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MOUTH DISSOLVING TABLETS OF LOSARTAN POTASSIUM: FORMULATION AND EVALUATION

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ABSTRACT

Losartan potassium is an angiotention receptor antagonist, used in the management of hypertension. The objective of the proposed research work is to prepare and evaluate the mouth dissolving/disintegrating tablets (MDTs) of losartan Potassium, which avoid the first-pass metabolism, improved the dissolution rate and enhance the bioavailability. Mouth dissolving tablets (MDTs) were prepared by direct compression method by using combination of superdisintegrant like Ac-Di-Sol and Polyplasdone-xl (1%,2%,3%&4%) and evaluated for physico-chemical evaluation parameter such as hardness, friability, weight variation, drug content uniformity, water absorption ratio, wetting time, *in-vitro* and *in-vivo* disintegration time, *in-vitro* dissolution studies. The control tablet (without superdisintegrant) was formulated and evaluated. The twelve formulations, B1to B8 were formulated and among these formulations, B8 was optimized. The hardness, friability, weight variation and drug content were found to be within pharmacopeias limits. The water absorption ratio, wetting time, *in-vitro* and *in-vivo* disintegration time of optimized formulation, B8 was found to be 86.1%, 8secs, 18secs and 25secs respectively. The formulation, B8 was considered to best formulation, which released up to 99.21% in 2 minutes. The comparison of dissolution rate profile of marketed formulation of Losartan potassium (Losacar) tablet with best formulation, B8 was conducted. The result showed that the formulation, B8showed complete drug release within 2 minutes and marketed formulation showed complete drug release in 5 minutes. The stability study was also conducted the best formulation, B8 and it indicates that there was no significant change in any parameters. Hence the formulation A4 was considered to be highly stable.

INTRODUCTION: The demand for mouth dissolving tablets has been growing over the other oral dosage forms (such as tablets, capsule, dry syrups, chewing gums/chewable tablets) among pediatric, geriatric, dysphasic, psychotic and non-cooperative patients and travelers. The main approach is to formulate mouth-dissolving tablets or mouth-disintegrating tablets which are dissolves rapidly in saliva without the need of water within few seconds due to the action of superdisintegrant in the formulations.

Hence, the basic approach used in development of mouth dissolving tablets is the use of superdisintegrant, which provide instantaneous disintegration of tablets after putting on tongue, thereby releasing the drug in saliva.

In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form [1]. To design rapidly disintegrating oral tablets of Losartan potassium for pediatric patients and elderly patients, in order to improve bioavailability, ease of administration and patient compliance. Losartan potassium indicated for hypertension, diabetic nephropathy and heart attacks disorders [2 & 3].

The bioavailability of Losartan is 33% due to extensively first pass metabolism [4, 5 & 6]. The terminal $t_{1/2}$ of losartan is 2 hours. Various techniques can be used to formulate rapidly disintegrating or dissolving tablets [7].

The objective of the proposed research work is to prepare and evaluate the mouth dissolving/ disintegrating tablets (MDT) of losartan Potassium, which avoid the first-pass metabolism and enhance the bioavailability.

MATERIALS AND METHODS: Losartan potassium was obtained as gift sample from Dr. Reddy's Laboratories, Hyderabad, Ac-Di-sol& Primogel was obtained from Colorcon Asia Pvt. Ltd. Goa, Polyplasdone-xl was obtained from Merck chemicals Ltd.,Mumbai, Sodium saccharine, Mannitol, Micro crystalline cellulose, Talc and Magnesium stearate were obtained from S.D. Fine Chemicals. Pvt Ltd, Mumbai, India. All chemicals and solvents used were of analytical grade.

Formulation of control tablet: (without use of superdisintegrant): Losartan Potassium control tablet (without using superdisintegrant) were prepared by the direct compression method using different excipients. The excipients used were Micro crystalline cellulose, Mannitol, saccharine sodium, talc and magnesium stearate. Compositions of formulation are shown in Table 01. All the ingredients of the control tablet of Losartan Potassium were weighed and mixed in mortar with the help of pestle. Then the blended material was slightly compressed on the 8mm flat–biconvex punch using a Rimek MINI PRESS-I MT tablet machine (Karnawati Engg. Ltd. Mehsana, India). The total weight of the formulation was maintained 200mg.

TABLE 1: FORMULATION OF CONTROL TABLETS: (WITHOUT USING SUPERDISINTEGRANTS)

Name of ingredients	Quantity (in mg)
Losartan potassium	25.0
Mannitol	105.0
MCC	62.0
Sod. Saccharin	2.0
Flavours	2.0
Magnesium stearate	2.0
Talc	2.0
Total	200

Formulation of Mouth Dissolving Tablets: (Combination of Superdisintegrant): Losartan Potassium mouth dissolving tablets were prepared by the direct compression method using different excipients. The excipients used were Micro crystalline cellulose, Mannitol, saccharine sodium, Ac-Di-Sol and Polyplasdone-xl (1%, 2%, 3%, and 4% superdisintegrant). Compositions of various formulations are shown in **Table 2**. All the ingredients of the mouth dissolving tablets of Losartan Potassium were weighed and mixed in mortar with the help of pestle. Then the blended material was slightly compressed on the 8mm flat–biconvex punch using a Rimek MINI PRESS-I MT tablet machine (Karnawati Engg. Ltd.,Mehsana, India). The total weight of the formulation was maintained 200mg.

TABLE 2: FORMULATION OF MOUTH DISSOLVING TABLETS: (COMBINATION OF SUPERDISINTEGRANTS)

Nameof ingredients	Quantity (in mg)							
	B1	B2	B3	B4	B5	B6	B7	B8
Losartan potassium	25	25	25	25	25	25	25	25
Ac-Di-Sol	**2**	**2**	**2**	**2**	2	4	6	8
Polyplasdone	2	4	6	8	**2**	**2**	**2**	**2**
Sodium Saccharin	2	2	2	2	2	2	2	2
Flavours	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2
Mannitol	105	105	105	105	105	105	105	105
MCC	58	56	54	52	58	56	54	52
Total	200	200	200	200	200	200	200	200

Drug-Excipients Compatibility Study: Compatibilities among the Drug-Excipients can be confirmed by carrying out infrared light absorption scanning spectroscopy (IR) studies. Infra red spectra of pure drug and mixture of formulations were recorded by dispersion of drug and mixture of formulations in suitable solvent (KBr) using Fourier Transform Infrared Spectrophotometer (FTIR). A base line correction was made using dried potassium bromide and then the spectra of the dried mixture of drug, formulation mixture and potassium bromide were recorded .The FTIR studies were conducted at Bright Laboratories, Hyderabad. The results are presented in **Figures 1 to 5**.

Preformulation studies:

Physicochemical Characterization of the Drug

Flow properties:

- **Angle of Repose:** A funnel with 10 mm inner diameter of stem was fixed at a height of 2 cm over the platform. About 2gm of drug was slowly passed along the wall of funnel until the tip of the pile formed touches the stem of the funnel. A rough circle was drawn around the pile base and the radius of powder cone was measured. Angle of repose was calculated from three averages using following formula.

$\theta = \tan^{-1} h/r$

Where, θ= angle of repose, h = height of powder cone, r = radius of the powder cone

Density Measurement: Different types of density calculations were done to characterize the drug. Generally two types of densities are determined i.e. bulk density and tapped density..

- **Bulk Density:** Bulk density of the drug was determined by pouring gently 2gm of drug sample through a glass funnel into a 10 ml clean dry graduated measuring cylinder. The volumes occupied by the sample were recorded. Bulk density was calculated;

$$\text{Bulk density (g/ml)} = \frac{\text{Weight of Sample in gms}}{\text{Volume occupied by the Sample}}$$

- **Tapped density:** Tapped density of the drug was determined by pouring gently 5gm of sample through a glass funnel into a 10ml clean dry graduated measuring cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after tapping were recorded and tapped density was calculated.

$$\text{Tapped density (g/ml)} = \frac{\text{Weight of Sample in gms}}{\text{Volume occupied by the Sample}}$$

- **Percentage Compressibility:** It is also one of the simple methods to evaluate flow property of a powder by comparing the bulk density and tapped density. An useful empirical guide is given by Carr's compressibility.

$$\text{Carr's Index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

Evaluation of Mouth Dissolving Tablets of Losartan Potassium: The evaluations of physic-chemical parameters of Losartan Potassium mouth dissolving tablets were done as per standard procedures The following parameters were evaluated.

- **Hardness [9]:** The test was done as per the standard methods. The hardness of three randomly selected tablets from each formulation (B1 to B8) was determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet broke down into two parts completely and the reading on the scale was noted down in Kg/cm^2. The results are presented in Tables 06.

- **Thickness [9]:** The thickness of three randomly selected tablets from each formulation was determined in mm using a vernier caliper (Pico India). The average values were calculated. The results are presented in Table 06.

- **Uniformity of Weight [9]:** Weight variation test was done as per standard procedure. Ten tablets from each formulation (B1 to B8) were weighed using an electronic balance and the average weight was calculated. The results are shown in **Table 6**.

- **Friability [9]:** The friability of tablets using 10 tablets as a sample was measured using a Roche Friabilator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were taken out, dedusted and reweighted. The percentage friability was calculated from the loss in weight as given in equation below. The weight loss should not more than 1%.The results are shown in table 06.

$$\%\text{Friability} = \frac{\text{initial weight- final weight}}{\text{(initial weight)}} \times 100$$

Drug Content [9]: Ten randomly selected tablets from each formulation (B1 to B8) were finely powdered and powder equivalent to 4 mg of Losartan Potassium was accurately weighed and transferred to 100 ml volumetric flasks containing 50 ml of phosphate buffer(pH 6.8). The flasks were shaken to mix the contents thoroughly. The volume was made up to the mark with phosphate buffer pH 6.8 and filtered. One ml of the filtrate was suitably diluted and Losartan Potassium content was estimated at 235 nm using a double beam UV-visible spectrophotometer. This procedure was repeated thrice and the average value was calculated. The results are presented in Table 6.

Wetting Time [10]: The tablets wetting time was measured by a procedure modified from that reported by Bi et al. The tablet was placed at the centre of two layers of absorbent paper fitted into a dish .After the paper was thoroughly wetted with distilled water, excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch. The results are presented in Table 6.

Water absorption ratio [10]: A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighted. Water absorption ratio, R was determined using following equation.

$$R = 100 \times Wa - Wb/Wa$$

Where, Wa = Weight of tablets after water absorption; Wb = Weight of tablets before water absorption.

The results are presented in **Table 6**.

***In- vitro* Dispersion Time [10]:** Tablets were added to 10 ml Phosphate buffer solution, pH 6.8 at 37± .5ºC. Times required for complete dispersion of tablets were measured. The results are presented in Tables 06.

***In-vivo* Dispersion Time:** *In-vivo* dispersion time of tablets were checked in healthy human volunteers by putting tablets on tongue and required for complete dispersion of a tablets were recorded.

The results are presented in Table 6.

***In-vitro* Dissolution study [11]:** *In-vitro* drug release rate of Losartan Potassium mouth dissolving tablets were carried out using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus. The dissolution test was carried out using 900 ml of 6.8 pH phosphate buffer at 37± .5^{0}C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 3, 4, 5, 6, 7 and 8 min. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through Whattman filter paper No 40 and analyzed for Losartan Potassium after appropriate dilution by UV spectrophotometer at 235 nm. The percentage drug release was calculated using an equation obtained from the calibration curve. The results are presented in figures 07 to 08.The dissolution testing was carried out in triplicate.

Accelerated stability studies: The Accelerated stability studies for optimized formulation; B8 was conducted at 40ºC ±2ºC/75% ±5%RH as per ICH guidelines. The stability studies were conducted after 30 and 60 days. The results are presented in Table 08.

RESULTS AND DISCUSSIONS:

Drug-Excipients compatibility study: The IR spectrum of Losartan potassium and other excipients were determined and it was found that there were no any extra peaks were observed, which indicating that there was no interaction between drug and excipients. The results are shown in **Figures 1 to 5**.

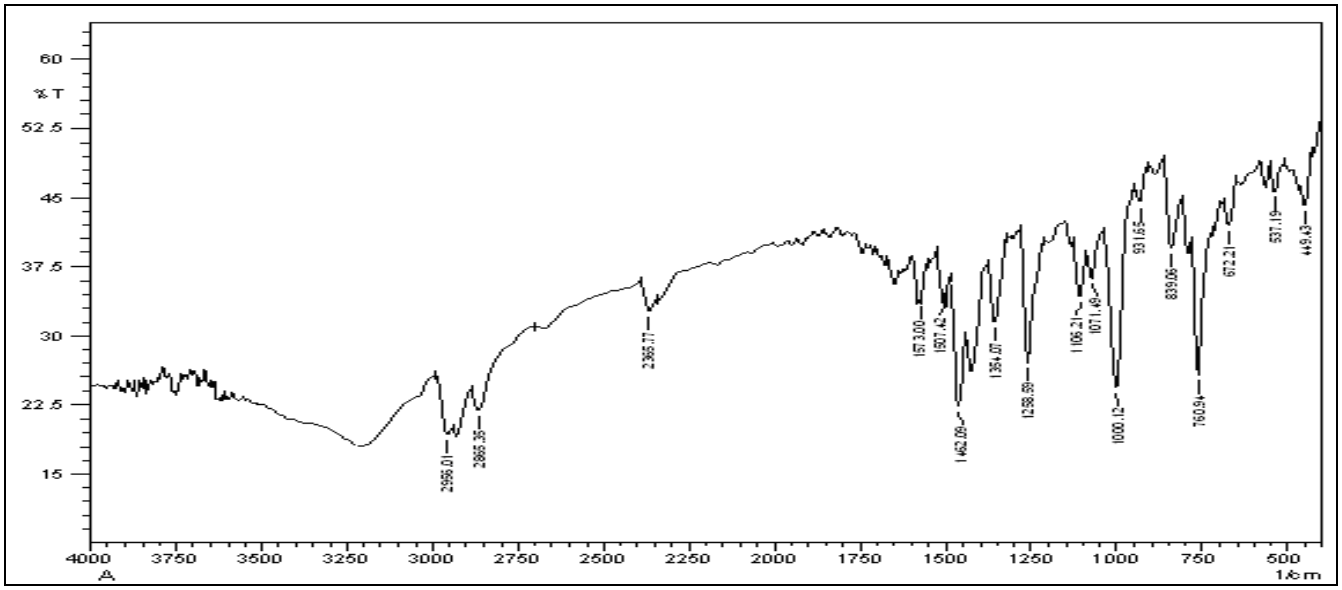

FIGURE 1: FT-IR -SPECTRUM OF LOSARTAN POTASSIUM DRUG

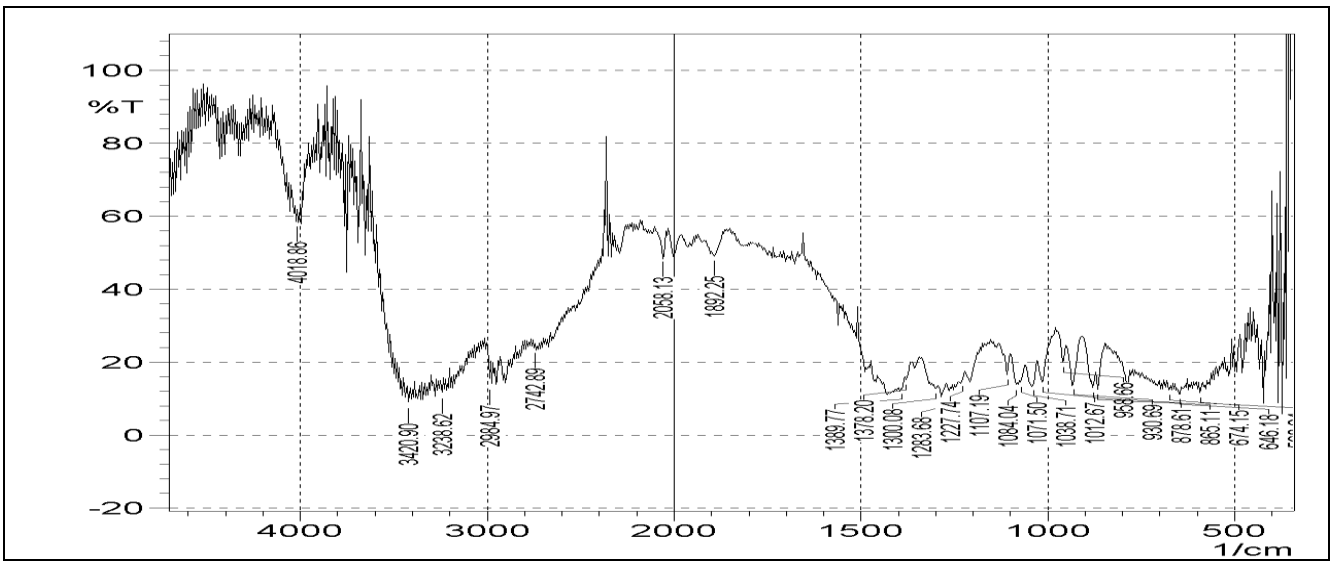

FIGURE 2 :FT-IR -SPECTRUM OF MANNITOL

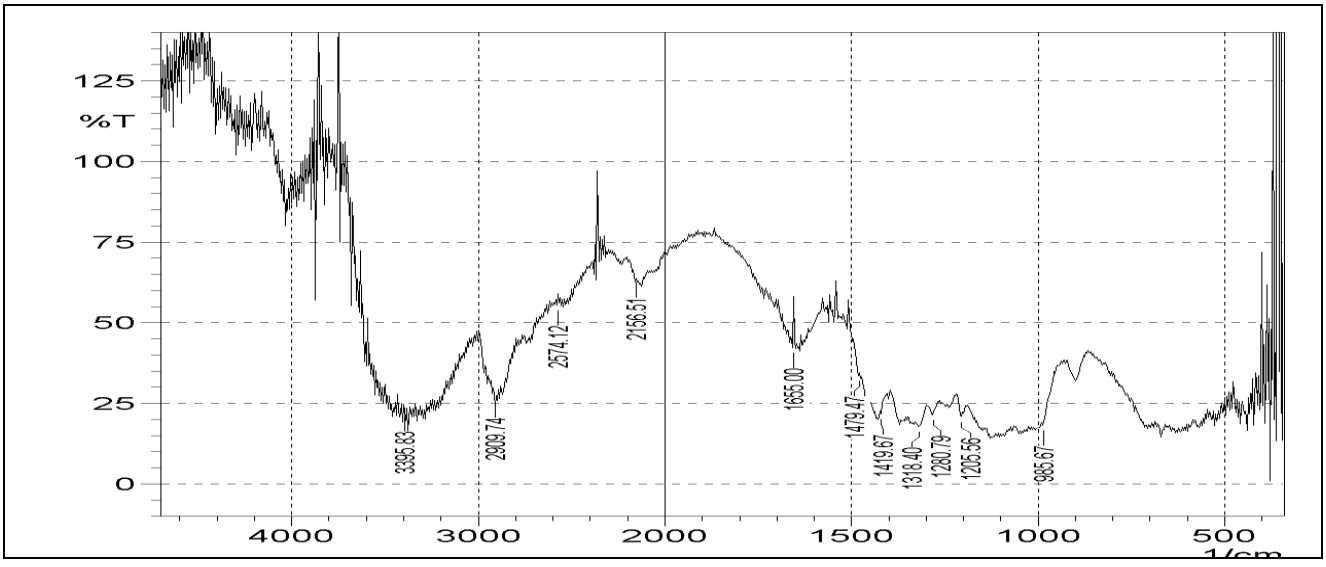

FIGURE 3: FT-IR -SPECTRUM OF MICROCRYSTALLINE CELLULOSE

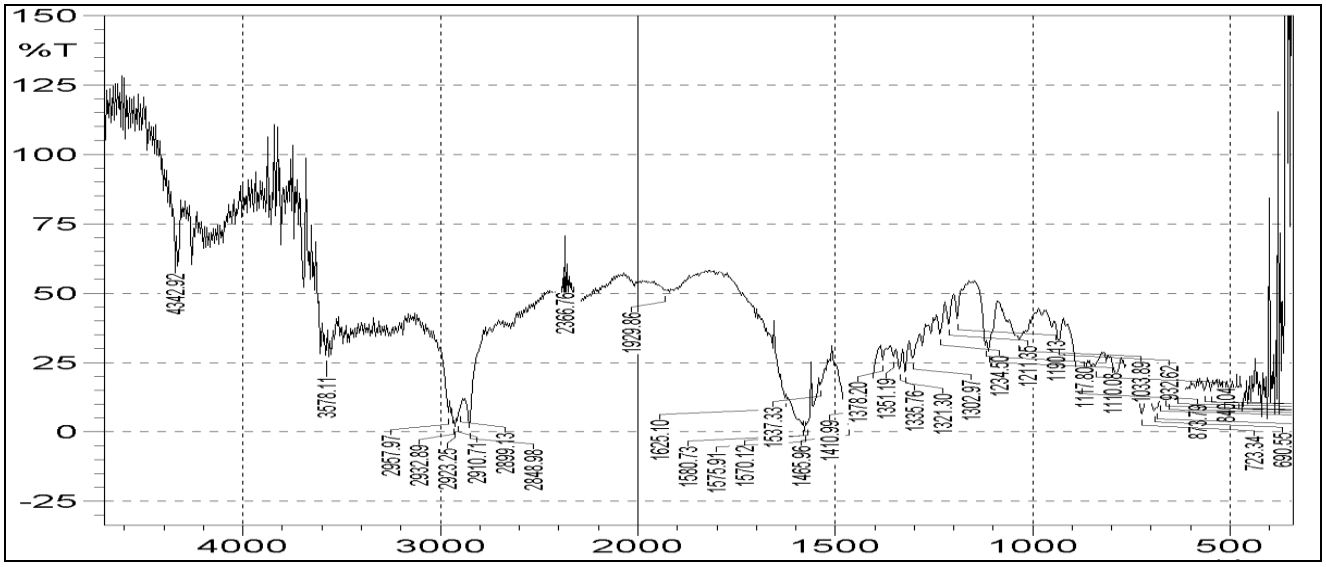

FIGURE 4: FT-IR -SPECTRUM OF MG.STEARATE

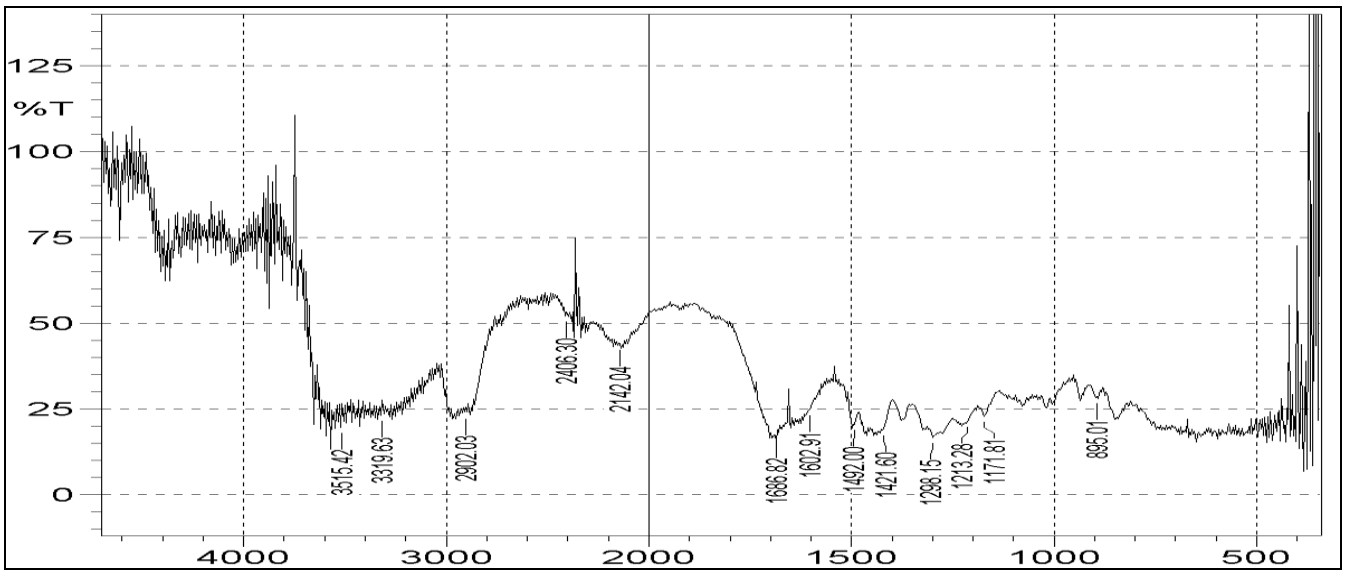

FIGURE 5: FT-IR -SPECTRUM OF AC-DI-SOL

Preformulation studies: In the Preformulation studies, blended powered drug were conducted for the angle of repose, bulk density, tapped density and Carr's index. From the results it indicated that in angle of repose was low, good compressibility and found excellent in flowability. It has also showed less porosity than powders containing superdisintegrant. The porosity of gets altered by the number of contact points and by the shape and diameter of constituent particles. As tablet porosity and average pore size decreases with increase in compression force due to high compressibility of microcrystalline cellulose, it was observed that there is decrease in porosity with increase in microcrystalline cellulose contents. The results are shown in **Table 3**.

TABLE 3: RESULTS OF PREFORMULATION STUDIES OF LOSARTAN POTASSIUM

Preformulation studies	Result
Identification test	Drug is pure
Melting point	263^{o} c
Partition coefficient	5.2
Bulk density	0.21 gm\ml
Tapped density	0.51 gm\ ml
Carr' index	56%
Angle of repose	22.32
Loss on drying	0.30%(0.50)
R_f	0.76
Drug polymer interaction	No interaction

Evaluation of Control Tablet: By comparing evaluation parameter of control tablet with mouth dissolving tablets prepared by using various concentrations of

superdisintegrant, it was found that control tablet had greater hardness while showing less water absorption ratio. Microcrystalline cellulose has more free hydroxyl group and thus the interaction forces in a contact point may be stronger because of stronger hydrogen bond of hydroxyl groups, which can cause increase in hardness. During manufacture of microcrystalline cellulose accessible amorphous region of cellulose molecules are hydrolyzed so that microcrystalline cellulose shows relatively high crystalline. So it can absorb only small amount of water and reaches equilibrium rapidly. The Hardness, Friability, Content uniformity (%), Water absorption (%), Wetting time (sec.) *in- vitro* disintegration time (sec.) and *in-vivo* dispersion time (sec.) were conducted for Control tablet. The results were found to be 3.5kg/cm^2, 0.62%, 97.43%, 45.23%,53 sec.,64 sec. and 74 sec. respectively. Hardness, friability and weight variation test result were found within acceptable limits. The results are shown in **Table 4**.

TABLE 4: EVALUATION OF CONTROL TABLET

Formulation properties	Control
Weight variation	Passes
Hardness (kg/cm^2)	3.5
Friability (%)	0.62
Uniformity of Content (%)	97.43
Water absorption Ratio (%)	45.23
Wetting time (sec)	53
In vitro Disintegration time (sec)	64
In vivo (sec)	74

Dissolution Rate Profile of Control Tablet: *In-Vitro* Dissolution studies were conducted for controlled tablet and It was observed that controlled tablet had shown complete drug release (99%) within 8 minutes. The results are shown in **Figure 6**.

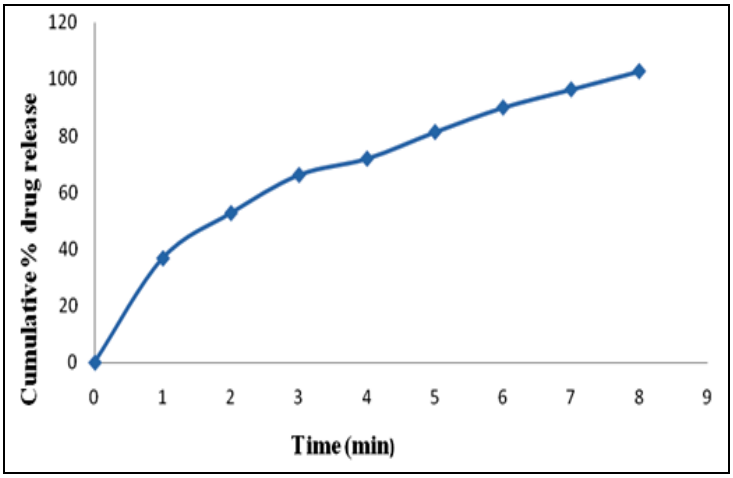

FIGURE 6: *IN-VITRO* DRUG RELEASE OF CONTROL TABLET

Preformulation studies of formulations containing combination of Ac-di-sol and Polyplasdone-xl: The powder properties of formulations containing combination of Ac-di-sol and Polyplasdone-xl (1% to 4%) as superdisintegrant, for direct compression had angle of repose in range of 28.30^o to 24.75^o ,while Carr's index values were ranged in 26.47 to 20%.The bulk density in the range of 0.28 to 0.25, similarly the tapped density in the range of 0.36 to 0.32.So all formulations (B1-B8) shown good flowability. The results are shown in **Table 5**.

TABLE 5: PREFORMULATION PROPERTIES OF FORMULATIONS CONTAINING AC-DI-SOL AND POLYPLASDONE.

Formulation properties	B1	B2	B3	B4	B5	B6	B7	B8
Angle of repose (^{o})	28.12	24.75	26.5	27.3	28.17	28.30	23.96	26.56
Bulk Density (g/cm^3)	0.26	0.25	0.27	0.26	0.26	0.28	0.25	0.28
Tapped Density (g/cm^3)	0.33	0 .32	0.34	0.36	0.33	0.36	0.34	0.35
Carr's index	21.21	21.78	20.58	27.7	21.21	22.2	26.47	20

Evaluation of Mouth Dissolving Tablets of Losartan Potassium:

Hardness and Friability: Tablets required certain amount of strength, or hardness and resistance to friability. It is necessary or important to withstand mechanical shocks of handling in manufacture, packaging and shipping. Adequate tablet hardness and resistance to powdering and friability are necessary requisites for consumer acceptance. Using tablets hardness tester, hardness of the tablets were checked.

The hardness of tablets prepared without superdisintegrant means control tablet have hardness 3.5 Kg/cm^{2}and friability 0.62%. The results are shown in table 40. By using the combination of two superdisintegrant (Ac-di-sol & polyplasdone) the hardness and friability of formulations B1 to B4 were found to be in the range of 3.0 to 3.5 kg/cm^2 & 0.61 to 0.65% respectively.

By using the combinations of two superdisintegrant i.e. Ac-di-sol & Polyplasdone ,the hardness and friability of formulations B4 to B8 were found to be in the range of 3.0 to 3.5 kg/cm^2 and 0.61 to 0.65% respectively. The results are shown in table 06. From the above studies it was found that hardness and friability are within the pharmacopeial limits.

Drug content uniformity: The results indicated that the content of Losartan potassium in all the formulations i.e B1 to B8 were found to be in the range of 98 to 99.12% which are within the Pharmacopeial limits. The results are shown in **Table 6**.

Water absorption ratio and Wetting time: The wetting time and water absorption ratio which are the important criteria for determining the capacity of disintegrates to swell in presence of little water. The results indicated that the water absorption ratio for control tablet was 45.23% and wetting time 53 sec By Using the combination of two superdisintegrant like Ac-di-sol and polyplasdone, the water absorption ratio and wetting time in the formulations B1 to B4 were found to be 72.2%, 74.3%, 78.5%, & 80.6% and 20, 17, 14 &,10 sec. respectively.

The results are shown in **table 6**. By Using the combination of two superdisintegrant like Ac-di-sol and polyplasdone, the water absorption ratio and wetting time in the formulations B5 to B8 were found to be 72.2%, 76.3%, 80.5%, & 85.6% and 19, 14, 12 & 8 sec. respectively. The results are shown in table 06. The best result has been shown by batch B8 tablets, it showed the water absorption ratio and wetting time was 85.6 % and 8 seconds. Thus the results indicated that the preparation was more water absorption ratio and minimum wetting time, so it will take less time for disintegrating.

***In- vitro* disintegration time:** The disintegration time of mouth dissolving tablets should be less because in a very short time it should be totally disintegrates. The disintegration time for control tablet was 64 sec., which was very high. This was due to no superdisintegrant was used. The combination of two superdisintegrants were used in tablets which shown the better result. When Ac-Di-Sol have been kept constant and the concentration of Polyplasdone have been changed the disintegration time of formulation, B4 gave the 20 seconds and when the Ac-Di-Sol concentration have been changed and Polyplasdone concentration have been kept constant then the result was found for formulation B8 was 18 seconds. Because, with increase in concentration of superdisintegrant, disintegration time decreases. The results are shown in **Table 6**.

***In- vivo* disintegration time:** The disintegration in mouth is a very important consideration during the formulation of mouth dissolving tablets. The *in vivo* disintegration time in the formulations B1 to B4 were found to be 35, 32, 30 and 28 sec. using the superdisintegrant i.e. Ac-Di-Sol & Polyplasdone-xl. The minimum and maximum *in vivo* disintegration time was found to be 28 and 35 seconds respectively. The *in vivo* disintegration time in the formulations B5 to B8 were found to be 35, 30, 28 and 25 sec. using the superdisintegrant i.e. Ac-Di-Sol & Polyplasdone-xl.

The minimum and maximum *in vivo* disintegration time was found to be 25 and 35 seconds respectively. On the basis of above discussion the tablet formulated by the combination of Ac-Di-Sol and Polyplasdone shown the less disintegration time in comparison to others preparation. When the concentration of Ac-Di- Sol in gradually increases up to the 4% and the Polyplasdone concentration have been kept constant then the disintegration time was 25 second. So that concentration of Ac-Di- Sol in gradually increases upto the 4% concentration then the disintegration time was decreased. The results are shown in **Table 6**.

***In-vitro* dissolution study:** Dissolution rate studies showed that about 95-99.21% drug release within 2 to 4 minutes for all formulations with using the superdisintegrant but in case for control tablet showed complete release of drug in 8 minutes without use of superdisintegrant. The results are shown in **Fig 7 & 8**. The results indicate that the formulation, B8which was prepared by the combination of two superdisintegrant Ac-Di-Sol with 4% and Polyplasdone 1% showed the complete drug released within 2 minutes.

TABLE 6: EVALUATION OF TABLETS WITH AC-DI-SOL AND POLYPLASDONE

Formulation properties	B1	B2	B3	B4	B5	B6	B7	B8
Weight variation	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Hardness (kg/cm^2)	3.5	3.0	3.0	3.5	3.5	3.5	3.0	3.0
Friability (%)	0 .65	0.63	0.61	0.62	0.62	0.63	0.62	0.61
Uniformity of Content (%)	98.63	99.31	98.63	98.97	98.22	99.31	98.87	99.12
Water absorption Ratio (%)	72.6	74.3	78.5	80.6	72.2	76.6	80.3	86.1
Wetting time (sec)	20	17	14	10	19	14	12	8
In-vitro Disintegration Time (sec)	28	25	23	20	27	24	24	18
In-vivo Disintegration Time (sec)	35	32	30	28	35	30	28	25

Thus, there was an indication that the formulation B8 has better result an comparison to others preparation. The dissolution rate profile of marketed formulation of Losartan potassium (Losacar) tablet was conducted. The results are shown in **Figure 9**. The complete drug release showed within the 5 minutes. The comparison graphs between the marketed preparation and best formulation, B8 is shown in **Figure 10**.

The result showed that the formulation, B8 showed complete drug release within 2 minutes and marketed formulation showed complete drug release in 5 minutes. Thus there was an indication that the formulation B8 has showed better result in comparison to other formulations and also marketed formulation. The evaluation parameter of marketed formulation is shown in **Table 7**.

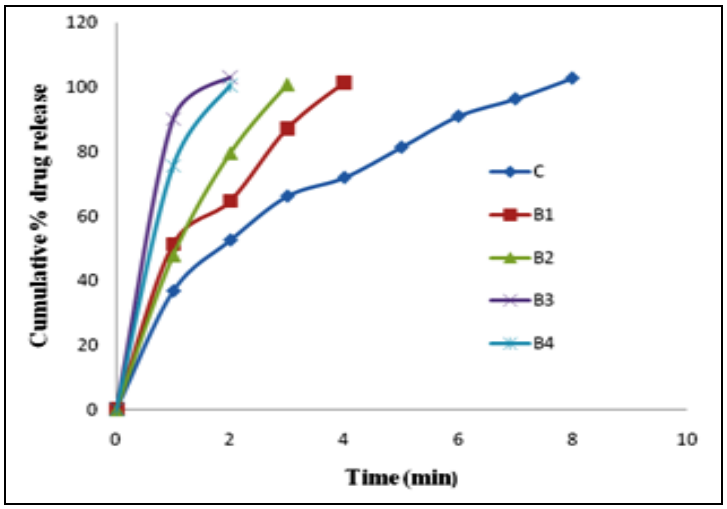

FIGURE 7: A COMPARISON *IN-VITRO* DRUG RELEASE OF TABLET BETWEEN CONTROL AND USING THE COMBINATION OF AC-DI-SOL AND POLYPLASDONE

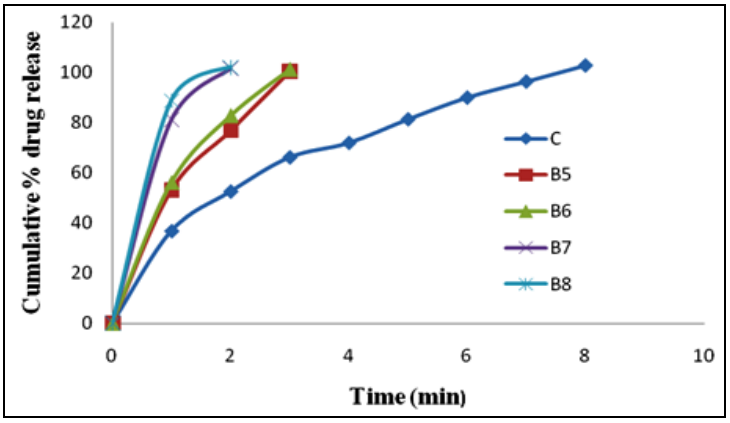

FIGURE 8: A COMPARATIVE STUDY OF *IN-VITRO* DRUG RELEASE OF TABLET BETWEEN THE CONTROL AND COMBINATION OF AC-DI-SOL AND POLYPLASDONE

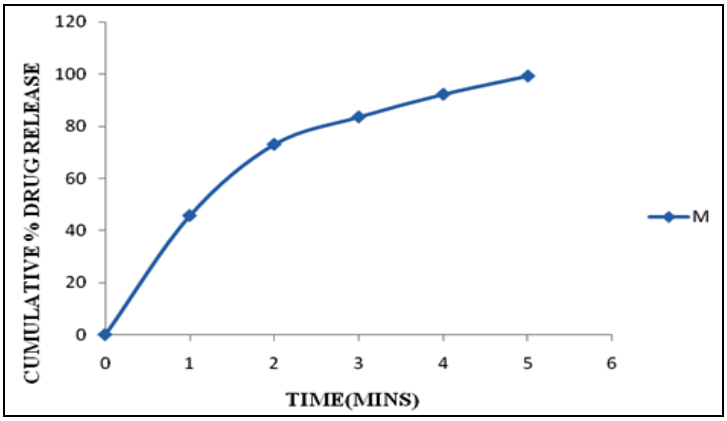

FIGURE 9: *IN-VITRO* DRUG RELEASES OF MARKETED TABLET (LOSACAR)

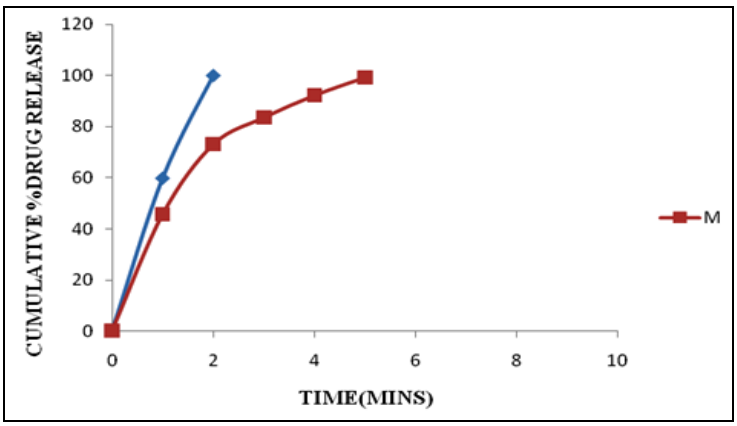

FIGURE 10: A COMPARISON BETWEEN *IN-VITRO* DRUG RELEASES OF MARKETED TABLET (LOSACAR) AND FORMULATION, B8

TABLE 7: TABLET PROPERTIES OF MARKETED TABLET

Formulation properties	M
Weight variation	Passes
Hardness(Kg/cm^2)	3.5
Friability(%)	0.68
In –Vitro Disintegration time(sec.)	52
In –Vivo Disintegration time (sec.)	75

Accelerated Stability Studies: The stability studies were carried out on the most satisfactory formulation, B8 at 40^{o}C±2^{o}C/75% RH ±5% for two months to assess their long term stability as per ICH guidelines. At various intervals of time (0, 15, 30, and 60 days) samples were evaluated. The parameter studies were hardness, weight variation, percentage drug contents and *in vitro* drug release studies. The results are shown in **Table 8**.

From the above results, it was concluded that there was no significant change in any parameters. Hence the formulation, B8 was considered to be highly stable.

TABLE 8: ACCELERATED STABILITY STUDIES OF FORMULATION B8 AT TEMPERATURE (40^{o}C ±2^{o}C/75% RH ±5%)

Physical parameter	Formulation, A4			
	0 days	15 days	30 days	60 days
Hardness (Kg/cm^2)	3.5	3.5	3.0	3.0
Weight variation (mg)	200	200	198	199
Percent drug content	99.12	99.10	99.10	99.10
In-Vitro drug release	99.21	99.10	98.75	98.50

CONCLUSION: Now days the more and more research is taking place in field of MDTs and the advanced technologies are utilized in the manufacturing of MDTs. An optimized formulation Mouth Dissolving tablets of losartan potassium was found and prepared in this study by direct compression method. The best *in-vitro* drug release observed in formulation B8 was found to be 99.21 % within 2 minutes which contain the drug (losartan potassium) and combination of Ac-Di-Sol (4%) and Polyplasdone (1%) (as super disintegrant) with other excipients. The formulation, B8 was found to be best among all other formulations because it has exhibited good wetting time, water absorption ratio and faster disintegration time with compared to all other formulations.

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