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Original Article

ANALYSIS OF *IN VITRO* DISINTEGRATION AND DISSOLUTION EFFECT OF *CUCURBITA MAXIMA* STARCH IN LOSARTAN FDT

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ABSTRACT

Objective: In this work, *Curcurbita maxima* was used as a superdisintegrant in the preparation of fast dissolving tablets containing Losartan. A Losartan is readily ionized in the presence of an acidic pH, resulting in decreased absorption via the GIT. Superdisintegrant can be used to solve this problem.

Methods: Losartan fast-dissolving tablets were made using the direct compression method and two distinct superdisintegrants, derived starch and *Curcurbita maxima* mucilage, in various quantities. Eleven formulations with varied concentrations of superdisintegrants were created to determine their efficacy and critical concentration levels. For each formulation, several pre-compression and post-compression assessment parameters were used.

Results: The disintegration time of the FDT (F1-F4) prepared with derived starch ranges from 4.28±1.02 min to 8.20±1.02 min, while the disintegration time of the FDT (F5-F8) prepared with *Cucurbita maxima* starch ranges from 1.02±0.02 min to 5.02±1.02 min. The remaining three formulations, F9-F11, have a disintegration time of more than 10 min. In comparison to other formulations, FDT containing *Curcurbita maxima* mucilage demonstrated improved organoleptic qualities, as well as outstanding *in vitro* disintegration and dissolution drug release.

Conclusion: It was determined that a lower concentration of *Cucurbita maxima* starch (10 mg) was the optimal concentration level for the Losartan FDT formulation.

Keywords: *Cucurbita maxima,* Fast disintegration tablet, Direct compression, Superdisintegrant, Losartan

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INTRODUCTION

Cucurbita maxima Duchesne, a member of the *Cucurbitaceae* family, is extensively planted for use as a vegetable and medicine all over the world. Although starches from diverse botanical sources have been studied, there seems to be little information on *Cucurbita maxima* pulp starch as a disintegrant in the research. Starch is a type of tablet disintegrant that was named one of the top ten pharmaceutical ingredients by the International Joint Conference on Excipients [1].

Starches found in tropical vegetables and fruits have long been used as a nutritious carbohydrate source. The majority of these crops grow in abundance with little or less agricultural help and include gluten-free carbs in the form of starch. They've been researched for their superior medicinal excipient capabilities in formulations, such as fillers, glidants, binders, and disintegrants. These starches can be exchanged for chemically modified starches that are commercially available. The various versions of the native forms of these starches have also been studied and shown to have features that make them potential candidates for controlled drug delivery systems. The modified forms of these starches had better disintegrant properties than commercial super-disintegrants, implying that they could be employed as an intra-granular disintegrant in tablet formulations with rapid release as a substitute for synthetic disintegrants [2-4].

Natural carbohydrate reserves in vegetable sources are often in the form of minute granules or cells ranging in diameter from 1 to 100 m or more. They normally account for 10-38 percent of the total weight of the vegetable, with the proportion varying based on the botanic origin of the starch, as well as other aspects such as collection and cultivation time, soil quality, and climatic conditions [5, 6].

Because of differences in amylose-amylopectin ratios, starch produced from diverse botanical sources has varied properties, resulting in different binder substrate interactions. In the food, cosmetics, and pharmaceutical sectors, starch is an inevitable fact, where it is utilized as fillers, glidants, thickeners, binders, disintegrants, gelling, bulking, and water retention agents [7-9].

The selection of disintegrants or superdisintegrants, as well as their consistency of performance, are critical in the development of tablet formulations. The inclusion of suitable superdisintegrants can improve drug release from a solid dosage form. In recent years, there has been a greater focus on developing fast-dissolving tablets that can be ingested, as well as orally disintegrating tablets that disintegrate quickly in the mouth [10].

Disintegrants are compounds or mixtures of substances added to a drug formulation to aid in the breaking up or disintegration of a tablet or capsule substance into tiny particles that dissolve more quickly. In the solid dosage form, super-disintegrants are normally utilized at a low level, typically 1–10% by weight compared to the total weight of the dosage unit. Croscarmellose, cross povidone, and sodium starch glycolate are types of superdisintegrant which act as cross-linked cellulose, cross-linked polymer, and cross-linked starch, respectively. Disintegration of tablets has attracted a lot of attention as a crucial step in achieving rapid medication release. The main purpose of the disintegrant is to counteract the tablet binder's efficiency and the physical forces that act under compression to form the tablet. In order for the tablet to release its medication, the disintegration agents must be more effective as the binder strength increases. It should disrupt the tablet not merely into the granules from which it was compacted, but also into the powder particles from which the granulation was made. It is water-soluble, alcohol soluble, and somewhat soluble in common organic solvents. Losartan was utilized as a prototype drug in this work to construct tablets with Cucurbita maxima starch to evaluate their disintegration characteristics [11-13].

The goal of this research is to compare the disintegration and dissolution characteristics of *Cucurbita maxima* pulp starch with official natural disintegrant in the formulation of Losartan tablets, as well as to optimize the concentration of *Cucurbita maxima* starch to be employed in direct compression (DC). The other goal is to extract native starch from *Cucurbita maxima* pulp and determine the percentage of *Cucurbita maxima* starch required for optimal Losartan tablet disintegration.

MATERIALS AND METHODS

Losartan was purchased from Microlabs Pvt. Ltd. India. Starch paste, Lactose, Magnesium stearate, Talc were obtained from LOBA Chemie Pvt. Ltd 107, Mumbai, India.

Extraction of *Cucurbita maxima* starch powder

Fruits of Cucurbita maxima (pumpkin) were obtained from a local wholesale market, and authentication from the Agricultural College was obtained prior to preparation. Following confirmation, the pumpkin should be washed with water to eliminate dust from the surface, and the peel should be discarded. The seeds are also removed and chopped into little pieces before being steeped in water overnight to extract the cyanogenic glycosides. After decanting the water, the pumpkin should be pulped and distilled water added to dilute the slurry. A muslin cloth was used to remove the pulp from the mixed pumpkin, and hand agitation was given. The resulting starch suspension will be allowed to settle for 12 h under gravity before the supernatant will be decanted. The sediment was centrifuged for 25 min at 3000rpm. The upper protein layer should be scraped off, and the starch suspension produced should be washed numerous times with water over three days, with occasional shaking and water changing. Isopropyl alcohol was used to purify the starch. The starch will next be dried in a hot air oven at 40 °C, sieved, and stored in a desiccator for later use [14-15].

Evaluation of powder properties of *Cucurbita maxima* starch

Identification tests for the presence of starch

1g of starch is boiled with 15 ml of water for the BP starch identification test. 2 drops of 0.1N iodine solution were applied to 1 ml of cooled mucilage, and colour change was noticed [15].

Organoleptic evaluation of isolated starch

Organoleptic qualities such as colour, odour, taste, and texture were assessed in the isolated mucilage [16].

Solubility Behaviour mucilage

The solubility of one part dry starch powder was measured by shaking it with various solvents [17].

Hydration capacity

In a 15 ml centrifuge tube, 10 ml of distilled water was added to 1g of starch. The contents were shaken for 2 min, set aside for 10 min, and centrifuged for 10 min at 1000rpm. The moist mass is weighed after the supernatant is decanted [18].

$$\text{Hydration capacity} = Ws/Wd$$

Where Wd and Ws are weight of the dry sample and weight of sediment, respectively.

Swelling capacity of isolated starch powder

In a 100 ml measuring cylinder, the tapped volume occupied by 10g of each starch (Vd) will be documented. The powder will be dispersed in 85 ml of distilled water, and the volume will be increased to 100 by adding more water. The amount of sediment (Vw) is assessed after 18 h, and the swelling capacity and swelling index are calculated [19].

$$\text{Swelling capacity} = Vw - Vd$$

$$\text{Swelling index} = Vw/Vd$$

Where: Vd and Vw are the initial volume of material before hydration and volume of hydrated material, respectively.

Determination of pH

A digital pH metre is used to determine the pH of a 1 percent solution of *Cucurbita maxima* starch at 37 °C.

Loss on drying

The amount of moisture in the starch content of Cucurbita maxima was determined using a modified version of a method described in B. P (1993) for acacia. Each sample was weighed and placed in a petri dish, which was subsequently dried in a 105 °C oven until it reached a consistent weight. The percent moisture content is calculated as the weight of moisture loss divided by the weight of the sample, represented as a percentage [19].

Preparation of stock solution

10 mg of Losartan will be accurately weighed and transferred to a 100 ml volumetric flask. Methanol will be added in 50 ml increments and sonicated for 15 min before being used to make up the volume. A standard stock solution of Losartan (100 g/ml) was prepared.

Preparation of working standard solution

A standard working solution of medication was generated by appropriate dilution and scanned in the whole UV range to determine the λmax of Losartan for the stock solution of 100g/ml. For the analytical wavelength selection, a 10g/ml Losartan solution was generated by dilution of a standard stock solution and scanned in spectrum mode from 400 to 200 nm. A maximum of 296 nm was chosen for investigation from the drug's spectra.

Standard calibration curve of losartan in phosphate buffer pH7.5

Losartan 10 mg is weighed precisely. To make a stock solution of 100 g/ml, the medication was dissolved in methanol and the volume was increased to 100 ml. Losartan concentrations of 3, 6, 9, 12, 15, and 18 g/ml were obtained by diluting different aliquots of this solution with pH 7.5 buffer. On a UV-Visible spectrophotometer, the absorbance of these solutions was measured at 296 nm against a pH 7.5 buffer as a blank. The standard curve will be replicated three times. A graph of absorbance vs. corresponding concentrations was plotted to establish linearity over the whole concentration range [20].

Preparation of granulation

A wet granulation process was used for formulations 1–10. For 5 min, the active component and disintegrant were combined together. Another 5 min were spent mixing the mixture. After that, the bulk was sieved at 1.7 mm and allowed to dry. It was then dried again after passing through a 1.66 mm sieve. For later usage, the prepared granules were stored in a desiccator according to the formulations. The direct compression method was employed to assess the compressibility of partly pregelatinized starch in formulation 11 [21-24].

Evaluation of granules

Angle of repose

The funnel method will be used to determine the angle of repose. A funnel was used to collect the precisely weighed granules. The height of the funnel will be adjusted such that the tip of the funnel just touches the top of the granular heap. The granules will flow freely through the funnel and onto the surface. The powder cone's diameter was measured, and the angle of repose was computed using the equation below [25]:

$$\text{Tan } \theta = {}^{h}/_{r}$$

Where *h* = height of the powder cone; *r* = radius of the powder cone.

Bulk density and tapped density

It is determined by both the loose bulk density (LBD) and the tapped bulk density (TBD). A total of 8g of powder from each formula was added to a 10 ml measuring cylinder after being lightly shaken to break up any agglomerates that had formed. After determining the initial volume, the cylinder is allowed to fall 30 times under its own weight onto a hard surface from a height of 2 cm. The tapping keeps going until there is no more change in the volume. The following formulas were used to calculate LBD and TBD: [26].

$$\text{LBD} = \text{Weight of the powder/Volume of the packing}$$

$$\text{TBD} = \text{Weight of the powder/Tapped volume of packing}$$

Compressibility index and Hausner's ratio

The compressibility index and Hausner's ratio have become common approaches for predicting powder flow characteristics because they are simple, quick, and easy to use. Because all of these factors can influence the observed compressibility index, the

compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials. By measuring both the bulk volume and the tapped volume of granules, the compressibility index and the Hausner's ratio can be calculated [27].

$$\text{Carr's index (\%)} = [(\text{TBD} - \text{LBD}) \times 100]/\text{TBD}$$

$$\text{Hausners Ratio} = \text{Tapped Density}/\text{Bulk Density}$$

Preparation of tablets

The different formulae used in the study are presented in table 1. Tablets containing 40 mg of Losartan will be manufactured, and the different formulae used in the study are shown in table 1. The granules will be compressed utilising a rotary tablet punching machine equipped with an 8.00 mm concave facing punch and a 6 metric tonne compression force die set. The surface of the die and punch were greased with magnesium stearate before compression, and 1.5 percent of talc would be added to the granulations. The tablets will then be placed for 24 h on silica gel to allow for elastic recovery and hardening [25-27].

Post-compression evaluation

Thickness

The thickness of the tablets was measured with a vernier calliper and the findings were represented as the mean of 10 measurements with standard deviations [28].

Table 1: Formulation code table of the formulated tablet batches

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Losartan	40	40	40	40	40	40	40	40	40	40	40
Derived Starch	40	30	20	10	-	-	-	-	145	-	155(PPG)
Cucurbita maxima starch	-	-	-	-	40	30	20	10	-	-	-
Starch paste	10	10	10	10	10	10	10	10	10	10	-
Lactose	105	110	115	120	125	130	135	140	-	145	-
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3	3	3
Total	200	200	200	200	200	200	200	200	200	200	200

Weight variation

The weight variation of all produced tablets was tested according to the USP XXIV monograph. The weight variation among tablets was evaluated using twenty tablets from each batch, and the mean and standard deviation were obtained [The United States Pharmacopoeial Convention, 2007]. A tablet containing a precise amount of medication. The weight of the tablet is frequently measured to guarantee that it contains the correct amount of medicine. From each batch, 20 tablets were chosen at random and the average weight was calculated. The standard deviation was calculated after calculating the deviation of individual weights from the average weight (as per the IP limit of 7.5 percent for 80-250 mg tablets) [29].

Friability

The Roche friabilator is a friability tester used in laboratories. 10 tablets are weighed and placed in a plastic chamber that spins at 25 rpm, dropping the tablets six inches with each revolution for a total of 100 revolutions. The tablets are then dusted and reweighed to determine the percent weight loss (which should be less than 1% according to the IP limit). The formula below is used to determine the tablet's friability. After that, the average hardness and standard deviation were determined [30].

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

Hardness

The Digital Force Gauge (Model: EL=500N, Electrolab) was used to determine the hardness of all batches. All batches were tested in triplicate according to the USP XXIV monograph for uncoated tablets. The Monsanto hardness tester is made up of two plungers and a barrel with a compressible spring within. Then, the bottom plunger is pressed against the tablet, and a zero reading is taken. By rotating a threaded bolt, the higher plunger is forced against the spring until the tablet cracks. A pointer travels along with a gauge in the barrel as the spring is squeezed, indicating the force, and the force of fracture is recorded [26-31].

Disintegration time

Water was used as the immersion fluid for the tablets in each of the six tubes of the basket of the disintegration equipment. The test took 30 min to complete. When no residue of the unit, except particles of insoluble coating, remained on the apparatus's screen, the disintegration time was recorded [32].

Drug content

The UV technique was used to determine the amount of losartan in the pills in triplicate. The drug content of six pills from each batch was tested at random. The tablets were crushed, and the contents of all six tablets were thoroughly mixed together. 50 mg of crushed tablet powder (equivalent to 10 mg of Losartan) was transferred to a 100 ml volumetric flask for a 40 mg tablet. Then 50 ml of methanol was added and sonicated for 15-20 min, after which the volume was made up to the mark with methanol. After that, the solution was filtered using Whattman filter paper. To obtain a solution with a concentration of 10 g/ml, the filtrate was diluted appropriately with the solvent. The absorbance (234 nm) of the sample was compared to a blank solution. Using the standard curve, the concentration of drug content in each tablet was calculated [33].

Dissolution profile study

The dissolution research of Losartan tablets was conducted according to the USP Type II Dissolution Testing Apparatus procedure. The paddle was rotated at 75RPM for 60 min with 900 ml of phosphate buffer at 7.5 pH. 5 ml of samples were collected at various time intervals of 5, 10, 15, 30, 45, and 60 min and replaced with 5 ml of replenishing 7.5pH phosphate buffer. The collected samples were evaluated for the percentage amount of Losartan released at 234 nm using a UV spectrophotometer [34, 35].

Stability studies

Tablets were tested for three months for stability (45 °C 2 °C/75% RH). The capacity of a certain formulation (dosage form or medicinal product) in a specific container/closure system to remain within its physical, chemical, microbiological, therapeutic, and toxicological parameters during its shelf life is known as the stability of a pharmaceutical preparation. The accelerated stability research is intriguing and appealing since satisfactory results may be verified under stressful settings, allowing for time savings. It generates data on which shelf life proposals for drugs or dosage forms, as well as their suggested storage conditions, are based [25-35].

RESULTS AND DISCUSSION

Table 2: Evaluation of powder characteristics of *Cucurbita maxima* starch

Parameters	Specification
Solubility test	Cold water: not soluble Warm water: partially soluble 95% ethanol: not soluble
pH test	6.5
Organoleptic evaluation	Yellowish white, fine powder, smooth texture, warm bland taste, odorless
Iodine test	Dark blue colour is seen. Presence of starch is confirmed.
Hydration capacity	1.86g
Swelling capacity	19.3 ml
Swelling index	2.41
Pasting temperature	47.23 °C
Moisture content	7.98%
Percentage yield	6.77%

Losartan's lambda max was discovered to be 234 nm using a UV-visible spectrophotometer, as illustrated in fig. 1(A). The standard graph of losartan in phosphate buffer pH 7.3, shown in fig. 1(B), shows good linearity (r^2 = 0.999) between losartan concentration and absorbance in nm. The concentration of losartan in phosphate buffer pH 7.5 obeys Beers-Lamberts' law, according to the data.

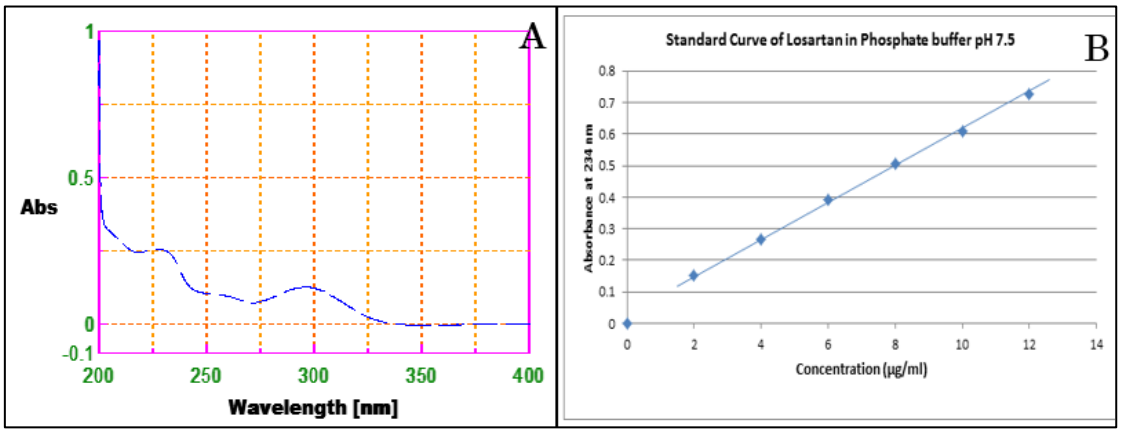

Fig. 1: Graph (A) shows λ_{max} of losartan at 234 nm; Graph (B) Linearity graph of losartan at 234 nm

DSC analysis

Cucurbita maxima starch was used to make a once-daily dosage version of FDT tablet with immediate release losartan. Differential Scanning Calorimeter was used to access the compatibility test. The thermogram revealed an endothermic peak, which is depicted in fig. 2. Losartan and *Cucurbita maxima* starch were shown to be compatible according to DSC curves. In the combination DSC, one peak was obtained at 171.10 °C for losartan and another at 78.60 °C for *Cucurbita maxima* starch as shown in fig. 2. In the individual DSC studies of the losartan, an endothermic peak was obtained at 170.48 °C. It was deduced from this data that there were no polymorphic changes in drug properties, and it was also proven that there was no drug-excipient interaction.

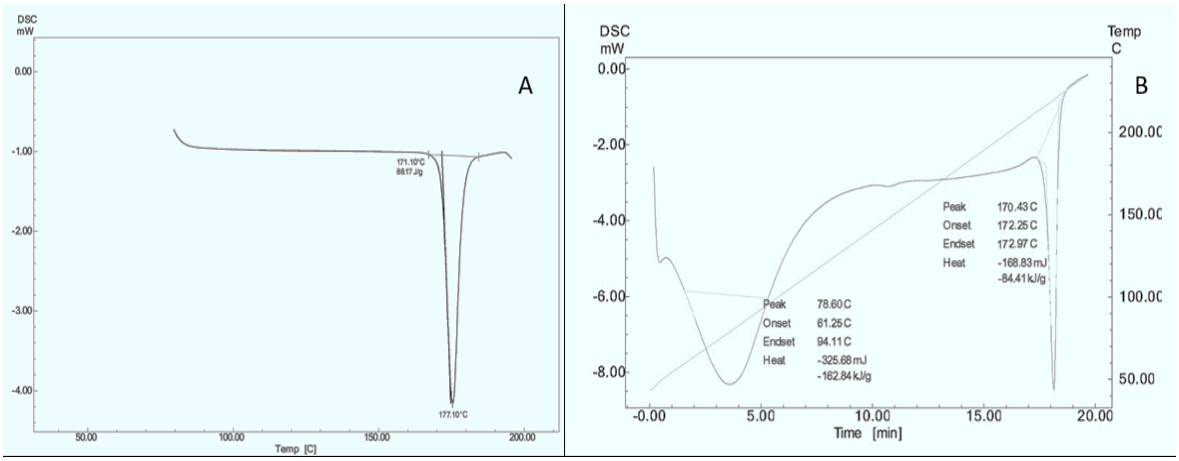

Fig. 2: Graph (A) DSC thermogram of losartan; (B) DSC thermogram of losartan with *Cucurbita maxima* mixture

Precompression parameter studies

Table 3: Pre-compression evaluation parameters of losartan granules

Formulation code	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index	Hausner's ratio
F1	25.6±0.98	0.469±0.015	0.342±0.014	5.78±0.31	1.098±0.009
F2	26.8±0.29	0.477±0.015	0.324±0.010	6.59±1.09	1.082±0.024
F3	25.3±0.72	0.465±0.031	0.346±0.012	5.50±0.40	1.061±0.007
F4	25.8±1.31	0.490±0.025	0.368±0.020	6.09±0.19	1.056±0.013
F5	29.1±0.51	0.484±0.014	0.372±0.012	7.32±0.37	1.076±0.009
F6	32.6±0.15	0.490±0.017	0.344±0.016	5.69±0.13	1.070±0.002
F7	26.2±0.62	0.479±0.018	0.326±0.012	5.31±0.64	1.075±0.014
F8	28.7±0.38	0.483±0.030	0.322±0.014	6.17±0.42	1.088±0.006
F9	25.2±0.55	0.464±0.008	0.342±0.016	6.06±0.54	1.085±0.032
F10	25.7±0.67	0.477±0.015	0.328±0.010	5.94±0.54	1.087±0.002
F11	25.2±0.17	0.489±0.012	0.334±0.012	5.88±0.54	1.083±0.010

Note: values are measured in mean±SD; n=3

The results are reported in table 3. 1. Bulk Density (gm/ml), Tapped Density (gm/ml), Carr's index, and Hausner's Ratio were all calculated for the manufactured Losartan IR granules, and the results are reported in table 3. The angle of repose data was in the range of 25.2±0.17 to 32.6±0.15, it shows that all of the granules from (F1-F11) have adequate flow properties and are within permissible limits (less than 35). The bulk density of all the formulations was in the range of 0.464±0.008 to 0.490±0.025. All of the granules have a high bulk density, indicating strong packaging quality. The true density of all the formulations was in the range of 0.322±0.014 to 0.372±0.012. The carr's index of all the formulations was in the range of 5.31±0.64 to 7.32±0.37. It shows that all of the granules from (F1-F11) have adequate flow properties and are within permissible limits, i.e., 5-15. The Hausner's ratio of all the formulations was in the range of 1.056±0.013 to 1.098±0.009. It shows that all of the granules from (F1-F11) have adequate flow properties and are within permissible limits, i.e., 1.2-1.3. The data indicates that all of the granules have acceptable flow qualities.

Post compression parameter studies

Table 3: Post-compression evaluation parameters of Losartan granules

Formulation code	Weight variation (mg)	Hardness kg/cm²	Friability %	Thickness (mm)	Diameter (mm)	Drug content (%)	Disintegration time (min)
F1	0.204±0.024	4.8±0.04	0.22±0.02	2.32±0.02	3.10±0.02	98.42±2.02	4.28±1.02
F2	0.210±0.044	5.4±0.06	0.64±0.02	2.34±0.00	3.12±0.02	98.12±2.12	4.50±1.00
F3	0.206±0.014	5.0±0.04	0.54±0.00	2.32±0.02	3.10±0.00	100.25±2.02	5.40±1.04
F4	0.212±0.026	4.8±0.06	0.26±0.02	2.34±0.00	3.12±0.02	99.42±2.22	8.20±1.02
F5	0.210±0.032	5.2±0.02	0.42±0.02	2.34±0.02	3.12±0.02	99.42±2.02	1.02±0.02
F6	0.204±0.040	5.4±0.04	0.38±0.02	2.32±0.00	3.10±0.00	100.42±2.12	2.12±0.62
F7	0.206±0.022	5.6±0.02	0.54±0.02	2.32±0.02	3.10±0.02	100.58±2.02	3.48±1.02
F8	0.212±0.034	6.0±0.04	0.42±0.00	2.34±0.00	3.12±0.02	99.54±2.12	5.02±1.02
F9	0.208±0.030	5.8±0.02	0.56±0.02	2.32±0.02	3.10±0.02	99.42±2.02	10.54±2.02
F10	0.214±0.056	5.6±0.02	0.62±0.02	2.34±0.00	3.12±0.02	98.14±2.32	11.54±1.02
F11	0.212±0.064	5.8±0.02	0.56±0.02	2.34±0.02	3.12±0.02	98.78±2.24	12.00±2.02

Note: values are measured in mean±SD; n=3

FDT (F1-F11) post-compression evaluations were found to be within acceptable limits. The weight variation of all formulations was found to be between 0.204±0.024 and 0.214±0.056 mg, indicating that the individual weight of each tablet does not depart from the average weight and meets the IP limit of 7.5 percent for 80-250 mg tablets. Because of the weight consistency, all of the formulations had strong content uniformity, ranging from 98.12±2.12 percent to 100.58±2.02 percent. The thickness and diameter of each batch were within a regulated range, and there were no flaws or variations. All of the batches' hardness was determined to be between 4.8±0.04 and 6.0±0.04 kg/cm², implying that all of the formulations were acceptable within the IP limit of 4-6 kg/cm². The friability of all the formulations was in the range of 0.22±0.02% to 0.64±0.02%, it shows the products' stability overstress due to packing and transportation. The drug content was found to be in the range of 98.12±2.12% to 100.58±2.02%. All the evaluated post-compression parameter values were within an acceptable range of Pharmacopoeial limits. It is reported in table 3.

The type and concentration of disintegrants utilised in formulations F1 through F11 influenced the disintegration time. The disintegration time of the FDT (F1-F4) prepared with derived starch ranges from 4.28±1.02 min to 8.20±1.02 min, while the disintegration time of the FDT (F5-F8) prepared with *Cucurbita maxima* starch ranges from 1.02±0.02 min to 5.02±1.02 min. The remaining three formulations, F9-F11, have a disintegration time of more than 10 min. According to the results, the *Curcurbita maxima* starch functions as a superdisintegrant, dominating the disintegrating impact of derived starch. It can also be concluded that all of the formulas were created within the IP limit. On the basis of cost-effectiveness, it was determined that the FDT F8 with a lower concentration of *Cucurbita maxima* (10 mg) was the ideal concentration for the formulation of *Cucurbita maxima.* F8 batch was observed as a promising batch based upon disintegration.

***In vitro* drug dissolution studies**

Cucurbita maxima starch FDT tablet (F8) vs. Derived starch FDT tablet vs. Marketed Losartan Tablet comparative *in vitro* drug dissolution investigations were graphed in fig. 3. When compared to derived starch FDT (98.14±4.42% at 15 min) and commercialized SART 40® tablet (94.38±3.24% at 15 min), it was determined that the FDT with Curcurbita maxima starch has an exceptional quick drug release pattern (99.12±3.42% at 10 min). This could be attributed to Curcurbita maxima's rapid disintegration effect. It improves inter particular wetting, which leads to increased biological fluid imbibition in between the particles, resulting in rapid disintegration and dissolution. Higher concentrations of Cucurbita maxima, on the other

hand, slow drug absorption, possibly because of viscous networks. In 15 min, F8 formulations released more than 80% of the medication. Based on dissolving statistics (100 percent drug release in 30 min), the F8 sample was deemed a promising batch.

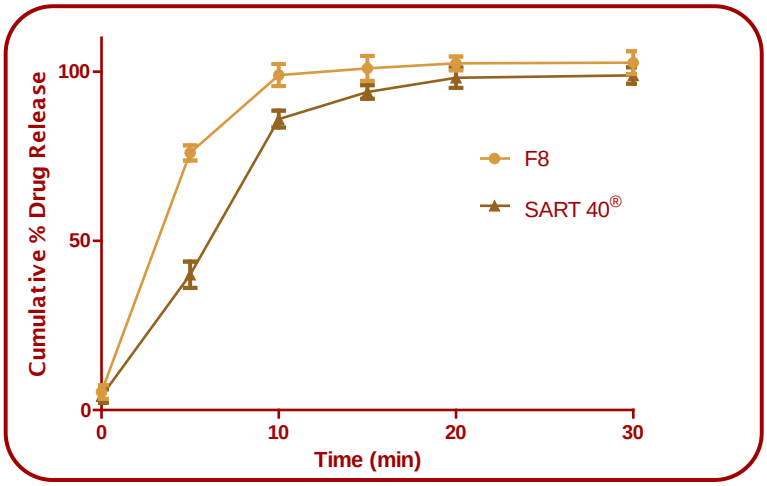

Fig. 3: Comparative *in vitro* drug dissolution studies of *Cucurbita maxima* starch, FDT tablet (F8) Vs. Derived starch FDT tablet Vs. marketed losartan tablet (Note: values are measured in mean±SD; n=3)

Stability studies

Table 4: Stability study data of optimized formulation F8

Parameter	Duration of evaluation			
	Initial	After 1 mo	After 2 mo	After 3 mo
Physical appearance	+++	+++	+++	+++
Color	Offset white	Offset white	Offset white	Offset white
Texture	Smooth and no defects	Smooth and no defects	Smooth and no defects	Smooth and no defects
Drug content (%)	100.42±2.12	100.12±2.02	100.08±2.42	99.98±2.12
% amount of drug release at 30 min	99.08±2.04	99.02±2.14	98.12±2.40	98.04±2.14

Note: *+++same as on zero day; Values are measured in mean±SD; n=3

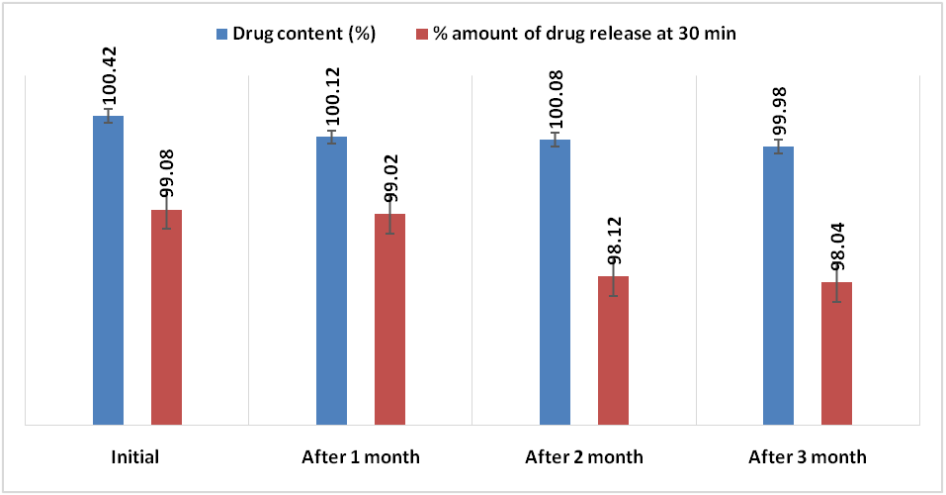

Fig. 4: Comparison of stability study data of optimized formulation F8 in various time interval (Note: values are measured in mean±SD; n=3)

Stability tests were conducted for 90 d at accelerated stability conditions (40 °C/75 % RH) using optimum batch F8 as per ICH guidelines. As shown in table 4, no significant changes in physicochemical properties or release profile were observed in batch F8. In order to identify the changes in physiochemical properties, drug content, and % amount of drug released at 30 min of the formulation, the formulation F8 was chosen as an optimal formulation and stored at 45 °C/75 5% RH. The initial drug content (%) and amount of drug released at 30 min were 100.42±2.12% and 99.08±2.04%, respectively. After one, two, and three months, it showed the drug content (%) as 100.12±2.02, 100.08±2.42, 99.98±2.12 and the amount of drug released at 30 min as

99.02±2.14, 98.12±2.40, 98.04±2.14. Table 4 and fig. 4 show that there have been no significant changes in the physical appearance, color, texture, drug content (%), and amount of drug released at 30 min, indicating that the formulation F8 was found to be the stable formulation.

CONCLUSION

Losartan fast disintegration tablets were made with *Curcubita maxima* starch and disintegration and dissolving investigations were performed. According to comparative disintegration and dissolving investigations, the lowest concentration of Cucurbita maxima (10 mg) was shown to be the ideal concentration level for the formulation of Losartan FDT, favoring cost effectiveness and patient compliance. As a result, it's possible to conclude that Losartan FDT made with *Curcubita maxima* starch superdisintegrant will be the best alternative and competitive dosage form, with a high marketability potential.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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