e-ISSN: 2349-2678, p-ISSN:2961-6050

available online on www.ijpba.in

International Journal of Pharmaceutical and Biological Science Archive

NLM (National Library of Medicine ID: 101732687)

Index Copernicus Value 2022: 72.59

Volume 12 Issue 5; 2024; Page No. 1-15

A Research on Formulation Design, Development and Evaluation of Post -Compressional Parameters of Fast Disintegrating Tablets of Losartan Potassium by Using Locast Bean Gum as Super Disintegrants

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Article Info: Received: 18-04-2024 / Revised: 17-05-2024 / Accepted: 11-06-2024

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Conflict of interest statement: No conflict of interest

Abstract

Fast dissolving medication delivery devices offer an option for patients who have difficulty swallowing pills, capsules, etc. Fast-acting tablets dissolve in the tongue instantaneously, thus water is not needed to consume them. The goal of the current experiment was to create potassium losartan pills that would dissolve quickly using locust bean gum, a naturally occurring superdisintegrant. Conduct pre-formulation research on the drug's identification, solubility, and partition coefficient. The impact of precompressional factors such as compatibility and interaction studies In addition to the influence of formulation factors on losartan potassium disintegration and in-vitro dissolving, other tablet qualities were also investigated. The results showed that locust bean gum at a 7.5% concentration created rapidly dissolving tablets and had good superdisintegrant properties. The optimal tablet formulation (F3) exhibited a maximum drug release of 98% after 30 minutes and a minimum disintegration time of 20 seconds. With a swelling index of 22, locust bean gum was shown to possess a noteworthy capacity for use as a superdisintegrant. There was no interaction of any kind with the tablet's formulation components, as shown by the DSC study and IR spectra. Accelerated short-term tests on the improved formulation reveal no discernible changes to the composition.

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

Introduction

FAST DISINTEGRATING TABLETS

Oral drug administration is still the preferred mode of medicine distribution despite a number of disadvantages since it is simpler to give and improves patient compliance. "Mouth Disintegrating Tablets" (MDTs), also called Fast Disintegrating Tablets (FDTs), are one approach to solve this problem with the novel drug delivery system. MDTs, or Fast Disintegrating Tablets, dissolve or disintegrate quickly in the mouth without the need for water in a matter of seconds due to the action of a super disintegrant or by optimizing the pore structure in the formulation. Fast-dissolving tablets are useful, particularly for patients—the young, old, or mentally ill—who find it difficult to swallow standard tablets and capsules. The paper addresses the many aspects of formulation, the technologies developed for multidisciplinary teams (MDTs), the super disintegrants employed, the various excipients,

the evaluation tests, the commercial formulation, and the drugs. Losartan potassium, the first non-peptide antihypertensive drug in the new family of Ang II receptor antagonists, was approved by the FDA in April 1995. Merck began selling losartan under the brand names Cozaar TM and Hyzaar TM. The revenue was divided equally between Merck and DuPont. The decreased adverse effects of losartan were likely influenced by its novel, selective mechanism of action. It turned out to be a highly successful course of action. The dry cough and skin rash that some ACE inhibitor users reported were not brought on by it. The fast-dissolving tablet is the most widely used product among the various dosage forms designed to improve administration convenience.[1] Patients who value easy-to-take dosage forms, particularly those in the pediatric and geriatric populations, strongly favor solid dosage forms that can be dissolved or suspended in water in the mouth.[2]

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.

Direct Compression Method

Direct compression consists of compressing tablets directly from powdered material without modifying the physical nature of the material itself. This method is suitable for a small group of crystalline chemicals having all the physical characteristics required for the formation of a good tablet. This includes chemicals such as potassium salts (chlorate, chloride, bromide, iodide, nitrate, permanganate), ammonium chloride. Direct compression process consists of three steps: raw material blending, tableting, and coating. These steps are interconnected in continuous processes, so that the raw materials are fed into the process, and the tablets are obtained from the process simultaneously.

Preparation of fast dissolving tablets

The fast dissolving tablets containing 20mg of losartan potassium were prepared by direct compression method using locust bean gum as super disintegrating agent. Compositions of various formulations are shown in table no. Avicel pH 102 was used as a directly compressible diluents. All the ingredients were weighed and mixed in mortar with the help of pestle, and then finally aspartame and magnesium stearate were added, and passed through 60 mesh to ensure better mixing and slightly compressed on 8mm flat-faced punches of 16 station rotary compression machine. The total weight of the formulation was maintained 200mg.

Table no.1: Composition of fast dissolving tablets of losartan potassium

Ingredients (mg)	FORMULATION CODE					
	F1	F2	F3	F4	F5	F6
Losartan Potassium	20	20	20	20	20	20
Locust bean gum	7	10	15	20	25	30
Avicel-102	135	130	127	122	117	112
Aspartame	30	30	30	30	30	30
Menthol	2	2	2	2	2	2
Magnesium Stearate	4	4	4	4	4	4
Talc	2	2	2	2	2	2
Total	200	200	200	200	200	200

PRECOMPRESSIONAL PARAMETERS

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.

POST COMPRESSIONAL PARAMETERS STUDIES

Following the punching of each batch, the tablets were assessed for thickness, weight uniformity test, hardness, friability, drug content, in vitro disintegration time, water absorption ratio, wetting time, and in vitro drug release studies, among other in-process and final product quality control tests.

Thickness

Using vernier calipers, the thickness of the tablets was measured from crown to crown. From each formulation, ten tablets were chosen at random, and the mean and standard deviation were computed.

Weight uniformity test[3]

A weight variation research was conducted in accordance with USP. From each batch, twenty tablets were chosen at random and weighed both separately and collectively. The weight of every tablet combined was used to get the average weight. The average weight and the individual weight were contrasted.

Hardness[4]

Hardness was measured using a Monsanto hardness tester. The test tablet was held between a moving and fixed jaw, and the indicator's reading was set to zero. By pushing the screw knob forward, you can progressively increase the stress exerted to the tablet's edge until it breaks. The scale's reading, which represents the amount of pressure needed in kilograms or pounds to shatter pills, is indicated. From each formulation, six tablets were chosen at random, and the mean and standard deviation were computed.

Friability[5]

Roche Friabilator was used to assess the tablets' friability. A total of ten tablets were weighed and then put inside the friabilator chamber, which rotated at a speed of 25 rpm, dropping the tablet six inches higher with each revolution. The tablets were removed after 100 rotations (4 minutes), dusted with a soft muslin towel, and then weighed once more. In order to calculate percentage friability, the following formula was used:

$$\% \text{ Friability} = \frac{\text{Initial wt. of tablets} - \text{Final wt. of tablets}}{\text{Initial wt. of tablets}} \times 100$$

Uniformity of drug content[6]

Six tablets were randomly selected and ground into a powder from each batch of manufactured tablets. 200 mg of this powder, or 20 mg of medication, was then precisely weighed and put into a 100 ml volumetric flask. With the help of phosphate buffer (pH 6.8), the capacity was increased to 100 ml. The sample was then subjected to a one-hour sonication to fully dissolve the medication. The solutions underwent appropriate filtration and diluting. Using a blank as a reference, the diluted solution's absorbance was measured spectrophotometrically at 209 nm. Using the standard calibration curve of losartan potassium in phosphate buffer (pH 6.8) solution, the amount of medication in each tablet was determined. Three copies of the test were administered.

In-Vitro Disintegration test[7, 8]

Using the Tablet Disintegration Tester ED-20 (Electrolab, Mumbai, India), six tablets were tested. The disintegration medium used was phosphate buffer 6.8pH at 37°C±2°C. The amount of time it took for the pill to completely dissolve and leave no discernible bulk inside the device was measured in seconds. Every glass tube has a tablet inserted, and the device is run until the tablet dissolves, at which point the amount of time needed to do so is recorded.

Water absorption ratio[9]

Within a 9cm-diameter Petri dish holding 10ml of filtered water was a piece of tissue paper folded twice. After positioning the tablet on the tissue paper, it was given time to fully saturate. After being taken out, the moist tablet was reweighted. The following equation was used to determine the water absorption ratio, or R: was determined according to the following equation:

$$\text{Water absorption ratio} = \frac{\text{Final wt. of tablet- Initial wt. of tablet}}{\text{Final wt. of tablet}} \times 100$$

Three tablets from each formulation were tested. Average and standard deviation was determined.

Wetting time[10]

A Petri dish with an internal diameter of 9 cm was filled with twice-folded tissue paper and 10 milliliters of water containing a modest amount of the water-soluble color methylene-blue. The tissue paper in the Petri dish was gently covered with a tablet. The wetting time was defined as the amount of time it took for water to reach the tablet's upper surface.

IN –VITRO DRUG RELEASE STUDY[5]

The produced tablets were subjected to in vitro drug release investigations utilizing a USP type-II (Paddle) dissolution device (Electro lab, Mumbai) operating at 50 rpm. The dissolution flask was filled with 900 ml of phosphate buffer (pH 6.8) solution, which served as the dissolution medium. The medium's temperature was adjusted to 37±0.5°C. To keep the volume constant and the sink condition, 5 ml of the sample was taken out of the dissolving medium and replaced with fresh medium at prearranged intervals. When necessary, dilutions were produced and samples were filtered. Using dissolving media as a blank, the sample solutions were examined using a UV-Visible spectrophotometer set at 209 nm. Drug concentration in the samples was computed.

KINETIC STUDY[11, 12, 13]

Numerous release models, including Higuchi, were examined in order to examine the release mechanism:

$$Qt = KH{-}t \text{ ----------} \quad 1$$

This is the most commonly used model to represent drug release from pharmaceutical matrices, where Qt is the amount of drug released at time t and KH is the higuchi release rate.

In zero order:

$$Qo + Kot = Qt \text{ --------} \quad 2.$$

Where Qo is the initial concentration of the drug in the solution as a result of a burst effect, Qt is the amount of drug released at time t, Ko is the apparent dissolving rate constant or zero order release constant, and in this instance the drug release runs at a constant rate. To begin with,

$$\ln Qt = \ln Qo + K1t. \text{ ----------} \quad 3.$$

In this situation, the first order release constant is denoted by K1.

$$/Q¥ = Kktn \text{ in Korsmeyer-Peppa ---------} \quad 4$$

where n is the release exponent, indicating the drug release mechanism, and Kk is a constant integrating geometric and structural characteristics of the drug dosage form. A release exponents value of n=0.45, 0.45 < n < 0.89, and 0.89 < n < 1.0, in accordance with the criteria for release kinetics from swellable systems, suggests fickian (case I) diffusion, non-fickian (anomalous) diffusion (case II), and zero order-super case II transport, respectively.

STABILITY STUDIES[14, 15]

The ability of a certain medication or dosage form in a certain container to maintain within its physical, chemical, therapeutic, and toxicological parameters is known as stability. Drugs degrade or break down during storage as a result of product instability or chemical changes to the active ingredients which lower the concentration of the medication in the dosage form. Rapid stability tests should be used to assess the stability of medicinal preparations. For the stability investigation, the losartan potassium tablet formulation that was most optimized was chosen. In compliance with ICH recommendations, the accelerated stability investigations were conducted for one month at 40±2oC and 75±5% relative humidity. Twenty tablets were randomly chosen from each batch, sealed in foil packs, and kept for a month at 40±2oC and 75±5% relative humidity. The tablets were compared to those that were assessed right away after production in terms of hardness, friability, drug content, weight fluctuation, and in vitro dissolution after a month had passed.

Reaching a 75% relative humidity

A wire mesh was positioned over the prepared saturated sodium chloride solution, the dosage

form was placed on top of the wire mesh, and the desiccator was sealed. A 40°C oven was used to maintain a 75% relative humidity in the desiccator.

RESULT AND DISCUSSION

PRE-COMPRESSIONAL PARAMETERS

DRUG POLYMER INTERACTION STUDY

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.).

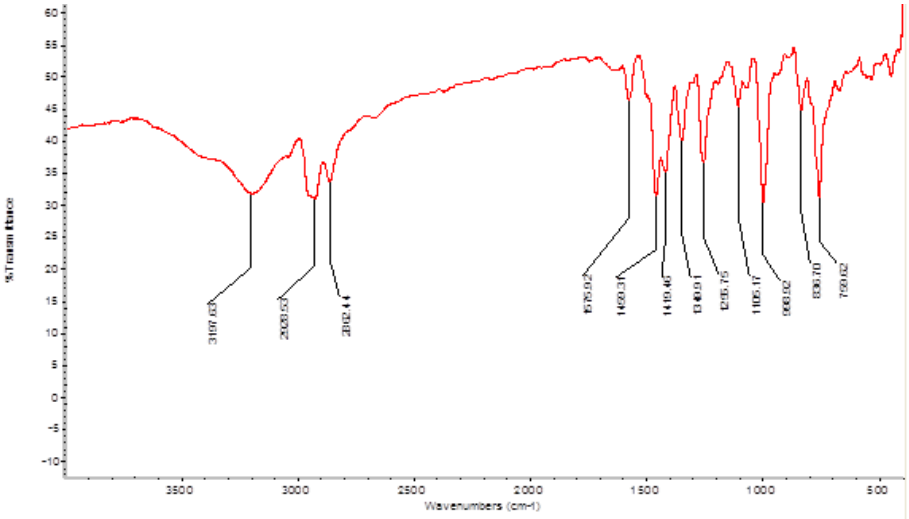

Fig.1 I.R. Spectra of losartan potassium

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.

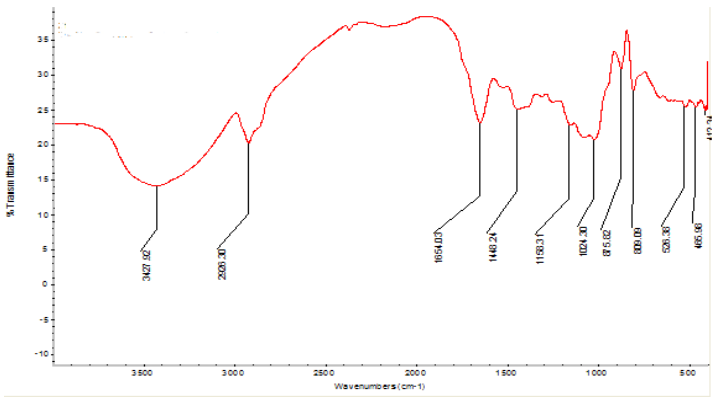

Fig. 2 IR spectra Locust bean gum pure polymer

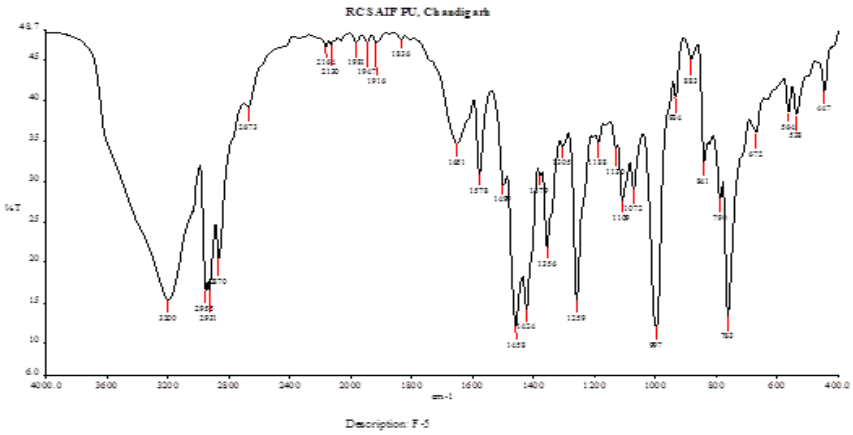

Fig. 3 IR spectra of physical mixture of pure losartan potassium+ locust bean gum

Table 2: 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_2OH(stretching)	1158.31	1100-1380
	CH_2 twisting (vibration)	1024.30	900-1100

Table:- 3 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 to 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_2OH(stretching)	1188	1100-1380
	CH_2 twisting (vibration)	1072	900-1100
	NH (Stretching)	3200	3077-3497

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 value[6] 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.

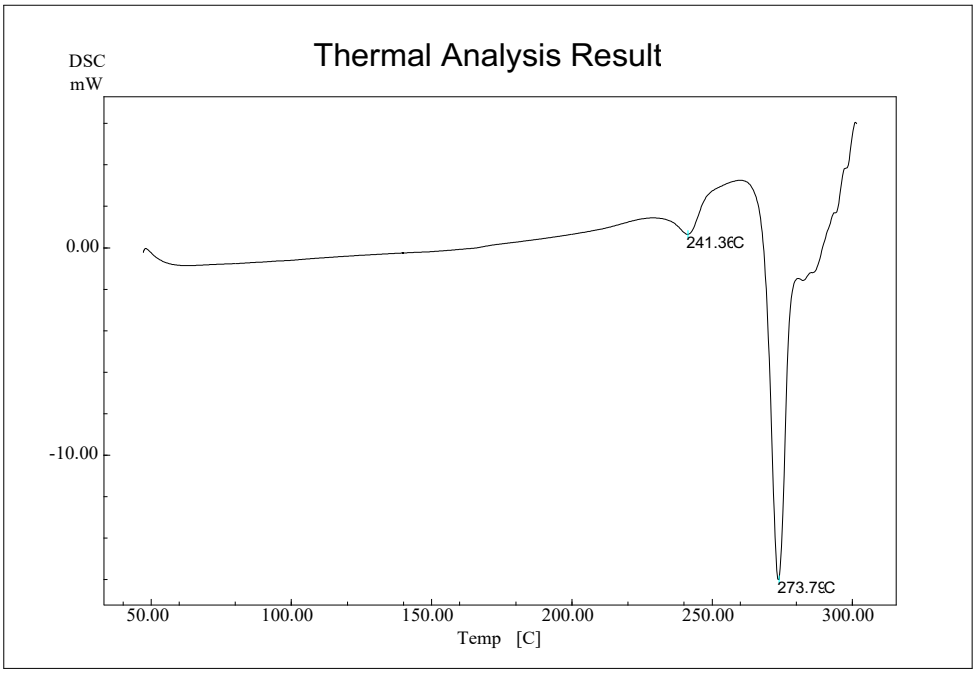

Fig. 4. DSC thermogram of losartan potassium pure drug

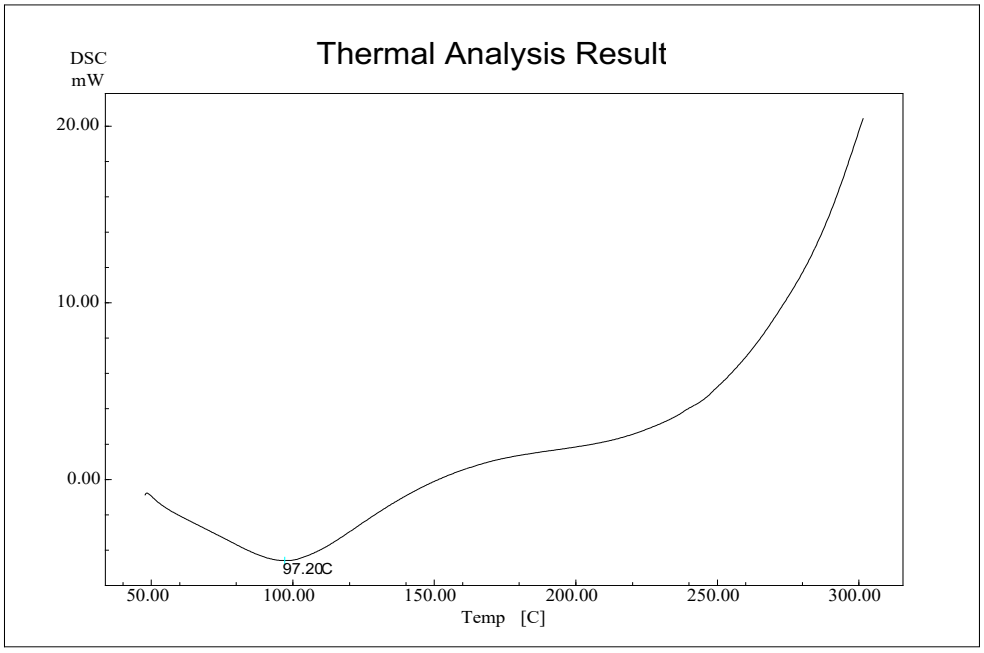

Fig.5 DSC thermogram of locust bean superdisintegrant

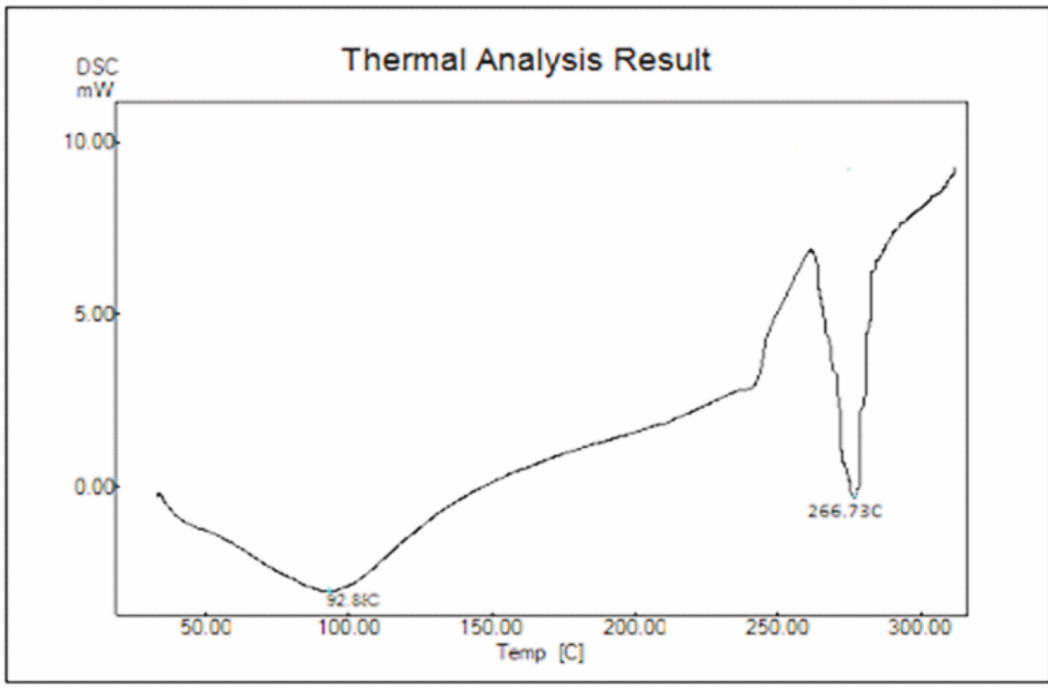

Fig. 6 DSC thermogram of physical mixture (drug+ superdisintegrant)

Post compressional parameters

Thickness

The thickness depends upon the size of the punch and the weight of the tablet. The mean thickness was (n=5) almost uniform in all the formulations and values ranged from 2.8±0.01mm to 2.94±0.1mm. The results of thickness for tablets were shown in table no. 2.

Weight variation test

Twenty tablets were randomly selected for weight variation. The weight variation was found in the range 199±1.23 to 200±1.84 mg and results are tabulated in table no. 2. The average percentage weight variation was within 7.5% within the pharmacopoeial limits.

Hardness

The hardness of tablets prepared by direct compression methods was maintained within the range of 2.5kg/cm^2 to 4.0 kg/cm^2. For fast dissolving tablets the hardness is generally kept low, because these disintegrate on the tongue between 15 sec. to 3 minutes. So, excessive hardness is not favoured for these formulations. The hardness for formulation F6 (3.9±0.05kg/cm^2) was found to be highest of all the formulations and for F1 (2.9±0.1kg/cm^2) was found to be least. The mean hardness test results are tabulated in table no. 2

Friability test

The friability was determined to evaluate the ability of the tablet to withstand abrasion in packing, handling and transportation. The friability of formulated tablets of losartan potassium was found in range 0.28±.057to 0.684±0.14% shown in the table 6. All the formulated tablets were shown the percentage friability within the official limits (<1%).

Drug content

The drug content uniformity was performed for all six formulations of losartan potassium and results are tabulated in table No.6. The percentage drugs content of the tablets were found to be between 92.53±0.23 to 99.13±0.278% of losartan potassium. The results were within the range and indicated uniformity of mixing.

Water absorption ratio

Water absorption ratio of all the formulations was found to be in the range41.21±5.48 to 95.98±2.21 %. The values of water absorption ratio have shown in table no.2 and figure 2

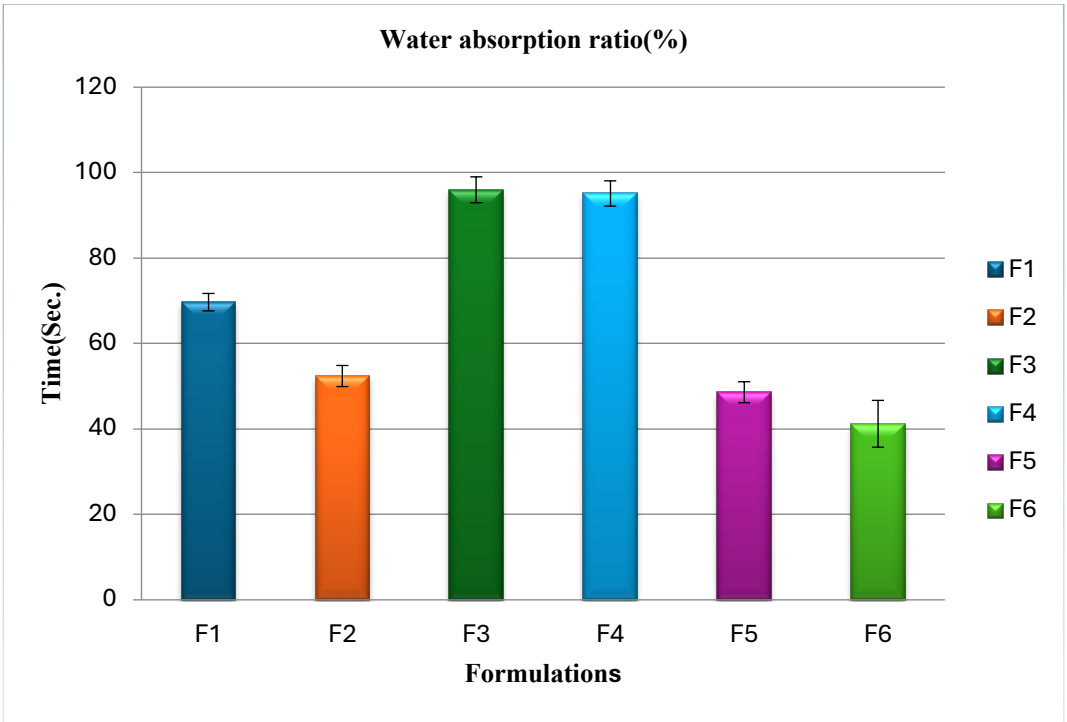

Fig. 7 Water absorption ratio

Wetting time

Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tissue paper in a petri dish. This method will duplicate the *In vitro* disintegration, as the tablet kept motionless on the tongue. The wetting time of losartan potassium prepared by direct compression were found to be in the range of 17.87±3.60 to 109.33±9.50 sec. The results of wetting time have shown in table no.2 and figure 2. Promising formulations F3 (7.5% Locust bean gum) and F4 (10% locust bean gum) showed a wetting time of 20.26±1.91 and 17.57±3.60 sec respectively, which facilitate the faster dispersion in the mouth.

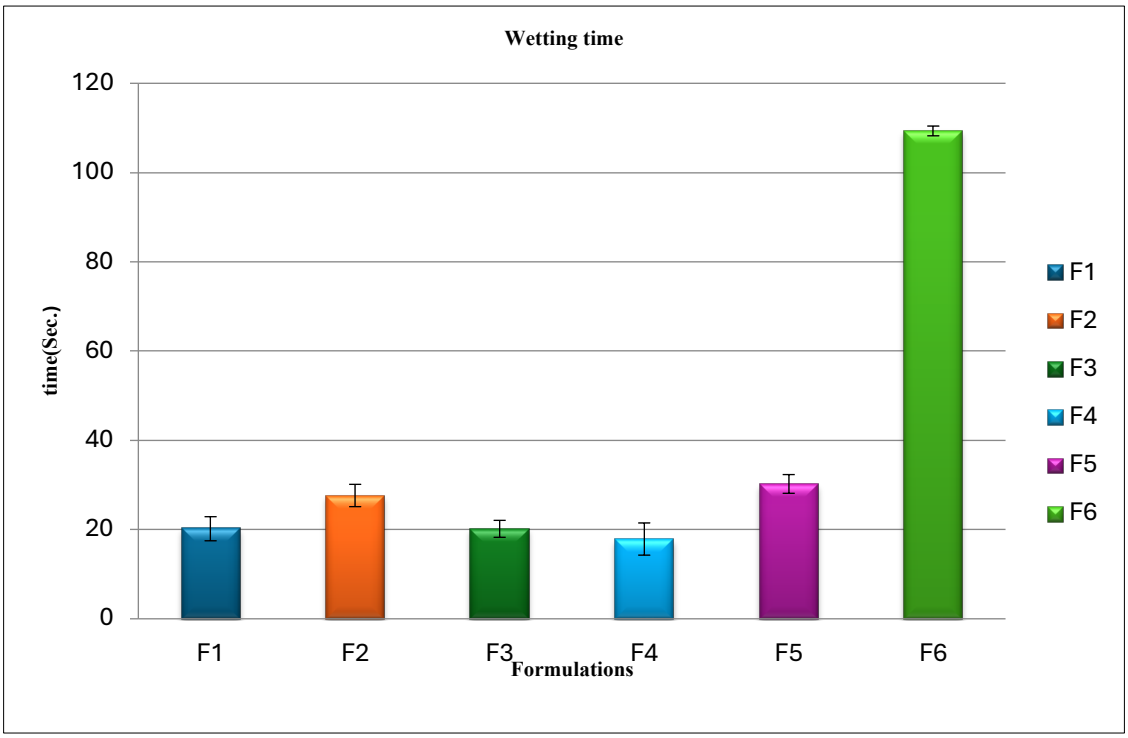

Fig 8 Wetting time of formulation F1-F6

Table no. 4: Physico-chemical evaluation of fast dissolving tablet

Formulation code	Thickness*(mm)	Weight variation*** (%)	Hardness test* (kg/cm^2)	Friability** (%)	Drug content* (%)	Water absorption ratio (%)	Wetting time(sec.)
F1	2.8±0.01	199±1.37	2.9±0.1	0.43±.19	95.86±1.031	69.67±2.05	20.18±2.74
F2	2.81±0.02	199±1.37	3.2±0.25	0.28±.057	97.58±1.490	52.39±2.47	27.63±2.57
F3	2.82±0.1	199±1.23	3.1±0.20	0.29±0.091	99.13±0.278	95.98±2.21	20.26±1.91
F4	2.94±0.1	200±1.43	3.6±0.20	0.68±0.14	92.97±1.80	95.12±2.95	17.57±3.60
F5	2.91±0.01	199±1.80	3.8±0.2	0.49±.010	92.53±0.23	48.59±2.46	30.22±2.12
F6	2.94±0.02	200±1.84	3.9±0.05	0.49±0.16	96.72±0.230	41.21±5.48	109.33±9.50

***In-vitro* disintegration time**

All the formulated tablets have shown *in-vitro* disintegration time less than 180 seconds (3 minutes). Based on the *In vitro* disintegration time, formulation F3 (7.5% locust gum) and F4 (10% locust gum) were found to be promising and showed *in-vitro* disintegration time 20.90±1.15 and 22.78±1.5 sec. respectively. Disintegrating study showed that the disintegrating times (Table 3, figure 3) of the tablets increased with increase in the concentration of locust bean gum. *In-vitro* disintegration time of formulation F5 (12.5% locust gum) were found to be 100.33±1.5 sec. and formulation F6 (15% locust gum) were also found to be 165.66±1.5 sec. Generally in the 1 to 10% concentration of total tablet weight, gum mucilage's can act as disintegrant. This is an important parameter to determine the application of gum mucilage in particular formulation. Disintegration times increased with increase in the concentration of locust bean gum in the formulation F5 & F6. It indicates that increase in the concentration of locust bean gum had a negative effect on the disintegration of the tablets. The results are in consistent with other results.

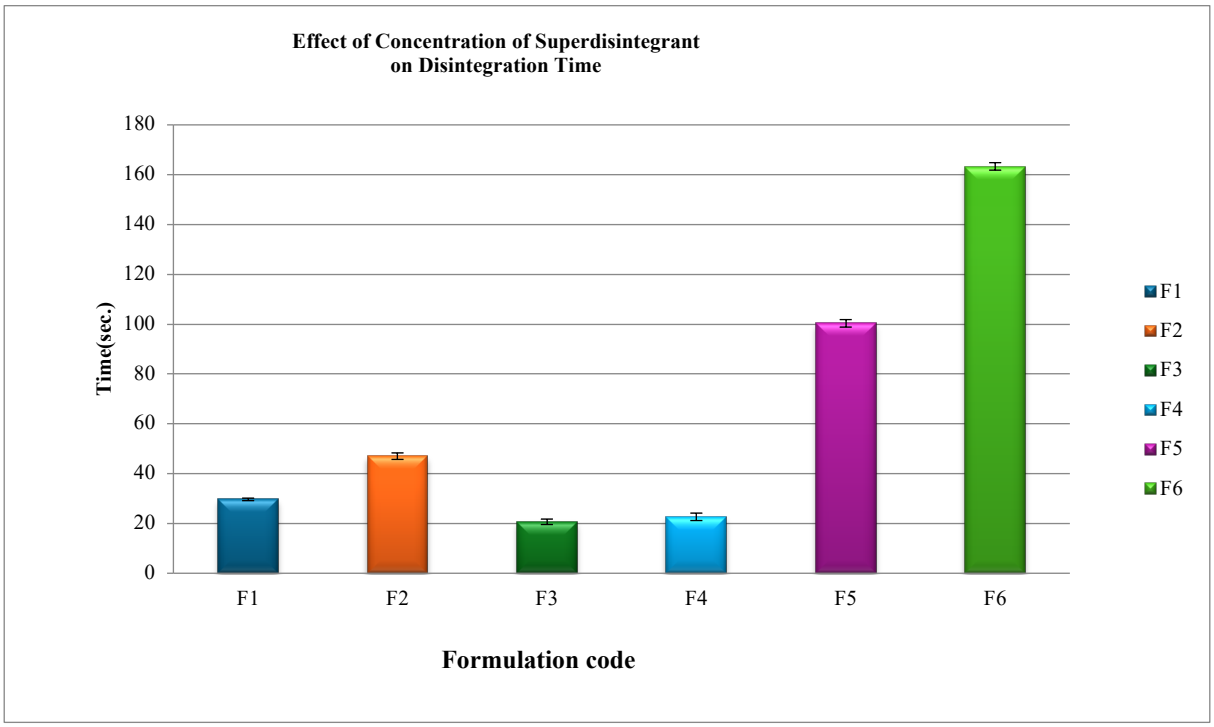

FIG 9: Disintegration Time For Formulation From F1- F6

Table no. 5 *In-vitro* disintegration time

Formulation code	USP disintegrating test
F1	29.76±0.5
F2	47±1.43
F3	20.66±1.23
F4	22.66±1.64
F5	100.33±1.2
F6	165.66±1.6

n=6, Sec. ±S.D.

IN –VITRO DRUG RELEASE STUDY

In vitro drug release studies for the prepared tablets were conducted using USP type-II (Paddle) dissolution apparatus (Electro lab, Mumbai.) at 50 rpm. The dissolution medium, 900 ml of phosphate buffer (pH 6.8) solution was placed into the dissolution flask and the temperature of the medium was set at 37±0.5°C. At predetermined interval of time, 5 ml sample was withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant and sink condition. Samples were filtered and dilutions were made whenever necessary. The sample solutions were analyzed by UV-Visible spectrophotometer at 209 nm, using dissolution medium as blank. The amount of drug present in the samples was calculated.

In-Vitro dissolution study

As there is no any specific dissolution test available for fast dissolving tablets, dissolution rate was studied as per USP specification of conventional tablets (USP type-II apparatus). Dissolution profiles of losartan potassium from the tablets are shown in figure5. Table 8 shows the cumulative % drug release profile of drug in 30 minutes. The order of drug release was found to be

F3>F2 >F1>F4>F5>F6

From formulation F1 (2.5% locust bean) percentage cumulative drug release of losartan potassium is approximately 91.688±2.0 in 30 min. In formulation F2 (5% locust gum) and F3 (7.5% locust gum), as increase in concentration of locust gum there is increase in the dissolution of losartan potassium formulation 93% and 98% after 30 minutes. The rapid increase in dissolution of losartan potassium with the increase in locust bean concentration may be due to rapid swelling and disintegrating tablets rapidly into apparently primary particles. While in formulation F4 (10% locust gum), F5 (12.5% locust gum) and F6 (15% locust gum) *In vitro* release of losartan potassium was 80%, 50% and 38%. The release was decreased with increase in concentration of super disintegrant may be due to the binding action of locust gum. *In-vitro* proving the super disintegrant property of locust bean gum release profile of formulation F3 showed maximum release 98% among all formulations.

Table 6: *In-vitro* release profile of losartan potassium fast dissolving tablets (Formulation F1)

Time(Min.)	% Cumulative Release of losartan potassium			Mean±S.D. (n=3)
2	11.391	12.206	8.211	10.602±2.1
4	14.063	19.694	14.290	16.016±3.1
6	19.287	25.837	20.729	21.951±3.4
8	36.426	33.832	30.588	33.615±2.9
10	47.007	49.307	50.228	48.84±1.6
15	73.155	77.709	75.375	75.41±2.2
20	80.554	79.971	76.809	79.111±2.0
25	86.091	84.078	83.549	84.573±1.3
30	89.807	91.467	93.790	91.688±2.0

Table 7: *In-vitro* release profile of losartan potassium fast dissolving tablets (Formulation F2)

Time(Min.)	% Cumulative Release of losartan potassium			Mean±S.D. (n=3)
	I.	II.	III.	
2	11.676	9.352	15.060	12.029±2.8
4	15.410	13.318	19.710	16.146±3.2
6	20.551	19.670	24.344	21.522±2.4
8	41.726	39.455	39.547	40.243±1.2
10	58.265	61.077	62.800	60.714±2.2
15	71.428	69.160	75.785	72.124±3.3
20	80.586	79.936	76.609	79.044±2.1
25	87.142	85.470	84.366	85.659±1.3
30	94.345	90.421	94.406	93.057±2.2

Table 8: *In-vitro* release profile of losartan potassium fast dissolving tablets (Formulation F3)

Time(Min.)	% Cumulative Release of losartan potassium			Mean±S.D. (n=3)
	I.	II.	III.	
2	12.002	14.188	15.142	13.777±1.6
4	19.897	20.790	17.305	19.330±1.8
6	24.859	27.428	26.818	26.368±1.3
8	44.427	46.333	48.925	46.562±2.2
10	54.049	54.743	57.961	55.584±2.0
15	74.935	76.244	78.257	76.479±1.6
20	88.189	91.340	87.452	88.994±2.0
25	91.322	97.548	92.0079	93.626±3.4
30	96.712	101.341	97.197	98.417±2.5

Table 9: *In-vitro* release profile of losartan potassium fast dissolving tablets (Formulation F4)

Time(Min.)	% Cumulative Release of losartan potassium			Mean±S.D. (n=3)
	I.	II.	III.	
2	7.638	7.7609	10.339	8.579±1.5
4	19.667	18.852	19.366	19.295±0.4
6	31.232	27.152	27.627	28.670±2.2
8	36.756	36.729	42.049	38.511±3.0
10	48.374	47.940	54.104	50.139±3.4
15	58.832	53.911	64.187	58.977±5.1
20	66.086	68.068	69.023	67.726±1.4
25	91.322	73.333	74.700	74.347±0.8
30	96.712	79.440	81.630	80.052±1.3

Table 10: *In-vitro* release profile of losartan potassium fast dissolving tablets (Formulation F5)

Time(Min.)	% Cumulative Release of losartan potassium			Mean±S.D. (n=3)
	I.	II.	III.	
2	10.983	11.793	9.540	10.772±1.1
4	26.562	27.050	28.347	27.319±0.9
6	32.905	30.789	30.543	31.412±1.2
8	38.556	33.274	36.419	36.083±2.6
10	40.095	36.435	33.765	36.765±3.1
15	42.488	37.210	41.696	40.465±4.3
20	44.662	38.977	44.777	42.806±2.9

25	48.258	44.594	47.874	46.909±2.0
30	52.600	48.185	52.211	50.998±2.4

Table 11: *In-vitro* release profile of losartan potassium fast dissolving tablet (Formulation F6)

Time(Min.)	% Cumulative Release of losartan potassium			Mean±S.D. (n=3)
	I.	II.	III.	
2	1.647	2.0548	2.544	2.081±0.4
4	7.934	6.0209	1.008	4.988±3.5
6	11.525	8.663	5.662	8.617±2.9
8	17.012	13.277	9.322	13.203±3.8
10	21.957	21.708	16.100	19.922±3.3
15	28.340	24.070	24.465	25.625±2.3
20	34.815	28.239	29.330	30.795±3.5
25	40.918	30.636	32.793	34.782±1.5
30	42.568	36.714	36.560	38.614±1.5

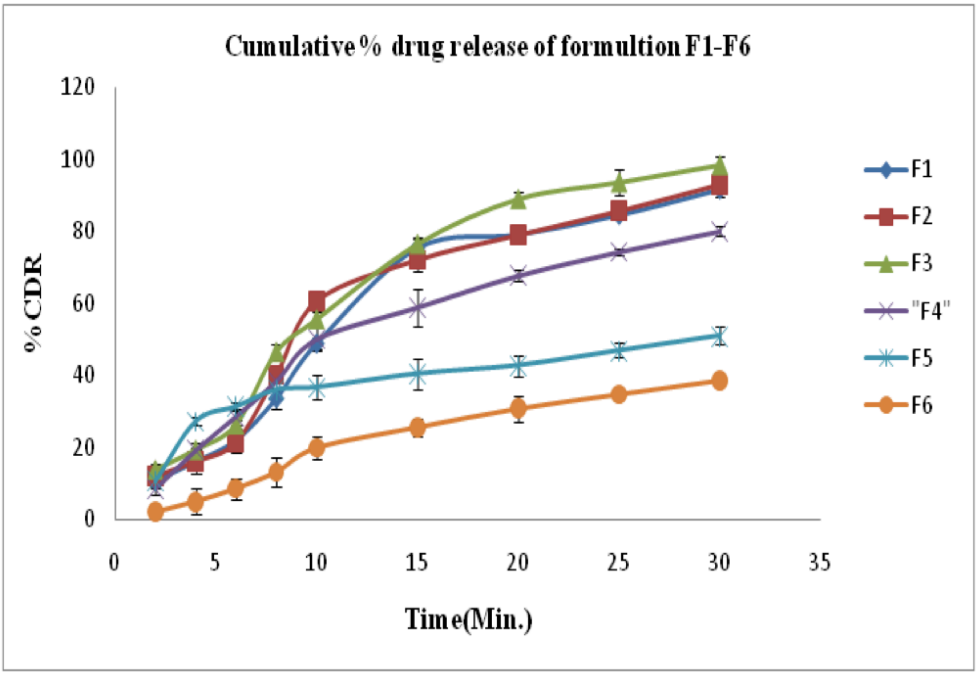

Fig 10 *In vitro* release profile of formulation F1-F6

Stability studies

The stability is defined as the ability of a particular drug or dosage form in a specific container to retain within its physical, chemical, therapeutic and toxicological specifications. Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, lowering the concentration of the drug in the dosage form. The stability of pharmaceutical preparation should be evaluated by accelerated stability studies. The optimized formulation of losartan potassium tablet was selected for the stability study. The accelerated stability studies were carried out according to ICH guidelines at 40±2ºC/75±5% RH for 1 month. 20 tablets from each batch were selected at random and were packed in aluminum foil packs and stored at 40±2ºC/75±5% RH for one month. After one month the tablets were evaluated for hardness, friability drug content, weight variation, in vitro dissolution and compared with tablets which were evaluated immediately after manufacturing.

Achieving of 75% RH

Saturated solution of sodium chloride was prepared and placed in the desiccators over

which a wire mesh was placed, the dosage form was placed on wire mesh and the desiccator was sealed. The desiccator was kept in oven maintained at 40°C to create the relative humidity of 75%.

CONCLUSION

The current study aims to create potassium losartan tablets that dissolve quickly. Fast dissolving tablets are a potential method for achieving a quicker onset of pharmacological action and would be more beneficial than the standard versions that are already on the market. The two main negative effects of tablets are dysphasia and trouble swallowing. Losartan potassium fast-dissolving tablets are produced via direct compression in order to meet the aforementioned requirements. The precompressional parameters of drug polymer interaction studies and the postcompressional parameters of weight variation, hardness, friability, uniform drug content, wetting time, water absorption ratio, in-vitro disintegration time, in-vitro dissolution studies, and stability study were applied to the prepared tablets. Weight variation of the tablet prepared using the direct compression method was found to be between 199±1.23 and 200±1.84 mg, hardness between 2.3 and 3.3 Kg / cm2, percentage friability between 0.28±.057 and 0.684±0.14%, in-vitro disintegration time between 20 and 165 sec, uniformity of drug content between 92.53±0.23 and 99.13±0.278%, wetting time between 17.87±3.60 and 109.33±9.50 sec, and water absorption ratio between 41.21±5.48 and 95.98±2.21% were observed. The formulation F3, which releases 98% of the medicine in vitro in 30 minutes and disintegrates in 20 seconds, was found to be the best based on the results. The created formulation did not exhibit any appreciable physical changes, according to the stability investigation, and formulation F3 was determined to be stable.

AKNOWLEDGEMENT

The author is thankful to Elfin Drug Pvt. Ltd. Baddi, Nalagarh (Himachal Pradesh) for providing gift sample of losartan potassium. I am sincerely thankful to professor Dr. Amit Kumar, Department of Pharmaceutical Science, Sunrise University, Alwar, Rajasthan India for their support and guidance and also thankful to sunrise university for providing me a platform where I had perform my all these post compressional evaluation parameters.

CONFLICT OF INTREST

Authors declare none of conflicts

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