

Formulation And Evaluation Of Preformulation Studies And Precompressional Parameters Of Anti Hypertensive Drug Losartan Potassium By Using Locust Bean Gum As Superdisintegrant

Kehar Singh^{*1}, Dr. Gaikwad Dushyant Dadabhau², Satbir Singh³

^{1*,3} Research Scholar, Department of Pharmaceutics, Sunrise University, Alwar, Rajasthan India. ² Professor, Department of Pharmaceutical Science, Sunrise University, Alwar, Rajasthan India.

***Corresponding Author:** Kehar Singh

*Research Scholar, Department of Pharmaceutics, Sunrise University, Alwar, Rajasthan India.

Email- keharpharma88@gmail.com, Contact No. 9896304553

ABSTRACT

Fast dissolving drug delivery systems offers a solution for those patients having difficulty in swallowing tablets/capsules etc. Fast dissolving tablets disintegrate instantaneously in the mouth so that they can be swallowed without the aid of water. The aim of the present study was to investigate pre formulation studies of drug losartan potassium using locust bean gum as a natural super disintegrant. Perform pre formulation studies like partition coefficient, solubility and identification of drug. The influence of precompressional parameters like angle of repose, swelling index and micromeritic properties on formulation of a tablet along with melting point, drug characterization like organoleptic properties, interaction studies and compatibility

Material and methods: Losartan potassium was received as gift sample from Elfin drug pvt ltd baddi, nalagarh (Himachal Pradesh). Locust bean gum was purchased from Lucid colloids, Mumbai. Microcrystalline cellulose (avice1102), aspartame and magnesium stearate was received as gift sample from helios pharmaceutical pvt. ltd. baddi (H.P). Menthol was purchased from Yarrow Chem. Mumbai (Maharashtra) and talc was purchased from Qualichems Fines Chemicals ltd New Delhi.

Result: The results suggested that locust bean gum in 7.5% concentration possess excellent super disintegrant property and resulted in fast dissolving tablets. Swelling index was found to be 22 which indicated appreciable capability of locust bean gum to be used as super disintegrant. IR spectra and DSC study showed that there was no any kind of interaction with formulation additives of the tablets.

Conclusion: Based on the pre formulation studies locust bean gum show a super disintegrant properties and it is clear that we can formulate fast dissolving antihypertensive tablet with losartan potassium by using locust bean gum as superdisintegrant.

Key words: Super disintegrant, preformulation, fast dissolving tablets (FDTs), locust bean gum, losartan potassium.

INTRODUCTION

The tablet is the most popular dosage form right now because of how easy it is to manufacture, how small it is, and how easy it is for patients to self-administer. However, some patients have problems swallowing, tremors in their hands, dysphasia in their older patients, and underdeveloped muscles and nervous systems in younger patients, so they don't take their medication as prescribed.

The inability to swallow, or dysphagia, affects people of all ages. Approximately 35% of the population, 30% to 40% of elderly patients in nursing homes, and 18% to 22% of all residents in long-term care facilities experience difficulty swallowing. Low therapy costs, convenience of administration, correct dose, self-medication, pain avoidance, variety, and high patient compliance continue to make the oral route the optimum means to provide therapeutic substances. On the other hand, a novel drug delivery system that incorporates an existing medicine can greatly enhance the drug's effectiveness, safety, and patient compliance."¹

The size, form, surface, and flavor of tablets are among the most frequently reported factors contributing to the difficulty ingesting pills. The patients who require easy-to-swallow dose forms the most include those who are elderly or young, as well as those who are traveling and might not always have access to water.² According to a literature review, these issues affect 50% of people. The urgent need for a novel dose form that can increase patient compliance is emphasized

by these research.³ A wide range of pharmaceutical research has been carried out in the last several decades in an effort to create novel dosage formulations. New developments in new drug delivery systems (NDDS) seek to improve patient compliance while creating a convenient dose form that will increase drug molecule safety and efficacy. The simplicity of medicine has been the main focus of these initiatives. The most popular product among the different dosage forms created to enhance administration convenience is the fast-dissolving tablet.⁴ for patients who prefer the ease of conveniently taken dose forms, especially Those in the paediatric and geriatric population, solid dosage forms that can be dissolved or suspended with water in the mouth are very preferred.”³

FAST DISSOLVING TABLETS

As an alternative to traditional oral dose forms, fast dissolving tablets (FDTs) and orally disintegrating tablets (ODTs) have gained popularity. Modern medicine has developed new types of medicines that break down in the mouth within seconds. A growing number of academics and businesspeople are realizing FDTs' value. A recent use of the term "orodispersible tablet" by the European Pharmacopoeia serves to emphasize their growing importance. Subsequent to three minutes, the ODTs ought to dissolve or scatter in accordance with the European Pharmacopoeia.⁵ Orally disintegrating tablet guidelines were first proposed in April 2007 by the Food and Drug Administration. Quickly dissolving in the mouth and having an in vitro disintegration time of 30 seconds or less are the criteria for oral disintegrants that meet the USP disintegration test technique or an equivalent.”⁶

Advantages of Fast Dissolving Tablets

1. Easy dosing for patients with swallowing difficulties, such as the elderly, those who have suffered a stroke, those who are bedridden, those with renal failure, and those in pediatric, geriatric, or mental health care who refuse to swallow.
2. The dose form can be swallowed without water, which is a very practical feature for patients who are on the go and do not always have access to water.
3. The medication will dissolve and absorb quickly, resulting in a quick start of action.
4. When saliva travels down into the stomach, certain medications are absorbed from the mouth, throat, and esophagus. In these circumstances, a drug's bioavailability is greatly enhanced.”
5. A pleasant mouth feel can assist patients, especially younger ones, stop viewing medications as bitter pills.
6. Because there is no physical obstruction during oral delivery of the standard formulation, there is less chance of choking or asphyxia, improving safety.⁷

Limitations of fast dissolving tablets

1. The mechanical strength of the tablets is typically inadequate. Therefore, handling must be done with caution.
2. If the tablets are not formed correctly, they may leave an unpleasant taste and/or grittiness in the mouth. ⁸

Desired characteristics for formulating fast dissolving tablets

1. It should dissolve, scatter, or disintegrate in the mouth in a couple of seconds without the need for water when taken orally.
2. The parent component must be stable, soluble, and quick to penetrate the mucosal barrier, dissolving quickly enough to allow for a long enough contact time at the administration site.
3. Adding excipients with hydrophilicity.
4. Capable of quickly absorbing water to cause the matrix to disintegrate quickly.
5. The tablet needs to be very porous.
6. After ingestion, there should be little to no residual in the mouth.
7. Have a taste that is appropriate. If there is an unpleasant taste that can be covered up with the right taste masking techniques
8. It should feel good in the mouth.
9. Need to be more robust and less pliable. Must demonstrate minimal susceptibility to external factors such as humidity and temperature. ⁹

MATERIAL AND METHODS

MATERIAL USED FOR FORMULATION

All the materials used in the formulation and evaluation are listed below: (Distilled water was used in the present study) Losartan potassium was received as gift sample from Elfin drug pvt ltd baddi, nalagarh (Himachal Pradesh). Locust bean gum was purchased from Lucid colloids, Mumbai. Microcrystalline cellulose (avice1102), aspartame and magnesium stearate was received as gift sample from helios pharmaceutical pvt. ltd. baddi (H.P). Menthol was purchased from Yarrow Chem. Mumbai (Maharashtra) and talc was purchased from Qualichems Fines Chemicals ltd New Delhi.

IDENTIFICATION OF DRUG

Physical appearance

Physical appearance of drug was examined by various organoleptic properties:

Table 1: Organoleptic characters of Losartan Potassium

Color	White crystal powder.
Taste	Slightly Bitter
State	Fine to crystalline powder

Melting Point

Melting point of losartan potassium was determined by Capillary fusion method; one sided capillary filled with drug and put in to the Melting point apparatus. Temperature was noted at which solid drug convert in to liquid.

Ultraviolet absorption

Ultraviolet absorption in the range 200 nm to 450 nm of a 10 μ g/ml solution in methanol was determined.

I.R spectra determination

IR (KBr) cm^{-1} of pure drug losartan potassium exhibited characteristics absorption bands Interpreted with reference standard of losartan potassium.

Partition Coefficient

The partition coefficient of losartan potassium was determined in n-octanol and double distilled water. Mixture saturated for a period of 24 h. 20 mg of losartan potassium was added to the mixture and was agitated for 1 h. These two layers were separated using separating funnel. Water phase was suitably diluted and absorbance was measured at 209 nm. The partition coefficient of losartan potassium was calculated as ratio of concentration of losartan potassium in n-octanol to that in the aqueous phase using following equation:

$$P_{O/W} = \frac{C_{org}}{C_{water}} \text{ equilibrium}$$

(Initial conc. – conc. in aqueous phase)

Solubility studies

An excess quantity of losartan potassium was added to 10 ml of different solvents like distilled water (pH 7.0) water and phosphate buffer of pH 6.8 in a shaking water bath at room temperature for 24 hrs. The solutions were then filtered through whatman filter paper (No. 41) and the filtrate was suitably diluted and analyzed using UV-visible spectrophotometer at 209 nm wavelength.

QUANTITATIVE ESTIMATION OF DRUG

In present study, a UV Spectrophotometric method is selected for the estimation of the drug because the method was simple, economic and gave reproducible results in the acceptable limits. The double beam UV spectrophotometer (UV-1800, Shimadzu) was used for the analysis.

Preparation of buffer ¹ Phosphate buffer (pH 6.8)

Phosphate buffer of pH 6.8 was prepared by dissolving 28.8gm disodium hydrogen orthophosphate and 11.45gm potassium dihydrogen orthophosphate in 1000 ml volumetric flasks and the pH was adjusted with the help of 0.1N HCl and 0.1N NaHCO₃ solution and volume was made up to 1000ml with distilled water.

Preparation of standard plot of Losartan potassium 1. Preparation of stock solution (stock solution I)

100 mg of losartan potassium was accurately weighed and transferred into a 100 ml volumetric flask and dissolved in phosphate buffer (pH 6.8). The volume was made up to 100 ml. This gives the standard stock solution of 1 mg/ml concentration.

2. Spectrophotometric scanning of losartan potassium in phosphate buffer (pH 6.8)

From the standard stock solution prepared in phosphate buffer (pH 6.8) one ml solution was pipetted out and volume was made up to 10 ml in a 10 ml volumetric flask and U.V. scan was taken between wavelength of 200-400 nm. The blank used here was phosphate buffer.

3. Preparation of calibration curve

From the standard stock solution of losartan potassium (**stock solution I**), 1ml was pipetted out and volume was made up to 100 ml in a 100 ml volumetric flask (**stock solution II**) From the stock solution II, aliquots of 0.1 ml, 0.2 ml, 0.3 ml,..... 1.0 ml pipetted out into 10 ml volumetric flask and volume was made up to 10 ml with phosphate buffer (pH 6.8). The absorbance of these dilutions was measured at 209 nm using UV spectrophotometer (Shimadzu, UV- 1800) against phosphate buffer as reference. The calibration curve was plotted between concentration and absorbance on X and Y axis respectively.

VALIDATION OF ANALYTICAL METHODS AND PROCEDURES (USP) ²

The USP has published specific guidelines for method validation for compound evaluation. USP defines six steps for validation. 1. Accuracy

2. Precision

3. Limit of Detection (LOD)

4. Limit of Quantitation (LOQ)

5. Linearity

6. Range

1. Accuracy

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. This is sometimes termed trueness.

2. Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels: repeatability, intermediate precision and reproducibility. The amount of drug was estimated by measuring the absorbance and by fitting these values to the straight-line equation of calibration curve.

3. Limit of Detection (LOD)

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

The limit of detection is the point at which a measured value is larger than the uncertainty associated with it. The limit of detection is frequently confused with the sensitivity of the method. The sensitivity of an analytical method is the capability of the method to discriminate small differences in concentration or mass of the test analyte. In practical terms, sensitivity is the slope of the calibration curve that is obtained by plotting the response against the analyte concentration or mass.

The Limit of detection (LOD) may be expressed as:

$$\text{LOD} = \frac{3.3 \sigma}{S}$$

Where σ = the standard deviation of the response
S = the slope of the calibration curve

Based on the Standard Deviation of the Blank

Measurement of the magnitude of analytical background response is performed by analyzing an appropriate number of blank samples and calculating the standard deviation of these responses.

4. Limit of Quantitation (LOQ)

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. The quantitation limit is a parameter of quantitative assays for low levels of compounds in sample matrices, and is used particularly for the determination of impurities and/or degradation products.

The Limit of quantitation (LOQ) may be expressed as:

$$= \frac{10 \sigma \text{ LOQ}}{S}$$

Where σ = the standard deviation of the response, S = the slope of the calibration curve

The slope S may be estimated from the calibration curve of the analyte. The estimate of σ may be carried out in a variety of ways including:

Based on Standard Deviation of the Blank

Measurement of the magnitude of analytical background response is performed by analyzing an appropriate number of blank samples and calculating the standard deviation of these responses. LOQ: $10 \sigma / S$

5. Linearity

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample.

6. Range

The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.

DRUG POLYMER INTERACTION STUDY

In the preparation of tablet formulation drug and polymer may interact as they are in close contact with each other, which could lead to the instability of drug. Therefore drug polymer interaction studies are very critical in selecting appropriate polymers. For the present study, the drug- superdisintegrants interaction studies were conducted by comparing it with the pure drug and physical mixture of drug-polymer and formulation by FTIR and DSC.

EVALUATION OF LOSARTAN POTASSIUM DRUG AND EXCIPIENTS Precompressional Parameters/ Micromeritic properties Angle of repose (θ)³

Angle of repose of losartan potassium and tablet blends was determined using fixed funnel method. The physical mixtures of drug with different excipients were prepared and the accurately weighed. A funnel was held in plane with a clamp on a ring spot over a plate. A fixed amount of powder was transfer in to the funnel, keeping the orifice of the funnel blocked by the funnel. As the thumb is removed the powder is emptied from the funnel.

The height (h) and diameter of the powder cone was measured and angle of repose was calculated by following formula:

$$\text{Angle of repose } (\theta) = \tan^{-1} (h/r)$$

Where, h = the height of powder cone and r = the radius of powder cone

Apparent bulk density and tapped density ⁴

Apparent bulk density and tapped density of losartan potassium and tablet blends were determined using bulk density apparatus. A weighed amount of drug or blend was poured into graduated cylinder and the volume (V_o) was noted. Then the graduated cylinder was fixed on the density apparatus and timer knob set for 100 tapping. The tapped volume was measured to nearest graduated unit. The bulk density and tapped density were calculated by following formula: Bulk Density = W/V_o Tapped density = W/V_f

W= weight of the powder

V_o = Initial volume of the powder

V_f = Final volume of the powder

Compressibility index (Carr's index) ⁵

Based on the apparent bulk density and the tapped density, the percentage compressibility of the powder mixture was determined by the following formula:

Tapped density - Bulk density

Compressibility index = $\times 100$

Tapped density

Hausner's ratio

Hausner ratio is an indirect index of ease of measuring the powder flow. It is calculated by the following formula:

Tapped density

Hausner's ratio =

Bulk density

Swelling Index of gum

Swelling index (B.P. Vol. II, 1988) is the volume in millilitres that is occupied by 1 gm of drug or any adhering mucilage after it has swollen in an aqueous liquid for 4 hours. The method of studying swelling index for locust bean gum was carried out as per BP specifications. Swelling index was calculated from mean readings of three determinations: Initial volume

Swelling index =

RESULTS AND DISCUSSION IDENTIFICATION

OF DRUG Melting Point¹

Melting point of Losartan Potassium was determined by Capillary fusion method. It was found to be 264-268°C which is similar to the reported in literature 263-265°C.

Ultraviolet absorption²

The absorption maxima (λ max.) of losartan potassium solution (10 μ g/ml) were found to be 209 nm which is concordant with the literature shown in figure 1 and table 2.

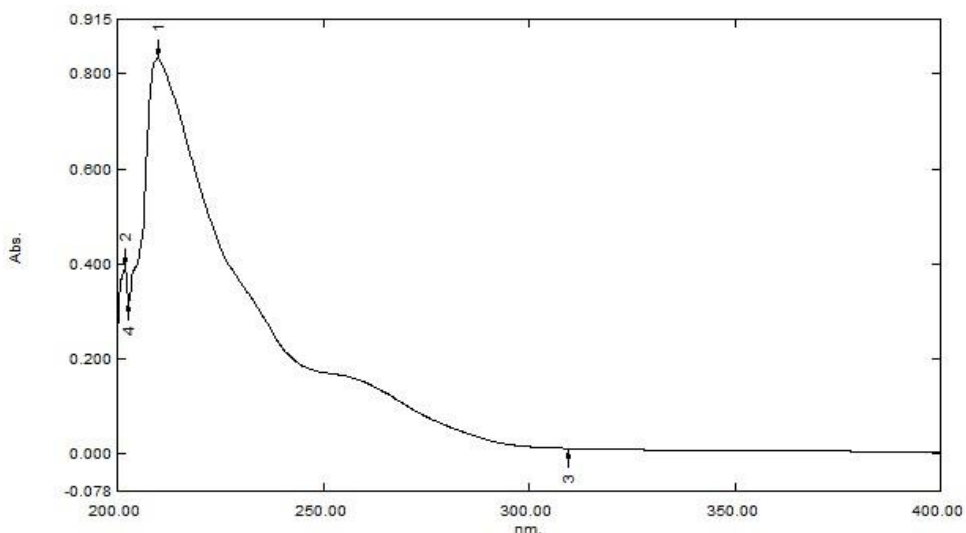


Fig.1 Spectrum of losartan Potassium in acid buffer pH 6.8

I.R. spectra determination

IR (KBr) cm^{-1} of pure drug losartan potassium exhibited characteristics absorption bands like 3197.63 (NH str.), 2928.53 (CH str., aliphatic), 1575.92 (Skeletal vibrations phenyl ring), 988.92 (Ring breathing mode, imidazole/ tetrazole), 759.62 (C-Cl str.).

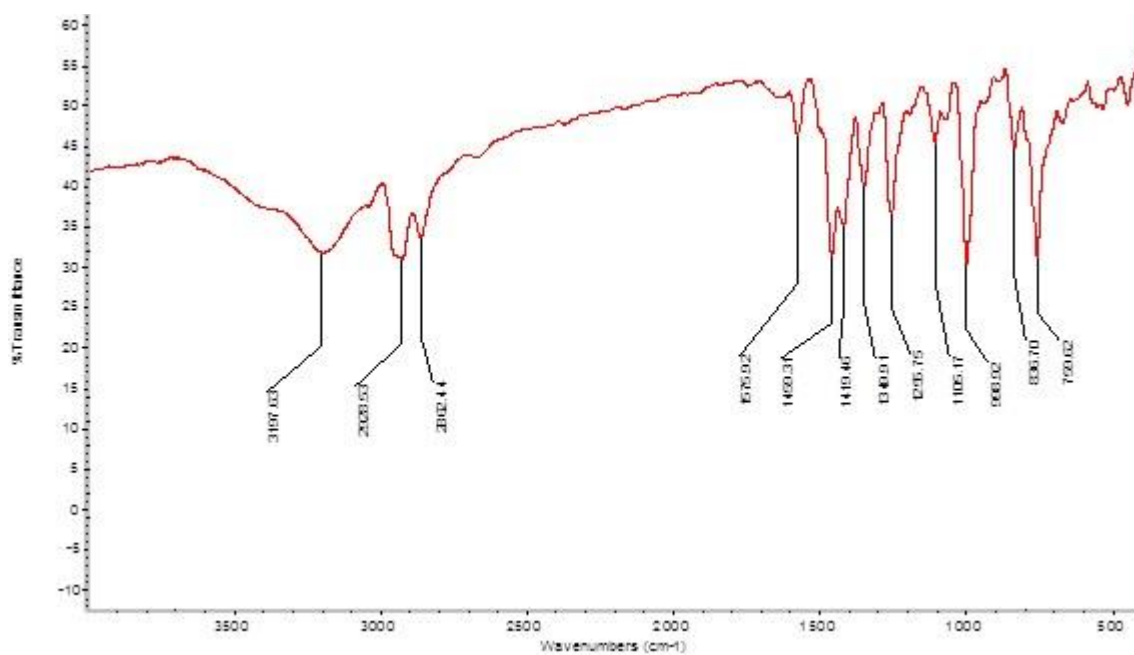


Fig.2 I.R. Spectra of losartan potassium

Partition Coefficient³⁻⁴

The partition coefficient of losartan potassium was calculated as ratio of concentration of losartan potassium in n- octanol to that in the aqueous phase and it was found 4.54 (shown in table 2).

Solubility studies⁵

The available literature on solubility profile losartan potassium indicated that the drug is very soluble in water, methanol, sparingly soluble in acetic acid and practically soluble in acetonitrile. The results of losartan potassium solubility in various media are shown in Table 2.

The study was carried out to select suitable dissolution medium for in-vitro release studies.

Table 2: Preformulation studies of losartan potassium

Studies	Identification* (UV)	Partition Coefficient	Solubility (gm/ml)*	
			Water	pH 6.8 (phosphate buffer)
Result	209	4.54		
Reported	209 & 210	4.5	1.230	1.289

*Average of 3 determinations

Scanning of losartan potassium in phosphate buffer pH 6.8

The absorption maximum (λ max.) of losartan potassium in pH 6.8 was found to be 209 nm. The results were shown in shown in figure 1 and table 2.

Preparation of standard plot of Losartan potassium

The calibration curve of losartan potassium was prepared in phosphate buffer (pH 6.8). The plot of different concentrations of losartan potassium versus absorbance was found to be linear in the concentration range of 0.1- 10 μ g/ml at 209nm. The absorbance at different concentrations was shown in table 7. The data of standard curve were linearity regressed. The slop and correlation coefficient values were found to be 0.096 and 0.997 respectively. The intercepts on Y-axis found to be 0.100. The calibration curve and regression data was shown in figure 3 and table 3.

Table: 3 Standard plot (calibration curve) for the estimation of Losartan Potassium in phosphate buffer (pH 6.8)

Sr. No	Concentration (μ g/ml)	Absorbance \pm S.D.*
1	1	0.107 \pm 0.011
2	2	0.214 \pm 0.008
3	3	0.326 \pm 0.007
4	4	0.433 \pm 0.012
5	5	0.533 \pm 0.007
6	6	0.623 \pm 0.009
7	7	0.728 \pm 0.002
8	8	0.800 \pm 0.010
9	9	0.893 \pm 0.008
10	10	0.984 \pm 0.013

*Average of three determinations

Table 4: Regression data of calibration curves

Sr. No.	Medium	Regression data		
		M	C	R
1	pH 6.8	0.096	0.031	0.997

m = slope, c = intercept, r = correlation co-efficient

The linear regression analysis was done on absorbance data points. A straight-line equation ($Y = mx + c$) was generated to facilitate the calculation of amount of drug. Absorbance = slope x concentration + Intercept

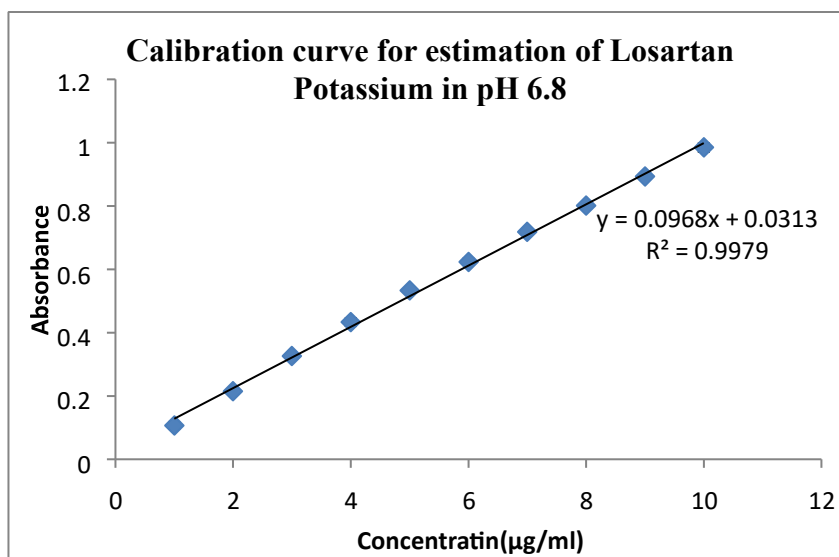


Fig. 3 Calibration curve of losartan Potassium

Table 5: Regression data of calibration curves

Validation Parameters	Phosphate buffer pH 6.8
Linearity Equation	$y = 0.096 + 0.031$
Linearity Range (b)	1-10 mcg/ml
Slope (m)	0.096
Intercept (C)	0.031
R ² Value	0.997
LOD, n=3	0.46 µg/ml
LOQ, n=3	1.40 µg/ml
Precision, n=3(%RSD)	10.49187
Accuracy, n=3	96.02%

DRUG POLYMER INTERACTION STUDY

As described in methodology section the FT-IR and DSC studies were carried out for pure drug alone and along with polymers.

FT-IR studies

FT-IR spectra of pure losartan potassium and polymer locust bean and physical mixture (drug + polymer) are shown in figure 12-14 and peaks are listed in table 10-11. The peaks given in table 10 matched with that of literature values for the functional groups present in losartan potassium. The peaks listed in the table 10 for pure drug under considered as characteristics peaks. The peak of the drug in presence of polymer were not affected and prominently observed in FT-IR spectra given in figures 12-14. This indicates that there is not any kind of interaction between losartan potassium and polymer and the drug was compatible with the formulation components.

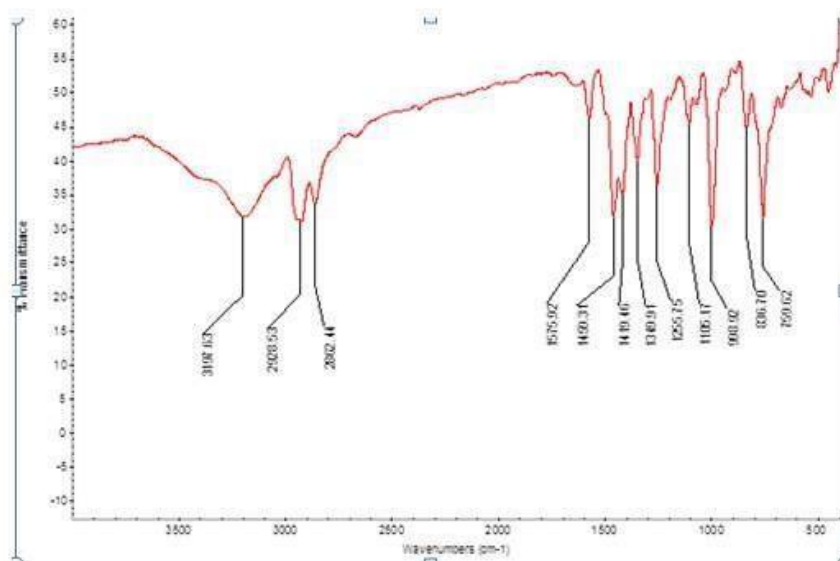


Fig. 4 IR spectra losartan potassium pure drug

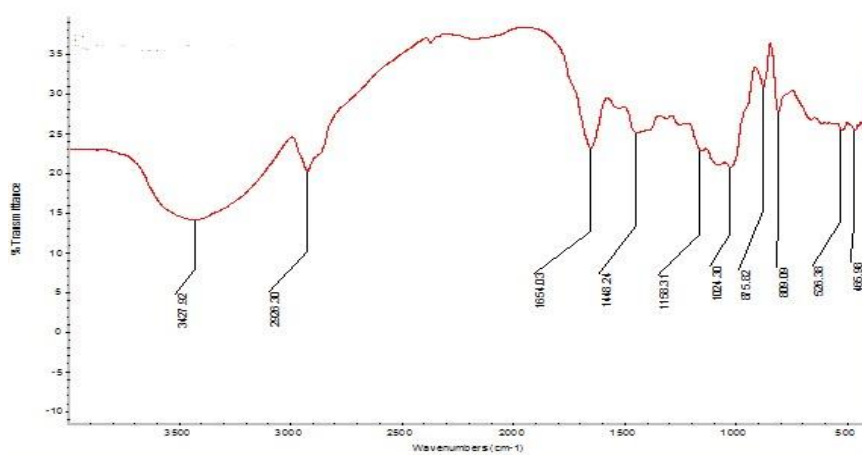


Fig. 5 IR spectra Locust bean gum pure polymer

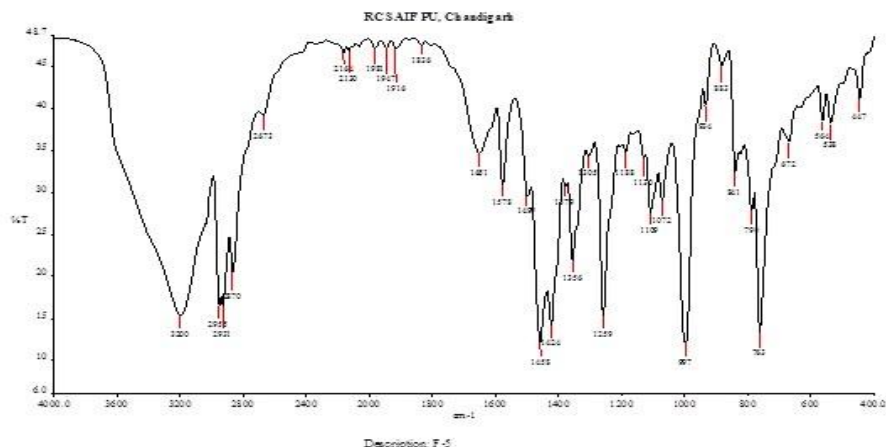


Table 6: IR spectra interpretation of Losartan Potassium (drug) and Locust bean gum (superdisintegrant) interaction study

Formulation Name	Functional group	Characteristics absorption peak cm^{-2}	Bond vibration Range
Losartan Potassium	NH (Stretching)	3197.63	3077-3497
	CH ₃ group C-H (bending)	1419.46,1459.31	1375-1450
	C-Cl (stretching)	759.62	550-850
	C-N(stretching)	1255.75	1020-1280
	C-C multiple bond(stretching)	1575.92	1510-1600
	CH aromatic hydrocarbon (stretching)	2928.53,2862.44	2800-3000
	Aromatic ring two adjacent H atom	836.70	855-910
Locust bean gum	O-H (stretching)	3427.92	3400-3700
	C-H (stretching) due to CH ₂ group	2926.30	2760-3000
	Galactose & mannose ring (stretching)	1654.03	1580-1650
	Deformation of CH ₂ &COH groups	1448.24	1440-1470
	CH ₂ OH(stretching)	1158.31	1100-1380
	CH ₂ twisting (vibration)	1024.30	900-1100

Table 7: IR spectra interpretation of physical mixture of drug+ gum interaction study (Losartan potassium + Locust bean gum)

Physical mixture	Functional group	Characteristics absorption peak cm^{-2}	Bond vibration range
(A)Due losartan potassium	NH (Stretching)	3200	3077-3497
	CH ₃ group C-H (bending)	1424,1458	1375-1450
	C-Cl (stretching)	763	550-850
	C-N(stretching)	1259	1020-1280
	C-C multiple bond(stretching)	1578	1510-1600
	CH aromatic hydrocarbon(stretching)	2955	2800-3000
	Aromatic ring two adjacent H atom	841	855-910
(B)Due to Locust bean gum	C-H (stretching) due to CH ₂ group	2931	2760-3000
	Galactose & mannose ring (stretching)	1651	1580-1650
	Deformation of CH ₂ &COH groups	1499	1440-1470
	CH ₂ OH(stretching)	1188	1100-1380
	CH ₂ twisting (vibration)	1072	900-1100

NH (Stretching)	3200	3077-3497
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DSC studies

DSC studies for pure losartan potassium, polymer locust bean and physical mixture (drug + polymer) were carried out. Thermo grams are shown in figure 15-17 for pure drug and polymer and physical mixture (drug + polymer) respectively. Figure 15 indicates that the melting point of losartan potassium has taken place at sharp at 273.79°C. It is matching with the literature value⁶ of losartan potassium 263-268°C. The thermogram indicates that the drug is pure. Figure 16 indicates that the melting of the polymer has taken place at 97.20°C. The comparative study of DSC thermogram revealed that there is no any appreciable change in the nature of the melting endotherms suggesting that the drug has not lost its characteristic properties even in its formulation form as there is no interaction of the drug with the polymer and other excipients used for the study.

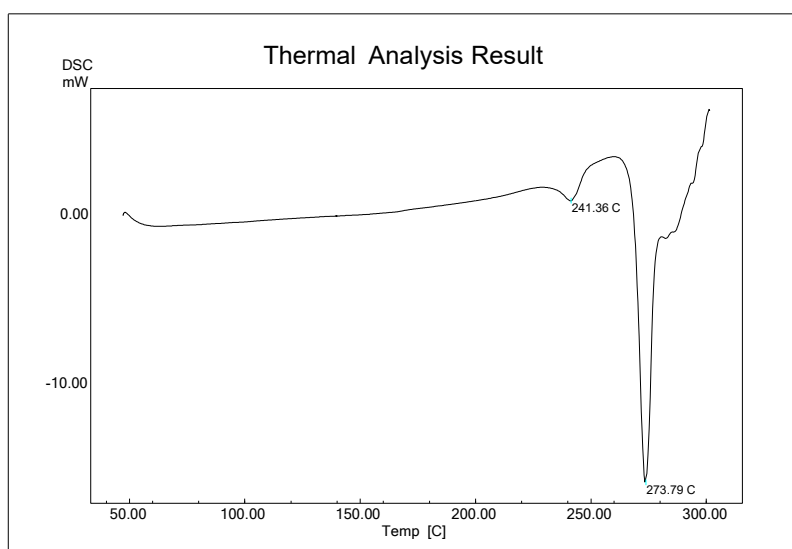


Fig.7 DSC thermogram of losartan potassium pure drug

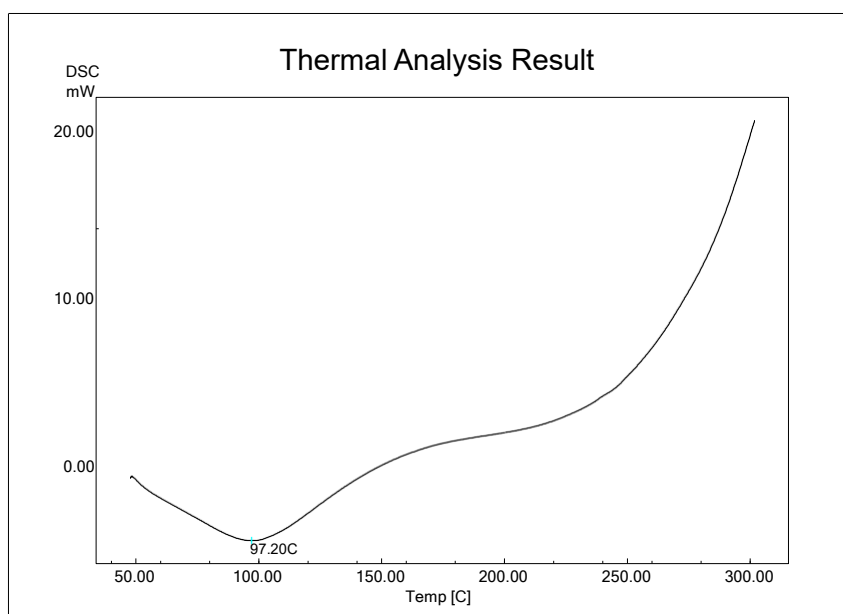


Fig.8 DSC thermogram of locust bean superdisintegrant

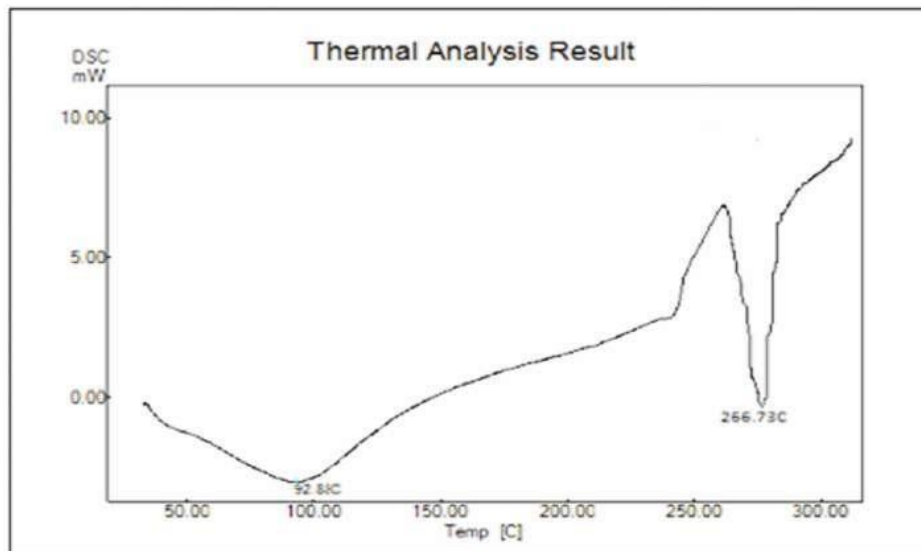


Fig. 9 DSC thermogram of physical mixture (drug+ superdisintegrant)

RESULTS OF PRECOMPRESSIONAL PARAMETERS MICROMERITICS PROPERTIES

Powder ready for compression containing drug and various excipients were evaluated for pre-compression parameters (Micromeritic properties) like flow properties of granules, bulk density and tapped density. The results of all the pre formulation parameters are given in table 9.

Angle of repose (θ)

Plain losartan potassium exhibited angle of repose value of (40.21 ± 0.16) indicating poor flow property. The data obtained from angle of repose after addition of magnesium stearate and talc as a lubricant for all the formulations were found to be in the range of $(25.08 \pm 0.61^\circ$ to $29.05 \pm 0.09^\circ)$. All the formulations prepared by direct compression method showed angle of repose less than 30 which reveals good flow property. The mean average of angle of repose results are tabulated in table 9.

Bulk density and Tapped density

Loose bulk density (LBD) and tapped bulk density (TBD) for the blend was measured. The loose bulk density for the entire formulation blend varied from $0.375 \pm 0.002 \text{ gm/cm}^3$ to $0.46 \pm 0.02 \text{ gm/cm}^3$ and tapped bulk density for the entire formulation blend varied from $0.41 \pm 0.001 \text{ gm/cm}^3$ to $0.53 \pm 0.02 \text{ gm/cm}^3$. The mean bulk density and tapped bulk density results are tabulated in table no. 9.

Carr's consolidation index Carr's index of plain losartan potassium exhibited 31.29 ± 0.14 indicating poor flow property. The results of Carr's consolidation index or compressibility index (%) after addition of magnesium stearate and talc, as a lubricant, for the entire formulation blend ranged from $6.00 \pm 1.07\%$ to $24.051 \pm 0.52\%$. The directly compressible granulations had shown excellent compressibility index values result in good flow properties after addition of lubricants. The mean Carr's index test results are tabulated in table no 9.

Hausner's ratio

Hausner's ratio of plain losartan potassium exhibited 1.42 ± 0.07 indicating poor flow property. Hausner's ratio of entire tablet blends was found between 1.06 ± 0.04 to 1.31 ± 0.01 . Lower Hausner's ratio (< 1.25) indicates better flow properties. All the blends show better flow properties. The mean Hausner's ratio test results are tabulated in table no 9.

Swelling Index of gum

Swelling index of locust bean gum exhibited in range of 21.32 ± 2.08 . This indicated appreciable capability of locust bean gum to be used as superdisintegrant. The mean swelling index results are tabulated in table no 8.

Table 8: Swelling index of locust bean gum

Swelling Index	
Locust bean gum	21.32 ± 2.08

Table 9: Micromeritic properties of precompressional powder blend

Z	Angle of repose (°)	Bulk Density	Tapped Density	Carr's Index (%)	Hausner's ratio
LP	40.21 ± 0.16	0.43 ± 0.01	0.82 ± 0.01	31.29 ± 0.14	1.42 ± 0.07
F1	25.08 ± 0.61	0.38 ± 0.002	0.52 ± 0.002	24.051 ± 0.52	1.31 ± 0.01
F2	30.38 ± 0.33	0.35 ± 0.002	0.41 ± 0.001	18.54 ± 0.18	1.24 ± 0.005
F3	26.40 ± 0.83	0.44 ± 0.02	0.53 ± 0.02	15.79 ± 2.88	1.17 ± 0.04
F4	26.19 ± 1.2	0.46 ± 0.02	0.49 ± 0.002	6.00 ± 1.07	1.06 ± 0.04
F5	26.39 ± 0.22	0.42 ± 0.005	0.49 ± 0.001	9.845 ± 1.14	1.17 ± 0.01
F6	29.05 ± 0.09	0.41 ± 0.02	0.51 ± 0.008	17.81 ± 1.69	1.29 ± 0.02

All values are expressed as mean LP (losartan potassium) \pm SD. n=3.

CONCLUSION

On the basis of pre formulation studies of losartan potassium and locust bean gum it can be concluded that all pre formulation parameters are found to be appropriate for formulation. All parameters like solubility, angle of repose, Carr's index, bulk density and tapped density was found ideal for preparation of fast dissolving tablet of losartan potassium. It is clear that we can formulate fast dissolving antihypertensive tablet with losartan potassium by using locust bean gum as super disintegrant.

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CONFLICT OF INTRESTS

Authors declare none of conflicts

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