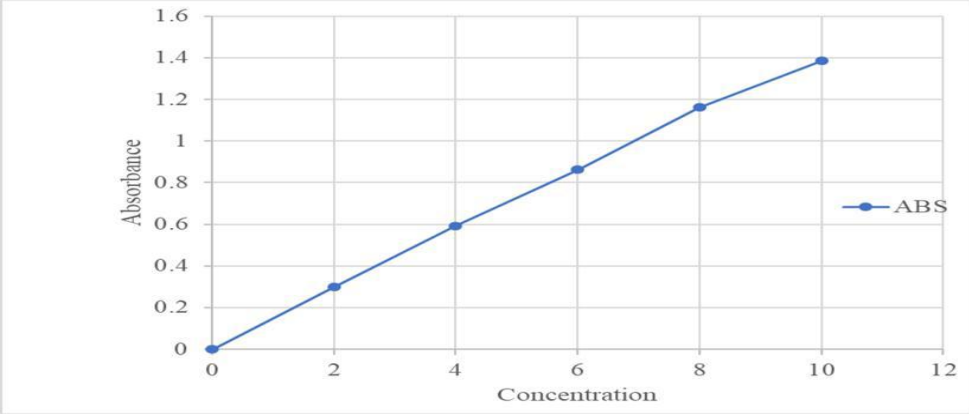

Figure 01: Standard calibration curve of losaratan potassium in pH 1.2 buffer.

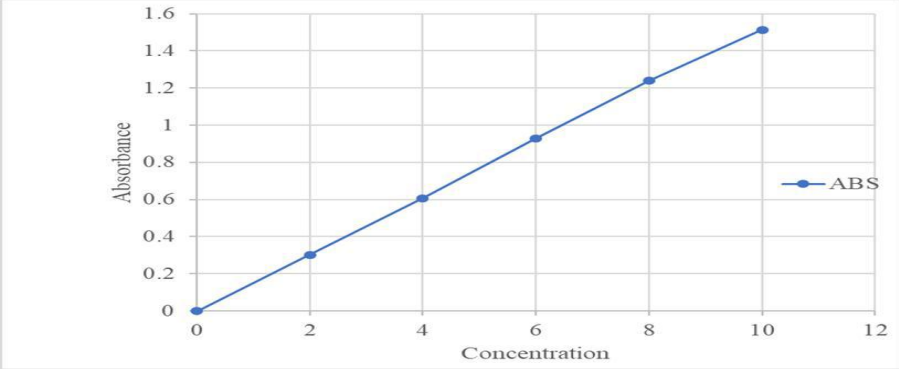

Figure 02: Standard calibration curve of losaratan potassium in pH 6.8 buffer.

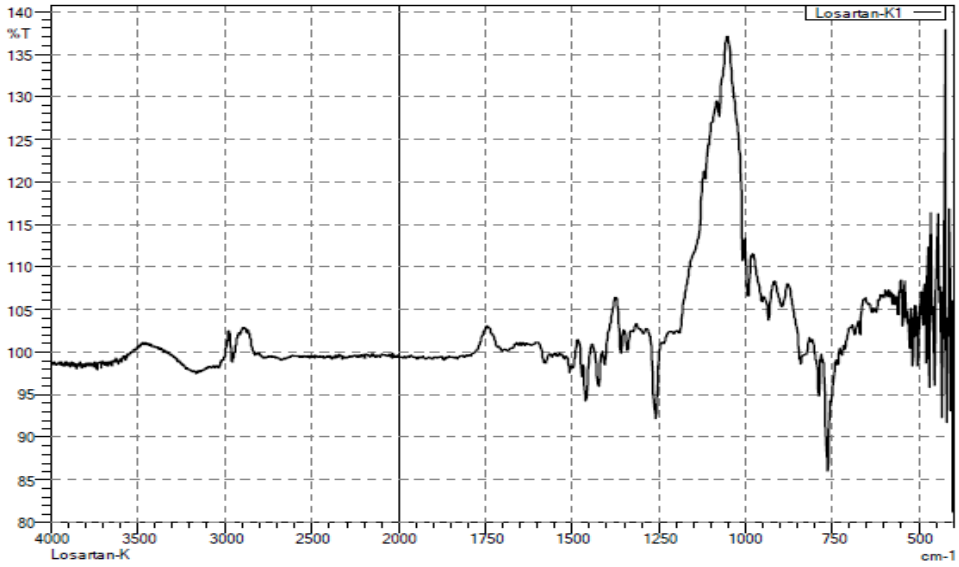

Figure 03: FT-IR of Losartan potassium drug.

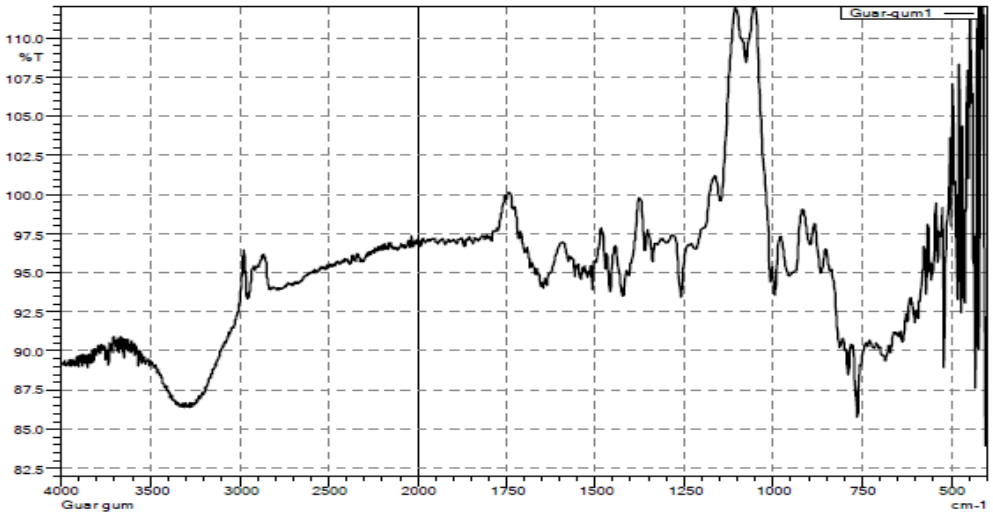

Figure 04: FT-IR of Losartan potassium + Gaur gum.

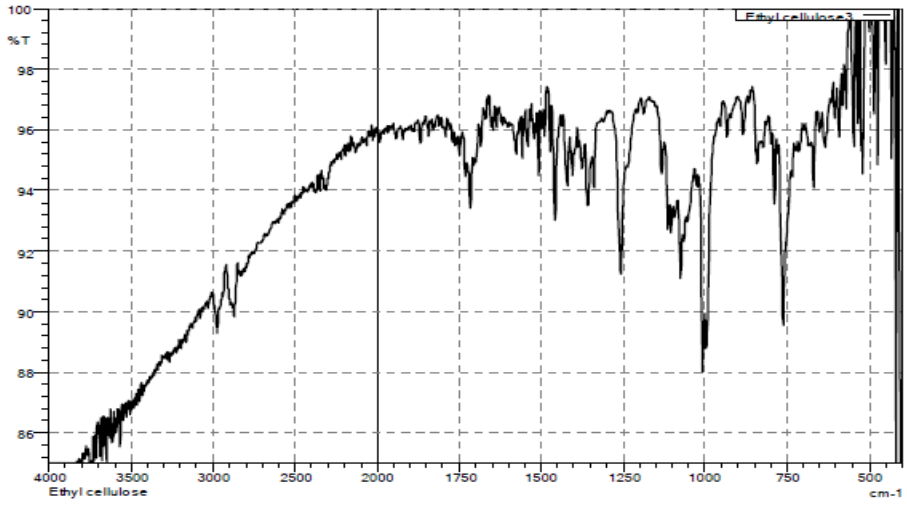

Figure 05: FT-IR of Losartan potassium + Ethyl cellulose.

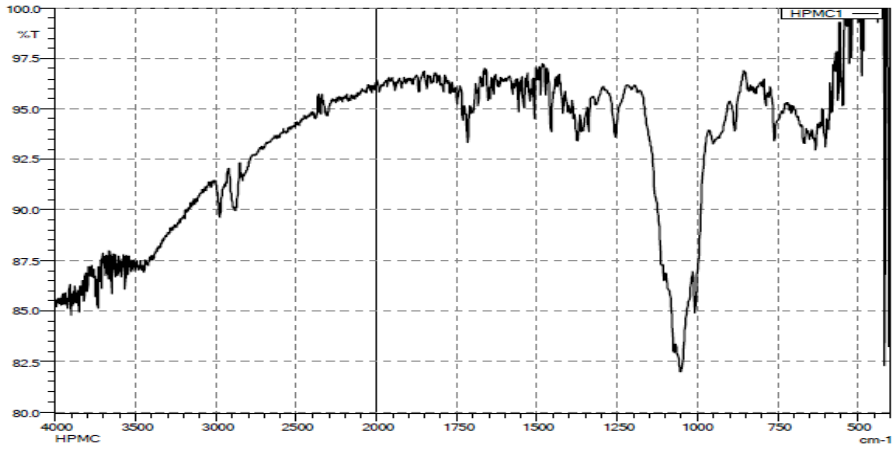

Figure 06: FT-IR of Losartan potassium + HPMC.

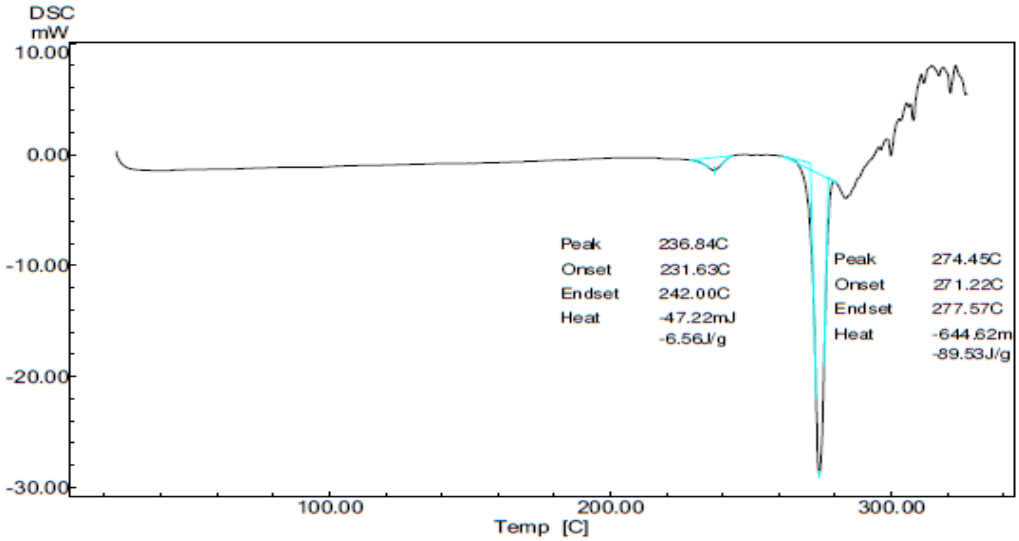

Figure 07: DSC thermograms of losartan potassium.

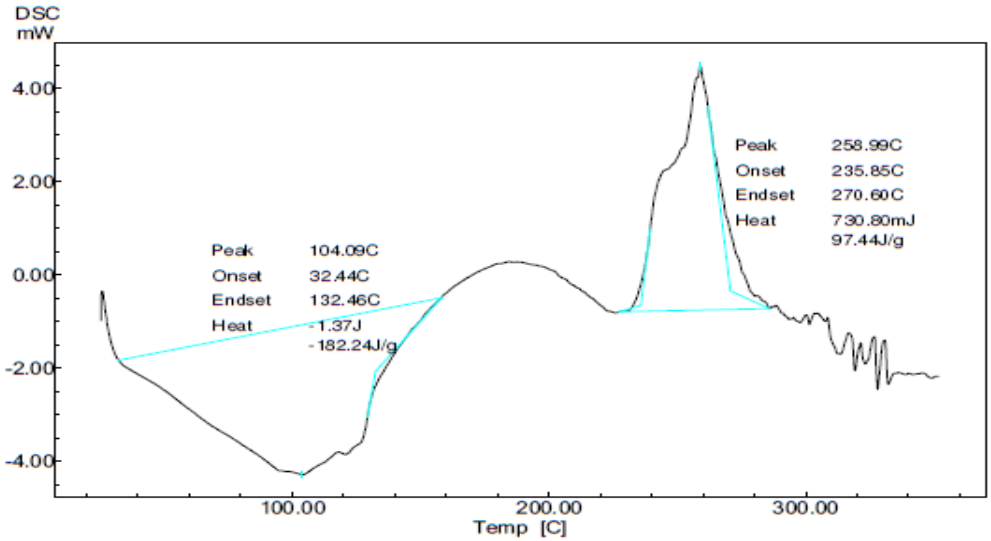

Figure 08: DSC thermograms of formulation F7.

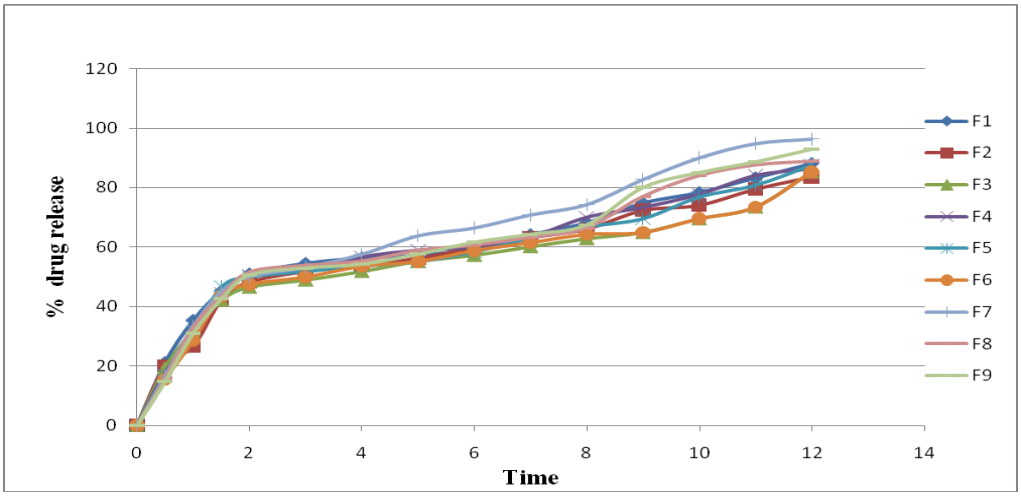

Figure 09: In-vitro drug release study of losartan potassium matrix tablet.

DISCUSSION

The sustained release matrix tablets of losartan potassium were prepared by direct compression method from polymers Gaur Gum, Ethyl cellulose and HPMC K4M.

The outcome of granules evaluation counseled that all the organized granules exhibited appropriate and first rate go with the flow properties, because the angles of repose values had been less or same to 30^0 an amazing packing potential of the granules changed into indicated by way of Carr's index and Hauser's ratio. The burden, thickness and drug contents of all drugs had been discovered to be shape with their low general deviation values. The hardness become in the variety of 5.4 to 6.8 kg/cm^2 and friability changed into within the variety of 0.2 to 0.4% and drug content material turned into in the range of 98.02% to 99.52%.

FTIR Spectroscopy of Pure drug losartan potassium has exhibited IR spectrum indicating the presence of O-H group and NH_2 group at 3300-3100cm^{-1}, Cl group at 750cm^{-1}. In the infrared spectra of drugs and various polymers obtained, there is no interaction between drug and polymers. Functional drug groups have been detected in both spectra of the infrared combination of drug also polymers. There bands confirm the structure of losartan potassium the similar peaks with the little alteration were observed in the septum mixture of the drug and other polymers. Figure no-03, 04, 05 and 06.

The thermal behavior of the matrix tablet was studied using DSC in order confirm the formulation solid inclusion. The DSC thermogram of losartan potassium shows an endothermic peak at 274.45^0c and corresponding to melting point. The characteristics endothermic peak at 236.84^0c disappears in the thermogram of F7 matrix formulation and shows 258.99^0c indicate the uniform dispersion the drug in the amorphous form in tablet. Figure no-07 and 08.

Stability studies were carried out at 40^0c /75 % RH for the selected formulation for the period of 3 months there was slightly acceptable changes was observed in physical and chemical parameter and slightly acceptable changes in drug release. F7 formulation was showed 99.45%, 99.42% and 99.40% up to 24 hrs in 1 month, 2 month, and 3 month respectively. Result was concluded F7 formulation was stable under specific temperature and humidity condition.

The dissolution profiles of losartan potassium are given in figure no 09; data are presented in above figure shows results of in-vitro drug release. 88.14%, 83.58%, 85.31%, 86.27%, 87.54%, 85.31%, 96.26%, 88.83% and 92.83% a drug was released from F1, F2, F3, F4, F5, F6, F7, F8, and F9 formulations respectively at the end of 12 hour, whereas results shows sustained drug released at the extended period of time.

CONCLUSION

A losartan potassium matrix tablet was prepared by the method of direct compression method using Guar Gum, Ethyl cellulose and HPMC K4M in different concentration. According to work plan, the tablets were evaluated for their hardness, thickness, weight variation, friability, drug content and in vitro release and drug excipients interactions. Among all the nine formulations, F7 formulation is optimized due to its good strength and capability to sustained release of the drug from the matrix over 12 hrs duration. The current study showed that the losartan potassium matrix tablets formulated using HMPC K4M showed promising prolong release of the drug compared to that of the formulation prepared by other formulation. However further studies are required to interpretative the effect of HPMC K4M in the improvement of the drug release in sustained or controlled manner

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